http://dx.doi.org/10.18623/rvd.v22.n3.3438

CLINICAL AND LABORATORY PREDICTORS OF SEVERE AND CRITICAL COVID-19 IN HOSPITALIZED CHILDREN

PREDITORES CLÍNICOS E LABORATORIAIS DA COVID-19 GRAVE E CRÍTICA EM CRIANÇAS HOSPITALIZADAS

Article received on: 30/6/2025
Article accepted on: 29/9/2025

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The authors declare that there is no conflict of interest

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Abstract
Background: Although coronavirus disease 2019 (COVID-19) in children is often mild, some develop severe or critical illness requiring hospitalization. Identifying predictors of severity is vital for timely management, particularly in resource-limited settings. Methods: A retrospective study was conducted on 906 children aged 0–16 years hospitalized with symptomatic COVID-19 at Vietnam National Children's Hospital. Demographic, clinical, laboratory, and imaging data were reviewed, and disease severity was classified as mild, moderate, severe, or critical. Factors associated with severe or critical outcomes were analyzed using univariate and multivariate logistic regression.
Results: Of 906 cases, 80.5% were mild, 9.9% moderate, 3.6% severe, and 6.0% critical. Severe and critical illness occurred mainly in infants under 12 months, malnourished children, and those with comorbidities. These groups showed higher rates of fever, cough, abnormal chest X-rays, elevated LDH, and lower lymphocyte counts. In multivariate analysis, only LDH > 376 U/L (OR = 10.53, p < 0.001) and chest X-ray abnormalities (OR = 24.24, p < 0.001) remained independent predictors. Conclusion: Most hospitalized children had mild disease, but severe forms were not uncommon. Elevated LDH and chest radiographic abnormalities were key predictors for early identification of high-risk patients.

Keywords: COVID-19. Children. Hospitalization. Predictors. Severity.

Resumo
Introdução: Embora a doença do coronavírus 2019 (COVID-19) em crianças seja geralmente leve, uma parcela pode evoluir para formas graves ou críticas que requerem hospitalização. Identificar preditores de gravidade é essencial para o manejo oportuno, especialmente em contextos com recursos limitados. Métodos: Realizou-se um estudo retrospectivo com 906 crianças de 0 a 16 anos hospitalizadas com COVID-19 sintomática no hospital. Foram revisados dados demográficos, clínicos, laboratoriais e de imagem, classificando a gravidade como leve, moderada, grave ou crítica. Os fatores associados a desfechos graves/críticos foram analisados por regressão logística univariada e multivariada. Resultados: Dos 906 casos, 80,5% foram leves, 9,9% moderados, 3,6% graves e 6,0% críticos. As formas graves e críticas ocorreram principalmente em lactentes menores de 12 meses, crianças desnutridas e com comorbidades, que apresentaram taxas mais altas de febre, tosse, alterações radiográficas e níveis elevados de LDH, além de linfopenia. Na análise multivariada, apenas LDH > 376 U/L (OR = 10,53; p < 0,001) e alterações radiográficas (OR = 24,24; p < 0,001) permaneceram como preditores independentes.
Conclusão: A maioria das crianças hospitalizadas apresentou doença leve, mas formas graves não foram incomuns. LDH elevado e alterações radiográficas mostraram-se marcadores importantes para identificação precoce de pacientes de alto risco.

Palavras-chave: *COVID-19. Crianças. Hospitalização. Preditores. Gravidade.*

1 INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has affected all age groups worldwide, including children. Although pediatric cases are generally milder compared with adults, a subset of children can develop severe or critical illness, particularly those requiring hospitalization. The burden of severe COVID-19 in hospitalized children, while less frequent, remains clinically significant and necessitates careful evaluation to inform healthcare strategies. Understanding the clinical and laboratory factors associated with severe outcomes in children is essential for optimizing management, guiding vaccination priorities, and developing targeted public health interventions.

The reported burden of severe COVID-19 among hospitalized children varies across regions. In Taiwan, during the Omicron wave, 6.5% of hospitalized pediatric patients were classified as severe cases, with a mortality rate of 0.6%. In Mozambique, the hospitalization frequency among children was 2.5%, yet mortality reached 30%, particularly in underweight children. Similarly, in Germany, approximately 3% of hospitalized children required intensive care, with severity differing according to circulating SARS-CoV-2 variants. These findings highlight the heterogeneous impact of COVID-19 on children across settings and underscore the importance of understanding local epidemiology and risk profiles.

Several studies have emphasized the importance of identifying risk factors for severe COVID-19 in children, which is crucial for prioritizing vaccination and allocating healthcare resources. Comorbidities such as obesity, cardiovascular disease, chronic lung disease, and neurological disorders have consistently been reported as major predictors of severe outcomes. Younger age, particularly infants under 12 months, and the presence of multiple comorbidities have also been linked with an increased risk of severe illness. Moreover, coinfections with pathogens such as respiratory syncytial virus (RSV) or bacterial infections may exacerbate disease severity, particularly in younger children. Nutritional status is another important determinant, with undernourished children shown to have worse outcomes and higher mortality.

Despite accumulating international evidence, data on the clinical and laboratory factors associated with severe and critical COVID-19 in children remain limited in Vietnam. A clearer understanding of these determinants in local populations is critical for early risk stratification and timely intervention. Therefore, we conducted this study to evaluate clinical and laboratory factors associated with severe and critical outcomes among children hospitalized with COVID-19 at the Vietnam National Children's Hospital.

2 MATERIALS AND METHOD

2.1 Study design and population

This retrospective descriptive study was conducted on pediatric patients aged 0 to 16 years who were diagnosed with symptomatic COVID-19 and admitted to the Vietnam

National Children's Hospital. The diagnosis of COVID-19 was confirmed either by rapid antigen testing or by polymerase chain reaction (PCR) performed on nasopharyngeal swab samples. Patients were excluded if they tested positive but had no clinical manifestations of COVID-19 or if their medical records lacked essential data. The study employed a convenience sampling approach, enrolling all eligible children who were hospitalized during the research period. A total of 906 patients who met the inclusion criteria were identified and included in the final analysis.

2.2 Data collection

Data were extracted from medical records and included demographic and clinical characteristics such as age, sex, nutritional status (normal, malnutrition, overweight, or obesity), and history of underlying conditions. Symptoms at admission were recorded, including fever, cough, vomiting or nausea, diarrhea, seizures, apnea, chest pain, and rash. Laboratory findings were also collected, consisting of hematological parameters such as white blood cell count (WBC), lymphocyte count, neutrophil count, hemoglobin (Hb), and platelet count (PLT). Biochemical tests included liver enzymes (GOT, GPT), urea, creatinine, LDH, ferritin, D-dimer, and C-reactive protein (CRP). Imaging results, particularly chest X-rays, were reviewed to assess pulmonary lesions.

2.3 Disease severity classification

Patients were categorized according to disease severity. Mild cases were defined as those presenting with upper respiratory tract symptoms without respiratory distress and with normal chest X-ray findings. Moderate cases were defined as pneumonia without respiratory failure, with chest X-ray showing mild abnormalities. Severe cases were defined as pneumonia accompanied by mild to moderate respiratory distress, indicated by an SpO_2 level of 90–94%, requiring supplemental oxygen administered through a nasal cannula or face mask. Critical cases were defined as severe pneumonia with respiratory failure, characterized by an SpO2 level below 90%, requiring invasive or non-invasive mechanical ventilation. Death was defined as any case of in-hospital mortality in patients who tested positive for COVID-19.

2.4 Statistical analysis

Data analysis was performed using SPSS version 26.0. Quantitative variables were expressed as mean ± standard deviation for normally distributed data or median with interquartile range for non-normally distributed data. Qualitative variables were presented as frequencies and percentages. The Pearson chi-square test was used to analyze categorical variables. For continuous variables, the Kruskal–Wallis test was applied in cases of non-normal distribution, while analysis of variance (ANOVA) was used for normally distributed data. A p-value of less than 0.05 was considered statistically significant.

2.5 Ethical considerations

The study protocol was reviewed and approved by the Ethics Committee. All data were collected and analyzed in accordance with ethical standards to ensure patient confidentiality and compliance with institutional regulations.

3 RESULTS

Between January 1, 2022, and December 31, 2022, a total of 906 children with symptomatic COVID-19 admitted to the Vietnam National Children's Hospital were included in the study. Regarding disease severity, 729 patients (80.5%) were classified as mild, 90 (9.9%) as moderate, 33 (3.6%) as severe, and 54 (6.0%) as critical. Males predominated across groups, although the difference compared with females was not statistically significant ($p = 0.307$). Infants younger than one month and those aged 1–<12 months accounted for a larger proportion of severe/critical cases, whereas children aged 1–5 years represented the highest proportion in the mild group ($p < 0.001$). Nutritional status was mostly normal (≥83%), but the prevalence of malnutrition was markedly higher in patients with moderate to critical disease ($p < 0.001$). Underlying comorbidities were also more common among children with severe and critical illness ($p = 0.003$). (Table 1)

Table 1.

General characteristics of the study population by disease severity

Characteristic	Mild (n=729)	Moderate (n=90)	Severe (n=33)	Critical (n=54)	p-value
Male, n (%)	461 (63.2)	52 (57.8)	24 (72.7)	30 (55.6)	0.307
Age group					
<1 month, n (%)	22 (3.1)	15 (16.7)	5 (15.2)	9 (16.7)	<0.001
≥1–<12 months, n (%)	173 (23.7)	47 (52.2)	15 (45.4)	20 (37.0)	
≥ 1–<5 years, n (%)	302 (41.4)	22 (24.4)	6 (18.2)	14 (25.9)	
≥5 years, n (%)	232 (31.8)	6 (6.7)	7 (21.2)	11 (20.4)	
Malnutrition, n (%)	71 (9.7)	28 (31.1)	9 (27.3)	8 (14.8)	<0.001
Comorbidity, n (%)	253 (34.7)	41 (45.6)	20 (60.6)	25 (46.3)	0.003

Note: n = number of patients; % = percentage.

Table 2 shows that children with severe or critical disease had significantly higher rates of chest X-ray abnormalities and elevated LDH compared with those with mild or moderate illness but fever was less frequent in severe/critical cases. Lymphocyte counts, while total white blood cell counts were both reduced in the severe/critical groups.

Table 2.

Clinical and laboratory characteristics by disease severity

Variable	Mild (n=729)	Moderate (n=90)	Severe (n=33)	Critical (n=54)	p-value
Fever, n (%)	672 (92.2)	68 (75.6)	22 (66.7)	38 (70.4)	<0.001
Cough, n (%)	327 (44.9)	78 (86.7)	30 (90.9)	33 (61.1)	<0.001
WBC (G/L), median [IQR]	8.56 (5.83–12.29)	10.73 (8.19–14.00)	9.15 (6.70–13.51)	8.29 (5.61–15.61)	<0.05
Lymphocytes (G/L), median [IQR]	2.06 (1.13–3.80)	4.20 (2.31–5.90)	3.26 (2.08–4.85)	1.67 (1.13–3.09)	<0.001
LDH (U/L), median [IQR]	278.75 (230.7–330.93)	327.75 (264.63–375.38)	417.0 (323.55–531.7)	758.05 (383.2–1687.7)	<0.001
Chest X-ray abnormalities, n (%)	118 (39.2) (n=308)	60 (75.0) (n=80)	30 (100) (n=30)	44 (91.7) (n=48)	<0.001

Note: LDH = lactate dehydrogenase; IQR = interquartile range.

In the univariate analysis, several factors were found to be significantly associated with severe or critical outcomes among children with COVID-19. These included age <1 month, presence of comorbidities, leukocytosis >17 G/L, CRP >10 mg/L, ferritin >237 ng/mL, LDH >376 U/L, and chest X-ray abnormalities ($p < 0.05$). Among these, LDH >376 U/L (OR = 12.85) and chest X-ray abnormalities (OR = 21.10) demonstrated the strongest associations. Conversely, fever and seizures had odds ratios below 1, indicating

that these features were more frequently observed in children with milder disease. (Table 3)

Table 3.

Univariate factors associated with severe/critical outcomes

Factor	OR	95% CI	p-value
Age <1 month	5.003	2.294–10.909	<0.001
Comorbidity	2.100	1.300–3.300	0.001
WBC >17 G/L	2.775	1.562–4.929	<0.001
CRP >10 mg/L	2.133	1.337–3.404	0.001
Ferritin >237 ng/mL	4.547	2.634–7.912	<0.001
LDH >376 U/L	12.846	7.307–22.584	<0.001
Chest X-ray abnormalities	21.098	7.562–58.865	<0.001
Apnea	2.898	1.211–6.937	0.017
Fever	0.237	0.142–0.395	<0.001
Seizure	0.485	0.246–0.957	0.037
Malnutrition	1.782	1.003–3.166	0.049

Note: CRP = C-reactive protein.

After adjustment for potential confounders in the multivariate logistic regression model, only LDH >376 U/L (OR = 10.53, p <0.001) and chest X-ray abnormalities (OR = 24.24, p <0.001) remained independent predictors of severe or critical disease. Other factors, although significant in the univariate analysis, lost significance after adjustment. These findings indicate that elevated LDH levels and chest radiographic abnormalities are highly valuable markers for identifying children at increased risk of disease progression.

Table 4.

Multivariate logistic regression of factors associated with severe/critical outcomes

Factor	OR (95% CI)	p-value
Age group		
Age <1 month	1.637 (0.331–8.093)	0.545
Age 1–<12 months	0.662 (0.216–2.028)	0.470
Age 1–<5 years	0.665 (0.202–2.181)	0.500
Age ≥5 years	1 (reference)	–
Nutrition		
Malnutrition	1.273 (0.398–4.077)	0.684
Overweight/obesity	0.750 (0.134–4.194)	0.743
Normal nutrition	1 (reference)	–
Apnea (Yes vs No[a])	1.430 (0.285–7.175)	0.664
Comorbidity (Yes vs No[a])	1.329 (0.531–3.330)	0.544
WBC >17 G/L (Yes vs No[a])	0.670 (0.230–1.958)	0.465
CRP >10 mg/L (Yes vs No[a])	1.716 (0.738–3.991)	0.210
Ferritin >237 ng/mL (Yes vs No[a])	1.480 (0.625–3.506)	0.373
LDH >376 U/L (Yes vs No[a])	10.527 (4.348–25.486)	<0.001

Factor	OR (95% CI)	p-value
D-dimer >1500 ng/mL (Yes vs No[a])	0.857 (0.342–2.148)	0.743
Chest X-ray abnormalities (Yes vs No[a])	24.238 (5.326–110.303)	<0.001

[a] reference group

4 DISCUSSION

This study identified clinical and laboratory predictors of severe and critical outcomes among 906 children hospitalized with symptomatic COVID-19 in Vietnam. Although the majority of children presented with mild disease, infants, malnourished children, and those with comorbidities were disproportionately represented in severe and critical groups. Elevated LDH levels and chest radiographic abnormalities were the strongest independent predictors of poor outcomes.

In our cohort, the majority of hospitalized children with COVID-19 presented with mild (80.5%) or moderate (9.9%) disease, while only a smaller proportion progressed to severe (3.6%) or critical illness (6.0%). This distribution is consistent with global findings that most pediatric cases remain mild to moderate. For example, in Chaozhou, China, 48.3% of children were classified as mild and 44.0% as moderate (Lin *et al*., 2024), while in Germany, nearly four out of five hospitalized children (79.3%) had moderate disease (Antoon *et al*., 2021). By contrast, severe or critical cases generally accounted for a minority, with 7.7% in Chaozhou (Lin *et al*., 2024), 11.3% severe and 9.4% very severe in the United States (Antoon *et al*., 2021), and 6.5% severe in Taiwan, where some children developed complications such as encephalopathy and shock (Huang *et al*., 2023). These findings reinforce the pattern that although pediatric COVID-19 is typically less severe, a notable proportion still progresses to serious disease requiring intensive care.

Infants and young children were disproportionately represented among severe and critical COVID-19 cases in our study, with 16.7% of neonates (<1 month) and 37% of infants aged 1–12 months falling into these categories. This finding is consistent with evidence that children under 12 months are more likely to experience severe outcomes than older children. Prior studies have demonstrated that infants not only have higher hospitalization rates but also exhibit elevated biomarkers such as LDH, reflecting more severe disease progression (Stopyra *et al*., 2022). Flores-Cisneros *et al*. (2023) further reported a strong association between young age and severe outcomes, reinforcing the

role of age as an important determinant of disease severity in pediatric COVID-19 (Flores-Cisneros *et al*., 2024).

Comorbidities also played a significant role in shaping disease severity. In our cohort, 60.6% of severe and 46.3% of critical cases had pre-existing conditions, compared with only 34.7% of mild cases. These findings align with international literature showing that chronic conditions substantially increase the risk of severe COVID-19 in children. Obesity, diabetes, chronic lung disease, and neurological disorders have been consistently linked to increased hospitalization and ICU admission (Gastesi *et al*., 2025; Verma *et al*., 2021). Children with congenital cardiovascular diseases, renal disease, or immunosuppression are also more vulnerable, with greater likelihood of requiring mechanical ventilation and facing higher mortality risks (Flores-Cisneros *et al*., 2024; Huang *et al*., 2023).

Nutritional status emerged as another relevant factor. While most children in the study had normal nutrition, malnutrition was more prevalent among severe and critical cases compared with mild disease. This observation is in line with previous research, which highlights the contribution of nutritional imbalances to disease progression. Obesity, for instance, is frequently cited as an important predictor of hospitalization and intensive care admission among children with COVID-19 (Oliveira *et al*., 2023). Together, these findings suggest that both ends of the nutritional spectrum—malnutrition and obesity—may predispose children to worse outcomes.

Laboratory and radiographic markers provided strong predictive value for severe disease. LDH >376 U/L remained a robust independent predictor, with an odds ratio of 10.53 after adjustment, consistent with prior studies linking elevated LDH to systemic inflammation and more severe illness (Zhou *et al*., 2021). Similarly, chest X-ray abnormalities were present in 91.7% of critical cases compared with 39.2% of mild cases, yielding an odds ratio of 24.24. Abnormal chest imaging, often accompanied by dyspnea or tachypnea, has been widely reported as a critical indicator of severe COVID-19 in children (Zhou *et al*., 2021). These results highlight the importance of objective biomarkers in distinguishing children at greater risk of progression to severe disease.

From a clinical perspective, our findings indicate that LDH >376 U/L and chest radiographic abnormalities should be considered red-flag markers for deterioration in children hospitalized with COVID-19. In settings with limited resources, these readily available assessments can guide early triage decisions, allocation of intensive care

resources, and prioritization of preventive interventions such as vaccination. Public health strategies should also emphasize nutritional support and targeted monitoring of infants and children with chronic conditions, who remain at highest risk.

This study has several limitations. First, its retrospective design carries inherent risks of incomplete data capture and misclassification. Second, the study was conducted in a single tertiary referral hospital, potentially over-representing more severe cases and limiting generalizability to community settings. Third, we did not analyze the role of viral variants, vaccination status, or coinfections, which may have influenced disease progression. Finally, causal relationships cannot be established from the observational design.

5 CONCLUSION

In summary, most hospitalized children with COVID-19 in Vietnam presented with mild disease, but severe and critical cases were not uncommon, particularly among infants, malnourished children, and those with comorbidities. Elevated LDH levels and chest radiographic abnormalities emerged as the strongest independent predictors of severity, highlighting their value for early identification of high-risk patients. Integrating these simple and accessible markers into routine clinical evaluation can improve risk stratification, guide timely interventions, and ultimately enhance outcomes for pediatric patients with COVID-19.

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Authors' Contribution

Both authors contributed equally to the development of this article.

Data availability

All datasets relevant to this study's findings are fully available within the article.

How to cite this article (APA):

Huong, T. T. T., Huyen, T. T. T., Loan, T. T., Son, N. H., Huong, N. T., Thao, N. P., & Vinh, N. A. CLINICAL AND LABORATORY PREDICTORS OF SEVERE AND CRITICAL COVID-19 IN HOSPITALIZED CHILDREN. Veredas Do Direito, e223438. https://doi.org/10.18623/rvd.v22.n3.3438