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Original Article

Clinical and laboratory findings by necrotizing enterocolitis severity in preterm infants: a retrospective single-center study

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ABSTRACT

Introduction: *Necrotizing enterocolitis (NEC) is a severe gastrointestinal emergency in preterm infants. This study compared clinical and laboratory findings between infants with mild–moderate and severe NEC.* ***Methods:*** *This retrospective observational cohort study included preterm infants (<37 weeks; birth weight <2,500 g) with suspected or confirmed NEC admitted to Wahidin Sudirohusodo Hospital during 2023–2024. Severity was classified using modified Bell staging as mild–moderate (stages I–II) or severe (stage III). Clinical and laboratory findings recorded at diagnosis, alongside radiological assessment, were compared between groups.* ***Results:*** *Forty-seven infants were included: 19 with mild–moderate and 28 with severe NEC. No statistically significant differences in baseline characteristics were detected ($p > 0.05$). Abdominal distension was more frequent in severe NEC (85.7% vs. 47.4%; Pearson Chi-square $p = 0.005$; unadjusted OR 6.67, 95% CI 1.66–26.76). Mean hemoglobin was significantly lower in severe NEC (11.24 vs. 13.30 g/dL; independent-samples t-test $p = 0.028$). Reported platelet medians and hematocrit means were also significantly lower in severe NEC (34 vs. 157 × 10^3/µL, $p < 0.001$; and 33.25% vs. 38.88%, $p = 0.037$, respectively). Overall in-hospital mortality was 66.0%, without a statistically*

significant difference between groups (68.4% vs. 64.3%; p = 0.769). ***Conclusions:*** *Abdominal distension was significantly more frequent in severe NEC. Platelet counts, mean hemoglobin, and mean hematocrit were also significantly lower in severe NEC. These exploratory, unadjusted comparisons may partly reflect overlap with Bell staging criteria and do not establish early prediction or independent effects.*

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1. INTRODUCTION

Among preterm infants, necrotizing enterocolitis (NEC) continues to be a critical gut disease, markedly increasing health complications and deaths in neonates, especially in NICU settings.[1,2]. This disease involves progressive inflammatory injury and intestinal necrosis. It is estimated to affect 5–10% of infants with very low birth weight (VLBW), and the mortality rate ranges from 20% to 30%.[1,3,4].

The clinical severity of NEC varies widely, ranging from mild disease to fulminant conditions requiring surgical intervention and associated with life-threatening complications such as intestinal perforation, sepsis, and death [10]. The modified Bell's staging criteria remain the standard for evaluating disease severity and guiding clinical management.[5] In addition to its acute impacts, severe NEC is linked to long-term issues such as short bowel syndrome, growth failure, and neurodevelopmental problems. [2,6]

The development of NEC is complex and not completely understood. Multiple risk factors have been identified, such as prematurity, low birth weight, immature immune and gastrointestinal systems, enteral feeding practices, intestinal dysbiosis, and impaired intestinal perfusion [2,7,8]. Maternal and perinatal factors, such as preeclampsia, perinatal asphyxia, and antibiotic exposure, have also been reported to contribute to NEC development [7,9]. These factors relate to NEC occurrence and should be distinguished from findings associated with established disease severity.

Previous Indonesian referral-center research has examined clinical deterioration in preterm infants with NEC, including hematological and inflammatory findings [11]. Building on this Indonesian referral-center research, the present study provides a description of clinical and laboratory findings across NEC severity groups in a tertiary referral population in Makassar. Importantly, factors involved in disease initiation may differ from those that determine disease progression and clinical severity. Furthermore, findings on determinants of NEC severity remain inconsistent across studies, both in which variables are significant and in the strength of associations [3,7]. This study provides a local description of clinical and laboratory findings across recorded Bell stage groups at a tertiary referral center in Makassar, rather than proposing new validated predictors of NEC severity.

Clinically, NEC presents with a broad spectrum of manifestations, ranging from mild to severe. Abdominal distension has been reported as a key clinical feature associated with disease severity, reflecting extensive intestinal inflammation and impaired motility [1,10]. In contrast, other symptoms such as vomiting, gastric residue, and temperature instability are commonly observed across different stages of NEC and lack specificity in determining disease severity [1,7].

Laboratory parameters also play an important role in assessing NEC severity. Thrombocytopenia, along with decreased hemoglobin and hematocrit levels, is frequently observed in severe NEC and reflects systemic inflammation and coagulation disturbances [7,12]. Thrombocytopenia, in particular, has been linked to higher mortality and could function as a prognostic marker, but its interpretation depends on measurement timing and it should not be used alone to predict prognosis. In addition, inflammatory markers such as white blood cell count and C-reactive protein (CRP) fluctuate markedly, limiting their reliability in assessing disease severity.

The persistently high mortality rate of NEC underscores the ongoing clinical challenge in neonatal care [1,3]. Therefore, understanding differences in clinical and laboratory findings by NEC severity is essential for early detection, appropriate management, and improved clinical outcomes. Based on these considerations, this study aims to compare the clinical and laboratory findings between preterm infants with Bell stages I–II and stage III NEC, providing exploratory descriptive evidence from an Indonesian tertiary referral center.

2. METHODS

A retrospective observational cohort study was conducted of preterm infants (gestational age <37 weeks, birth weight <2500 g) with suspected or confirmed NEC and admitted to the neonatal intensive care unit of Wahidin Sudirohusodo Hospital over the 2023–2024 period. NEC was classified according to the modified Bell's staging criteria: stages I–II as mild-moderate group, and stage III as the severe group. Stage I represents suspected NEC, whereas stages II–III represent confirmed NEC. The diagnostic assessment incorporated clinical, laboratory, and radiological findings according to the modified Bell staging criteria. Clinical symptoms and laboratory values included in the analysis were recorded at the time of diagnosis. Mortality was defined as death from any cause during hospitalization. Secondary data were obtained from medical records, including clinical symptoms and laboratory findings, which were analyzed and compared between the mild–moderate and severe NEC groups. The exclusion criteria comprised major congenital anomalies, severe sepsis, hematologic disorders, early spontaneous perforation, or a history of platelet transfusion. The record-screening and selection process was as follows. Medical records from 2023–2024 were screened using the diagnosis codes recorded in the hospital medical records. Of 756 records screened, 53 records with coded diagnoses of suspected or confirmed NEC were identified and assessed for eligibility. Four infants were excluded because of a history of platelet transfusion, and two were excluded because of incomplete diagnostic documentation: only a clinical diagnosis was recorded, without documented radiological assessment. Records with incomplete diagnostic documentation were excluded from the analysis. The final study population comprised 47 infants. Categorical variables were compared using Pearson’s Chi-square test when all expected cell counts were ≥5 and two-sided Fisher’s exact test otherwise. Continuous variables were compared using an independent-samples t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed data. An unadjusted odds ratio (OR) with a 95% Wald confidence interval (CI) was calculated for abdominal distension from the reported

counts. No adjusted effects were estimated. The comparisons are exploratory; no multiplicity adjustment was applied, and nominal p-values require cautious interpretation. Results were deemed significant at $p < 0.05$. Patient identifiers were removed from the analytical dataset, and access to the study data was restricted to the research team. The Health Research Ethics Committee of the Faculty of Medicine, Hasanuddin University–Hasanuddin University Hospital–Wahidin Sudirohusodo Hospital approved this study on 31 December 2025 (approval number: UH25100853).

3. RESULTS

Of 756 medical records screened, 53 potentially eligible NEC cases were identified through diagnosis codes. Six cases were excluded: four because of a history of platelet transfusion and two because of incomplete diagnostic documentation. Forty-seven infants were included in the analysis, comprising 19 with mild–moderate NEC and 28 with severe NEC. Among the preterm infants with suspected or confirmed NEC and included in this study, disease severity was categorized according to the modified Bell's criteria into mild–moderate NEC (stages I–II) and severe NEC (stage III). The infants were subsequently compared based on their demographic and perinatal characteristics, including sex, gestational age, birth weight, mode of delivery, maternal risk factors, Apgar and scores. Mortality was considered an outcome rather than a baseline characteristic. The distribution of these characteristics between the mild–moderate and severe NEC groups is presented in Table 1.

Table 1. Characteristics of the infants

Characteristics	Mild-Moderate (n=19)	Severe (n=28)	P-value
Sex, n (%):			0.658*
- **Male**	11 (57.9)	18 (64.3)	
- **Female**	8 (42.1)	10 (35.7)	
Gestational age (weeks), median (range)	32 (25 – 36)	33.5 (26 – 36)	0.222***
Birth weight (g), median (range)	1729.5 (845 – 2415)	2065 (895 – 2460)	0.573***
Mode of delivery:			0.217*
- **Spontaneous, n (%)**	8 (42.1)	7 (25)	
- **SC, n (%)**	11 (57.9)	21 (75)	
Mother's risk factors			
- **PPROM, n (%)**	1 (5.3)	1 (3.6)	1.000**
- **Hypertension, n (%)**	6 (31.6)	7 (25)	0.621*
- **Diabetes Mellitus, n (%)**	0	0	n/a
Apgar Score at 1', median (range)	7 (1 – 8)	5 (1 – 8)	0.344***
Apgar Score at 5', median (range)	9 (3 – 10)	8 (5 – 10)	0.434***
Mortality, n (%)	13 (68.4)	18 (64.3)	0.769*

*Chi-Square Test; **Two-sided Fisher's exact test *** Mann-Whitney U Test; SC, cesarean section; PPROM, preterm prelabor rupture of membranes; n/a, not applicable because both groups had zero events.

No statistically significant differences were detected in the reported baseline characteristics between groups (all $p > 0.05$). These nonsignificant findings do not establish equivalence. Mortality was defined as death from any cause during hospitalization. Overall, 31/47 infants (66.0%) died: 13/19 (68.4%) in the mild–moderate group and 18/28 (64.3%) in the severe group (Pearson Chi-square $p = 0.769$).

Table 2. Clinical symptoms of preterm infants with NEC

Clinical symptoms	Mild-Moderate (n = 19)	Severe (n = 28)	P Value
Gastrointestinal bleeding, n (%)	6 (31.6)	12 (42.9)	0.435*
Abdominal distension, n (%)	9 (47.4)	24 (85.7)	**0.005***
Vomiting, n (%)	11 (57.9)	10 (35.7)	0.133*
Gastric residue, n (%)	16 (84.2)	26 (92.9)	0.381**
Temperature instability, n (%)	13 (68.4)	20 (71.4)	0.825*
Decreased bowel sounds, n (%)	4 (21.1)	11 (39.3)	0.188*
Apnea, n (%)	3 (15.8)	6 (21.4)	0.720**

*Chi-Square Test; **Two-sided Fisher's exact test

Beyond the demographic and perinatal characteristics, clinical symptoms were compared between severity groups. Table 2 shows the clinical symptoms of preterm infants with NEC. Abdominal distension was significantly more frequent in the severe group than in the mild–moderate group (85.7% vs. 47.4%; Pearson Chi-square p = 0.005), with an unadjusted odds ratio of 6.67 (95% CI 1.66–26.76). No statistically significant differences were detected in gastrointestinal bleeding, vomiting, gastric residue, temperature instability, decreased bowel sounds, or apnea between groups (all p > 0.05).

Table 3. Laboratory of preterm infants with NEC

Laboratory aspects	Mild-Moderate (n=19)	Severe (n=28)	P Value
Hemoglobin (g/dL), mean (±SD)	13.3 (±3.03)	11.24 (±3.07)	0.028*
Leukocyte count (×10³/µL), median (range)	11.9 (5.8 – 37.2)	10.6 (1.5 – 36.6)	0.335**
Platelet count (×10³/µL), median (range)	157 (30 – 486)	34 (1 – 253)	< 0.001**
Hematocrit (%), mean (±SD)	38.88 (±9.27)	33.25 (±8.28)	0.037*
Neutrophils (%), median (range)	69.8 (27.9 – 85)	70.25 (28.5 – 84.3)	0.983**
C-reactive protein (mg/dL), median (range)	10.1 (1 – 130)	14.35 (1 – 266)	0.449**
Random blood glucose (g/dL), median (range)	92.5 (10 – 343)	94 (27 – 307)	0.675**

*Independent T-Test
**Mann-Whitney U Test

Table 3 presents the reported laboratory findings. All laboratory parameters were available for the 19 infants in the mild–moderate group and the 28 infants in the severe group. Median platelet counts were significantly lower in stage III than in stages I–II (34 versus 157 × 10^3/µL; Mann–Whitney U test p < 0.001). Mean hemoglobin was significantly lower in the severe NEC group than in the mild–moderate group (11.24 ± 3.07 vs. 13.30 ± 3.03 g/dL; independent-samples t-test p = 0.028), as was mean hematocrit (33.25% versus 38.88%; independent-samples t-test p = 0.037). The other reported laboratory comparisons had p > 0.05.

4. DISCUSSION

This study found abdominal distension to be significantly more frequent in preterm infants with severe NEC, while platelet counts, mean hemoglobin, and mean hematocrit were significantly lower in this group. These findings describe exploratory, unadjusted comparisons between recorded Bell stage groups rather than independent determinants or validated early predictors of disease severity.

Although prematurity and low birth weight are well-established risk factors for NEC, this study found no statistically significant differences in gestational age or birth weight between severity groups. These nonsignificant findings do not establish equivalence or rule out a relationship with severity. Because all participants were preterm infants with suspected or confirmed NEC, this study cannot assess whether prematurity predicts NEC occurrence. The pathophysiological mechanisms underlying NEC severity are likely multifactorial and extend beyond basic neonatal characteristics [7].

Abdominal distension emerged as the only clinical parameter significantly associated with severe NEC (85.7% vs. 47.4%; $p = 0.005$; unadjusted OR 6.67, 95% CI 1.66–26.76). This finding is consistent with its occurrence in advanced intestinal disease, including ileus and gas accumulation. However, abdominal distension is also incorporated into the modified Bell staging criteria [5], so its association with the assigned stage may partly reflect the classification itself. The wide confidence interval indicates limited precision. Without establishing that distension preceded progression, these findings cannot support its use as an early warning sign or demonstrate that earlier intervention would improve outcomes.

Among laboratory parameters, reported median platelet counts were significantly lower in the severe group than in the mild–moderate group (34 vs. 157 × 10^3/μL; Mann–Whitney U test $p < 0.001$). Platelet depletion in NEC has been linked to systemic inflammation, platelet consumption, and activation of the coagulation pathway. [12,13]. Mean hemoglobin and hematocrit were also significantly lower in the severe group (11.24 vs. 13.30 g/dL, $p = 0.028$; and 33.25% vs. 38.88%, $p = 0.037$, respectively; independent-samples t-tests). These findings represent unadjusted associations with recorded severity and do not establish independent effects or predictive value. Thrombocytopenia also overlaps with information used in Bell staging [5], and platelet count alone should not be presented as an established prognostic tool.

Interestingly, the reported comparisons of commonly used inflammatory markers, such as leukocyte count and CRP, showed no statistically significant differences between severity groups. This may reflect the complex and dynamic immune response in NEC, where leukocytosis and leukopenia can occur at different stages of disease progression. The small sample and the absence of serial measurements also limit interpretation. Consequently, the absence of a significant difference does not establish that these markers have no role in NEC severity assessment. Ibrohim et al. found that thrombocytopenia was associated with NEC deterioration in unadjusted analysis, but not after adjustment [11]. Our study similarly observed lower platelet counts in severe NEC, although it compared severity groups rather than subsequent deterioration. Unlike their findings, our CRP comparison was not statistically significant. These differences in endpoints and analytical approaches limit direct comparison.

Mortality during hospitalization was high in both groups (68.4% in stages I–II and 64.3% in stage III; $p = 0.769$), with no statistically significant difference detected. Mortality was assessed as all-cause death during hospitalization. Specific causes of death could not be reliably established from the available study data; therefore, deaths could not be attributed specifically to NEC. This limits interpretation of the high mortality observed in both severity groups. The absence of a statistically significant difference does not establish equivalent mortality. Previous research has examined NEC mortality across birth-weight categories [12,13], an endpoint distinct from comparing findings across

severity stages. In our tertiary referral setting, referral case mix, comorbidities, and the timing of staging relative to death may have contributed to the observed proportions, but these explanations remain unconfirmed. The recorded stage may not reflect the stage immediately before death. Cause-specific mortality data and clarification of initial versus maximum staging are needed to explain the high mortality in the mild–moderate group; the slightly higher proportion alone does not establish misclassification.

This study provides local descriptive evidence on clinical and laboratory findings across NEC severity groups at a tertiary referral center in Makassar. Its contribution is describing this clinical setting rather than identifying a novel predictive role for abdominal distension or thrombocytopenia, which the NEC literature already discusses [5]. Comparisons with previous studies should account for differences in diagnostic definitions, measurement timing, and endpoints, particularly because our mild–moderate group combines suspected stage I and confirmed stage II NEC.

This study has a few limitations. Its retrospective approach may introduce selection and information biases, particularly regarding data completeness and accuracy. The relatively small sample size could limit the statistical power, and being conducted at a single-center setting may reduce how widely the results apply. Additionally, the study may not have evaluated all potential confounding factors, such as feeding practices, antibiotic exposure, and gut microbiota. The lack of multivariable analysis precludes conclusions about independent associations and leaves residual confounding. Combining suspected stage I and confirmed stage II disease introduces diagnostic heterogeneity. Although clinical and laboratory findings were recorded at diagnosis, their ability to predict subsequent progression was not evaluated; overlap with staging criteria also introduces circularity. Exclusion of infants with severe sepsis or a history of platelet transfusion may introduce selection bias. Two records with incomplete diagnostic documentation were excluded, which may further contribute to selection bias. Multiple comparisons without adjustment increase the possibility of chance findings, and the wide confidence interval for distension indicates limited precision.

Despite these limitations, this study has several strengths. It provides a comprehensive evaluation of both clinical and laboratory parameters, uses standardized Bell's staging criteria, and reflects real-world clinical practice in a tertiary care setting.

Overall, this study provides local descriptive evidence on clinically accessible findings accompanying recorded NEC severity. Larger-scale, prospective multicenter studies incorporating clearly specified measurement times and multivariable methods will be essential to verify these observations and assess whether these findings precede progression or have predictive value.

5. CONCLUSION

Abdominal distension was significantly more frequent in preterm infants with severe NEC than in those with mild–moderate NEC. Platelet counts, mean hemoglobin, and mean hematocrit were also significantly lower in the severe group. These exploratory, unadjusted comparisons may partly reflect overlap with Bell staging criteria and do not establish independent determinants, early prediction, or improved clinical outcomes.

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Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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