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Clinical and Laboratory Predictors of Disease Severity in Hospitalized Children with COVID-19: A Study from the Early Pandemic Period

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ABSTRACT

Introduction: Although COVID-19 generally follows a mild course in children, a subset required hospitalization during the early pandemic period. Data from the pre-vaccination phase remain important for understanding risk factors associated with severe disease, particularly in upper-middle-income healthcare settings. The aim of this manuscript is to evaluate the clinical, laboratory, and radiological characteristics of hospitalized children with COVID-19 and to compare findings according to disease severity.

Material and methods: This retrospective study included 97 children hospitalized with confirmed COVID-19 between October and December 2020 at a tertiary center in Türkiye. Patients were classified as non-severe or severe. Demographic, clinical, laboratory, radiological, and outcome data were compared between groups.

Results: Of 97 patients, 75 (77.3%) were non-severe and 22 (22.7%) were severe. Severe patients were significantly older (median age: 136.5 months vs. 18 months, p = 0.036) and more frequently had ≥2 infected household contacts (p=0.034). Cough, dyspnea, and comorbidities were more common in severe cases. Severe disease was associated with lymphopenia, higher neutrophil-to-lymphocyte ratio, elevated CRP and D-dimer levels, increased troponin, and greater CT severity (all p<0.05).

Conclusions: During the early pandemic period, older age, multiple household contacts, comorbidities, elevated inflammatory and cardiac biomarkers, and more extensive radiological involvement were associated with severe disease among hospitalized children. In exploratory multivariable analyses, D-dimer remained significantly associated with disease severity. These findings are specific to the early pandemic period before the emergence of SARS-CoV-2 variants and pediatric vaccination and require validation in contemporary pediatric cohorts.

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Predictores clínicos y de laboratorio de la gravedad de la enfermedad en niños hospitalizados con COVID-19: un estudio del periodo inicial de la pandemia

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RESUMEN

Introducción: Si bien la COVID-19 generalmente tiene un curso leve en niños, un subgrupo requirió hospitalización durante la fase inicial de la pandemia. Los datos de la fase previa a la vacunación siguen siendo importantes para comprender los factores de riesgo asociados con la enfermedad grave, particularmente en entornos de atención médica de ingresos medios-altos. El objetivo de este manuscrito es evaluar las características clínicas, de laboratorio y radiológicas de niños hospitalizados con COVID-19 y comparar los hallazgos según la gravedad de la enfermedad.

Material y métodos: Este estudio retrospectivo incluyó a 97 niños hospitalizados con COVID-19 confirmado entre octubre y diciembre de 2020 en un centro de atención terciaria en Turquía. Los pacientes se clasificaron como leves o graves. Se compararon los datos demográficos, clínicos, de laboratorio, radiológicos y de resultados entre los grupos.

Resultados: De los 97 pacientes, 75 (77,3 %) presentaron un cuadro leve y 22 (22,7 %) un cuadro grave. Los pacientes con enfermedad grave eran significativamente mayores (mediana de edad: 136,5 meses frente a 18 meses, p = 0,036) y presentaban con mayor frecuencia ≥2 contactos domésticos infectados (p = 0,034). La tos, la disnea y las comorbilidades fueron más frecuentes en los casos graves. La enfermedad grave se asoció con linfopenia, mayor índice neutrófilos/linfocitos, niveles elevados de PCR y dímero D, aumento de troponina y mayor gravedad en la tomografía computarizada (p < 0,05 en todos los casos).

Conclusiones: Durante el inicio de la pandemia, la edad avanzada, los múltiples contactos domésticos, las comorbilidades, los biomarcadores inflamatorios y cardíacos elevados y una mayor afectación radiológica se asociaron con la enfermedad grave en niños hospitalizados. En los análisis multivariables exploratorios, el dímero D se mantuvo significativamente asociado con la gravedad de la enfermedad. Estos hallazgos son específicos del inicio de la pandemia, antes de la aparición de las variantes del SARS-CoV-2 y la vacunación pediátrica, y requieren validación en cohortes pediátricas contemporáneas.

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1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread rapidly worldwide and resulted in substantial morbidity and mortality. Although children have generally experienced milder disease compared with adults, a proportion of pediatric patients required hospitalization, particularly during the early phase of the pandemic when clinical knowledge and management strategies were still evolving [1, 2].

While most pediatric cases were non-severe, children remained at risk of complications, including multisystem inflammatory syndrome in children (MIS-C), severe pneumonia, and systemic inflammatory responses [3]. Pediatric COVID-19 exhibits a broad clinical spectrum, ranging from mild upper respiratory symptoms to severe respiratory failure and multiorgan involvement [4].

Hospitalized pediatric patients constitute a heterogeneous group with diverse clinical manifestations, laboratory abnormalities, and radiological findings [5, 6]. Although several studies have described the characteristics of hospitalized children with COVID-19, determinants of disease severity remain incompletely understood. Data from the early pandemic period are particularly valuable because they reflect the natural course of infection before the introduction of pediatric vaccination and the emergence of SARS-CoV-2 variants [7, 8].

Identifying clinical, laboratory, and radiological markers associated with disease severity may contribute to early risk stratification and optimized management strategies. Therefore, this study aimed to identify demographic, clinical, laboratory, and radiological factors associated with disease severity among children hospitalized with confirmed COVID-19 during the early pandemic period in Türkiye.

2. MATERIAL AND METHODS

This retrospective observational study included 97 children with confirmed COVID-19 who were hospitalized in the Pediatric Department of Sancaktepe Training and Research Hospital, Istanbul, Türkiye, between October 1 and December 31, 2020. Among these patients, 90 had positive SARS-CoV-2 Reverse Transcription Polymerase Chain Reaction (RT-PCR) test results, whereas 7 were RT-PCR negative but fulfilled the Turkish Ministry of Health clinical case definition for COVID-19 based on compatible clinical, radiological, and epidemiological findings. Confirmed cases were defined as children with compatible clinical symptoms and either a positive RT-PCR test or radiological findings consistent with COVID-19 in the presence of confirmed epidemiological contact, according to the Turkish Ministry of Health COVID-19 guideline in use during the study period (9). Nasopharyngeal swab samples were obtained for RT-PCR testing. Demographic characteristics (age, sex, contact history), clinical features, comorbidities, need for pediatric intensive care unit (PICU) admission, laboratory findings, radiological imaging (chest X-ray and computed tomography [CT]), treatments, and clinical outcomes were retrospectively reviewed from medical records.

Patients were classified according to the disease severity categories documented in their medical records at the time of hospitalization. These categories had been assigned by the treating physicians as asymptomatic, mild, moderate, severe, or critical according to the Turkish Ministry of Health COVID-19 clinical severity definitions in use during the study period (October–December 2020). For statistical analysis, these disease severity categories were numerically coded as follows: asymptomatic = 1, mild = 2, moderate = 3, severe = 4, and critical = 5. Since the present study included only hospitalized children, only patients with moderate (code 3), severe (code 4), or critical (code 5) disease were eligible for inclusion. Patients with moderate disease (code 3) were categorized as Group 1 (non-severe), whereas patients with severe (code 4) or critical (code 5) disease were categorized as Group 2 (severe). Because only five patients were classified as having critical disease, severe and critical cases were analyzed together due to the limited sample size in the critical disease group. The clinical criteria corresponding to each disease severity category are presented in Supplementary Table 1.

Laboratory parameters analyzed included complete blood count, C-reactive protein (CRP), ferritin, D-dimer, neutrophil-to-lymphocyte ratio (NLR), absolute lymphocyte count (ALC), procalcitonin, and troponin I. Lymphocytopenia was defined as an absolute lymphocyte count <1500 cells/mm³. Thrombocytopenia was defined as a platelet count <150,000 cells/mm³. Hypoxemia was defined as oxygen saturation <92% on room air. Age-specific tachypnea was defined according to established pediatric respiratory rate thresholds. Chest radiography was performed for all hospitalized patients. Chest CT was reserved for patients with hypoxemia, respiratory distress, or clinical deterioration. CT findings were categorized according to the Radiological Society of North America (RSNA) classification as normal, typical/probable COVID-19 pattern, indeterminate, or non–COVID-19. CT severity grading was performed only in patients with COVID-19–related CT findings. The extent of pulmonary involvement was visually estimated and categorized as mild (<25%), moderate (25–50%), or severe (>50%).

The study protocol was approved by the Sancaktepe Şehit

Table 1: Clinical disease severity classification used in the study according to the Turkish Ministry of Health COVID-19 guideline in use during the study period (October–December 2020)

Disease severity category	Statistical code	Clinical definition
Asymptomatic	1	Laboratory-confirmed SARS-CoV-2 infection without clinical signs or symptoms.
Mild	2	Symptoms of upper respiratory tract infection without evidence of pneumonia, hypoxemia, or respiratory distress.
Moderate	3	Clinical and/or radiological evidence of pneumonia without features of severe or critical disease. Patients in this category constituted Group 1 (non-severe).
Severe	4	Pneumonia with severe clinical findings, including hypoxemia and/or marked respiratory distress. Patients in this category were included in Group 2 (severe).
Critical	5	Respiratory failure requiring mechanical ventilation, shock, or multiorgan dysfunction requiring intensive care management. Patients in this category were included in Group 2 (severe).

SARS-CoV-2: severe acute respiratory syndrome coronavirus.
The numerical codes (1–5) were assigned solely for statistical analysis and do not represent an official scoring system of the Turkish Ministry of Health. Disease severity categories were assigned by the treating physicians according to the Turkish Ministry of Health COVID-19 clinical severity definitions in use during the study period (October–December 2020).

Table 2: Demographic, clinical characteristics, and outcomes of hospitalized children with COVID-19 according to disease severity

Characteristic	Group 1 (n=75)	Group 2 (n=22)	P value
Gender n (%)			
Female	40 (53.3%)	13 (59.1%)	0.815
Male	35 (46.7%)	9 (40.9%)	
Number of infected household contacts n (%)			
0 contact	14 (18.7%)	4 (18.2%)	1.000
1 contact	46 (61.3%)	8 (36.4%)	0.067
≥ 2 contacts	15 (20%)	10 (45.5%)	**0.034**
Symptoms at admission n (%)			
Cough	32 (42.7%)	17 (77.3%)	**0.009**
Fever	62 (82.7%)	18 (81.8%)	1.000
Shortness of breath	10 (13.3%)	15 (68.2%)	< **0.001**
Vomiting, diarrhea, weakness	27 (36%)	4 (18.2%)	0.188
Myalgia	7 (9.3%)	4 (18.2%)	0.264
Comorbid conditions	10 (13.3%)	8 (36.3%)	**0.026**
Asthma	4 (5.3%)	3 (13.6%)	
Neurologic	1 (1.3%)	4 (18.1%)	
Familial Mediterranean fever	2 (2.6%)	0 (0%)	
Glycogen storage disease	1 (1.3%)	0 (0%)	
Immunosuppression	0 (0%)	1 (4.5%)	
Phenylketonuria disease	1 (1.3%)	0 (0%)	
Down syndrome	1 (1.3%)	0 (0%)	
PICU admission	1 (1.3%)	15 (68.2%)	< **0.001**
Length of hospital stay (days) median (min-max)	7 (2–14)	11.5 (4–28)	< **0.001**
Age, months median (min-max)	18 (1–207)	136.5 (1–214)	**0.036**

Prof. Dr. İlhan Varank Training and Research Hospital Scientific Research Ethics Committee (date: 08.12.2021, number: 2021/135)and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from parents or legal guardians.

2.1. STATISTICAL ANALYSIS

Statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using visual inspection and the Shapiro–Wilk test. Since most variables were not normally distributed, continuous data were presented as median (minimum–maximum) values. Comparisons between the non-severe and severe groups were performed using the Mann–Whitney U test for continuous variables. Categorical variables were expressed as frequencies and percentages and were compared using the Pearson chi-square test or Fisher's exact test, as appropriate. Demographic variables, comorbidity status, household contact history, complete blood count parameters (including lymphocyte count and neutrophil-to-lymphocyte ratio), and C-reactive protein values were available for all patients. D-dimer and troponin measurements were available for 54 and 76 patients, respectively, because these laboratory tests were performed according to clinical indications. Therefore, multivariable logistic regression analyses including these variables were performed using complete-case analysis. Given the limited number of severe or critical cases (n = 22), the multivariable logistic regression analyses were considered exploratory and should be interpreted with caution. Accordingly, no adjustment for multiple comparisons was performed because the analyses were hypothesis-generating rather than confirmatory.

All statistical tests were two-tailed, and a p-value < 0.05 was considered statistically significant.

3. RESULTS

3.1. STUDY POPULATION

A total of 97 hospitalized pediatric patients diagnosed with COVID-19 were included in the study.

Seventy-five patients (77.3%) had moderate disease and were classified as Group 1 (non-severe). Among the remaining 22 patients (22.7%), 17 (17.5%) had severe disease and 5 (5.2%) had critical disease; these patients were classified as Group 2 (severe).

The median age was significantly higher in the severe group compared with the non-severe group (136.5 months [1–214] vs. 18 months [1–207], p = 0.036). Overall, 53 patients (54.6%) were female and 44 (45.4%) were male. There was no significant difference in sex distribution between the groups (p = 0.815). The distribution of contact history differed significantly between groups (p = 0.034). Contact

with two or more infected household members was more frequent in severe cases (45.5%) than in non-severe cases (20.0%) (Table 2).

The single patient in the non-severe group who required PICU admission was admitted for close monitoring and supportive care based on clinical judgment, despite not meeting the criteria for severe disease, and remained classified as having moderate disease throughout hospitalization. The median duration of hospitalization was significantly longer in the severe group (11.5 days [4–28]) compared with the non-severe group (7 days [2–14], p < 0.001) (Table 2).

Table 3: Demographic, clinical characteristics, and outcomes of hospitalized children with COVID-19 according to disease severity

Characteristic	Group 1 (n=75)	Group 2 (n=22)	P value
White blood cell count (WBC) (median (min–max))	6900 (2800–37350)	6345 (1790–18110)	0.354
>10000 cells/mm³ n (%)	18 (24%)	4 (18.1%)	0.774
<4000 cells/mm³ n (%)	9 (12%)	6 (27.2%)	0.099
Absolute neutrophil count (ANC) (median (min–max))	2570 (410–28820)	2850 (510–16750)	0.412
>3000 cells/mm³ n (%)	27 (36%)	9 (40.9%)	0.709
<1500 cells/mm³ n (%)	23 (30.6%)	5 (22%)	0.456
Absolute lymphocyte count (ALC) (median (min–max))	2610 (460–10020)	1330 (330–8090)	0.052
<1500 cells/mm³ n (%)	15 (20%)	12 (54.5%)	**0.004**
NLR (median (min–max))	0.98 (0.5–16.8)	2.32 (0.13–13.62)	**0.044**
Eosinophil (median (min–max))	70 (0–790)	40 (0–2160)	0.087
>250 cells/mm³	10 (13.3%)	5 (22.7%)	0.329
<50 cells/mm³	25 (33.3%)	12 (54.5%)	0.086
Platelet count ((×10³/µL) median (min–max))	290 (43–573)	235 (52–563)	0.287
<150000 cells/mm³	7 (9.3%)	6 (27.3%)	0.098
CRP (mg/dL median (min–max))	0.2 (0.07–12.5)	3.65 (0.02–40.7)	**< 0.001**
AST (U/L median (min–max))	34 (14–112)	29 (12–247)	0.564
AST >40 U/L n (%)	26 (34.6%)	7 (31.8%)	1.000
ALT (U/L median (min–max))	18 (6–96)	18 (6–218)	0.651
ALT >40 U/L n (%)	10 (13.3%)	4 (18.1%)	0.730
LDH (U/L median (min–max))	265 (100–1275)	285 (179–720)	0.550
LDH >240 U/L n (%)	50 (66.6%)	19 (86.3%)	0.115
D-Dimer (mg/L median (min–max))	0.56 (0.17–3.70)	1.56 (0.26–10.90)	**< 0.001**
D-Dimer > 0.55 mg/L n (%)	18 (24%)	16 (72.7%)	**< 0.001**
Ferritin (ng/mL median (min–max))	121 (8.5–325)	105 (20–1143)	0.977
Ferritin >220 ng/mL n (%)	3 (4%)	7 (31.8%)	**0.001**
PCT ng/mL median (min–max)	0.1 (0.10–0.12)	0.24 (0.09–8.44)	0.071
Troponin–I (pg/mL median (min–max))	1.5 (0.1–134)	3 (0.5–1404)	**0.033**
Troponin–I > 28.9 pg/mL n (%)	3 (4%)	6 (22.7%)	**0.004**
SARS-CoV-2 RT-PCR positive (n (%))	70 (93.3%)	20 (90%)	0.655

NLR: Neutrophil-to-lymphocyte ratio; CRP: C-reactive protein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LDH: Lactate dehydrogenase; PCT: Procalcitonin; PICU: Pediatric intensive care unit; RT-PCR: Reverse transcription polymerase chain reaction.

3.2. CLINICAL PRESENTATIONS

Fever was the most common presenting symptom (82.5%), followed by cough (50.5%), vomiting/diarrhea/weakness (32.0%), shortness of breath (25.8%), and myalgia (11.3%). Cough was significantly more frequent in severe cases (77.3% vs. 42.7%, p = 0.009). Shortness of breath was markedly more common in the severe group (68.2% vs. 13.3%, p < 0.001). No significant differences were observed between groups regarding fever, vomiting/diarrhea/weakness, or myalgia. Nineteen patients (19.6%) had at least one comorbidity. The presence of comorbidity was significantly higher in the severe group compared with the non-severe group (36.4% vs. 13.3%, p = 0.026). Sixteen patients (16.5%) required pediatric intensive care unit (PICU) admission. PICU transfer was significantly more frequent in severe cases (68.2% vs. 1.3%, p < 0.001).

3.3. LABORATORY FINDINGS

Laboratory findings are summarized in Table 3. Median white blood cell count, absolute neutrophil count, eosinophil count, platelet count, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Lactate dehydrogenase (LDH), ferritin, and procalcitonin levels were similar between groups. The median absolute lymphocyte count was numerically lower in severe cases (1330 [330–8090] vs. 2610 [460–10020]); however, the difference did not reach statistical significance and remained borderline (p = 0.052).

In contrast, the frequency of lymphopenia (<1500 cells/mm³) was significantly higher in the severe group (54.5% vs. 20.0%, p = 0.004). Median neutrophil-to-lymphocyte ratio (NLR) was significantly higher in severe patients (2.32 vs. 0.98, p = 0.044). C-reactive protein (CRP) levels were significantly higher in severe cases (p < 0.001), as were D-dimer levels (p < 0.001). Elevated D-dimer (>0.55 mg/L) was significantly more common in severe cases (72.7% vs. 24.0%, p < 0.001). Ferritin levels did not differ significantly in median values; however, ferritin >220 ng/mL was significantly more frequent in severe cases (31.8% vs. 4.0%, p = 0.001).

Troponin I (Trop-I) levels were significantly higher in severe patients (p = 0.033), and elevated Trop-I (>28.9 pg/mL) was more common in severe cases (27.3% vs. 4.0%, p = 0.004).

3.4. EXPLORATORY MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS

In the exploratory multivariable logistic regression analysis including age and D-dimer levels (n = 54), D-dimer remained significantly associated with severe disease (adjusted OR 2.57, 95% CI 1.24–5.33, p = 0.011), whereas age was no longer statistically significant (p = 0.280). In a second exploratory model including D-dimer and comorbidity, D-dimer remained significantly associated with severe disease (adjusted OR 2.57, 95% CI 1.24–5.33, p = 0.011), whereas comorbidity showed borderline significance (adjusted OR 3.70, 95% CI 0.87–15.80, p = 0.078). In a third exploratory model including D-dimer and NLR, D-dimer remained significantly associated with severe disease (adjusted OR 2.56, 95% CI 1.23–5.31, p = 0.012), whereas NLR was not significantly associated with disease severity after adjustment (p = 0.354).

3.5. RADIOLOGICAL FINDINGS

Chest radiographs were performed for all hospitalized patients. In the non-severe group, 28 patients (37.3%) had normal findings, whereas 47 (62.7%) had abnormal chest X-ray findings. All severe cases had abnormal chest radiographs. The difference between groups was statistically significant (p = 0.001; Figure 1A). Chest CT was performed in 34 of 97 patients (35.1%), primarily in cases with hypoxemia, dyspnea, or clinical deterioration. Among non-severe cases, 21 patients underwent CT: 2 (9.5%) had normal findings, 11 (52.4%) had classical/probable COVID-19 patterns, 6 (28.6%) had indeterminate findings, and 2 (9.5%) had non-COVID-19 findings. Among severe cases, 13 patients underwent CT: 1 (7.7%) had normal findings and 12 (92.3%) demonstrated classical/probable COVID-19 patterns. CT severity analysis was performed only in patients with COVID-19–related CT findings. Therefore, severity grading was available for 17 non-severe and 12 severe patients. Because chest CT was performed only in selected patients with hypoxemia, dyspnea, or clinical deterioration, comparisons of CT severity between the study groups are subject to selection bias and should be interpreted as descriptive findings only. CT severity differed significantly between groups (p < 0.001; Figüre 1B). In the non-severe group, 6 patients (35.3%) had mild and 11 (64.7%) had moderate involvement. In the severe group, 3 patients (25.0%) had moderate and 9 (75.0%) had severe CT involvement.

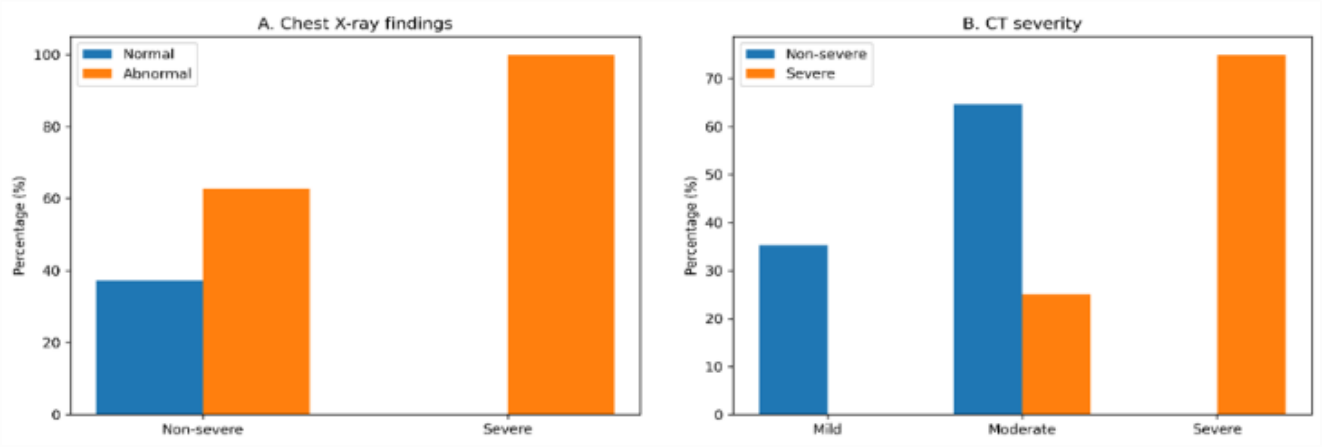

Figure 1: *Radiological findings. (A) Chest X-ray findings according to disease severity (p = 0.001). (B) Computed Tomography severity according to disease severity (p < 0.001).*

4. DISCUSSION

In this retrospective study evaluating children hospitalized during the early phase of the COVID-19 pandemic, we

identified several demographic, clinical, laboratory, and radiological factors associated with disease severity. Although most pediatric patients experienced a non-severe course, a substantial proportion developed severe disease requiring intensive care support. Consistent with previous reports, the majority of our patients were classified as non-severe. However, 22.7% were categorized as severe, and 16.5% required PICU admission, nearly all of whom belonged to the severe group. The only patient in the non-severe group who required PICU admission remained classified as having moderate disease and was admitted for close monitoring and supportive care without progressing to severe disease. These findings are comparable to previous reports from the early pandemic period, which described considerable heterogeneity among hospitalized children [7, 10-12]. Severe patients in our cohort were significantly older than non-severe patients. It suggests that adolescents and older children may be more vulnerable to severe pulmonary and inflammatory manifestations. Similar associations between increasing age and worse clinical outcomes have been reported in previous pediatric studies from Europe and Asia [7, 10, 12]. In our study, this association was observed in the univariable analysis; however, age was no longer significantly associated with disease severity after adjustment in the exploratory multivariable analyses. The observed age-related difference may reflect a more pronounced inflammatory response and greater pulmonary involvement in older pediatric patients.

Household transmission was common in our cohort, and contact with two or more infected family members was significantly more frequent among severe cases. Household exposure has been recognized as the primary route of infection in children during the early pandemic period [11, 12]. Our findings further suggest that repeated or intense household exposure may be associated with increased disease severity, potentially reflecting higher viral burden.

Regarding clinical presentation, fever was the most common symptom at admission, consistent with previous pediatric studies evaluating hospitalized children with COVID-19 [7, 13].

Cough and dyspnea were significantly more frequent among severe patients, underscoring the importance of respiratory symptoms as early indicators of severity. Dyspnea, in particular, may serve as a practical clinical marker warranting closer monitoring and early escalation of care.

Severe disease was associated with a higher frequency of lymphopenia, suggesting greater immune dysregulation in these patients. Lymphopenia has been widely reported as a marker of immune dysregulation in COVID-19 [14].

In addition, severe patients demonstrated higher neutrophil-to-lymphocyte ratios (NLR), elevated CRP levels, and markedly increased D-dimer concentrations. These findings reflect the inflammatory and thromboinflammatory nature of severe COVID-19 and are consistent with prior pediatric studies linking elevated inflammatory markers with worse outcomes [7, 10]. Elevated D-dimer levels have also been associated with adverse outcomes and thromboinflammatory activation [15-17].

In exploratory multivariable logistic regression analyses, D-dimer remained significantly associated with severe disease, whereas age, comorbidity, and NLR were no longer statistically significant after adjustment. Because of the limited number of severe events and the incomplete availability of some laboratory variables, these multivariable findings should be interpreted with caution and considered exploratory.

This finding suggests that thromboinflammatory activation may play a central role in the progression to severe disease in hospitalized children.

Because the present study was conducted during the early pandemic period, before the emergence of SARS-CoV-2 variants and the implementation of pediatric vaccination, these findings should be interpreted within this historical context and may not be directly generalizable to children infected during later phases of the pandemic.

Elevated troponin levels were more frequent in severe cases in our cohort, suggesting possible myocardial involvement or systemic inflammatory stress. Although median ferritin levels did not differ significantly, elevated ferritin above the defined cut-off was more common among severe patients, further supporting the contribution of hyperinflammatory mechanisms.

Radiologically, all severe patients had abnormal chest radiographs, and CT severity scores were significantly higher in this group. Standardized evaluation using the RSNA classification facilitated objective comparison of imaging findings [8]. The greater extent of pulmonary involvement among severe patients aligns with previous studies demonstrating that radiological severity parallels clinical severity in pediatric COVID-19 [4]. However, because chest CT was performed only in selected patients with clinical indications, these radiological findings should be interpreted descriptively and with caution due to the potential for selection bias.

5. CONCLUSIONS

In conclusion, although COVID-19 generally followed a non-severe course in children during the early pandemic period, a substantial proportion of hospitalized patients

developed severe disease requiring intensive care support. In this cohort, older age, multiple household contacts, comorbidities, lymphopenia, elevated neutrophil-to-lymphocyte ratio, increased inflammatory and thrombotic biomarkers, and more extensive radiological involvement were associated with greater disease severity. These findings highlight the importance of early clinical and laboratory risk stratification in hospitalized pediatric patients. However, these findings are specific to the early pandemic period before the emergence of SARS-CoV-2 variants and the implementation of pediatric vaccination programs. Therefore, validation in contemporary pediatric cohorts is warranted before these findings can be generalized to current clinical practice.

6. LIMITATIONS

This study has several limitations. First, its retrospective and single-center design may limit the generalizability of the findings. Second, the relatively small sample size, particularly in the severe group, may have reduced the statistical power to detect differences in certain variables and limited our ability to adjust for all potential confounding factors in the exploratory multivariable analyses. Third, management strategies and hospitalization thresholds during the early phase of the pandemic were evolving, which may have influenced clinical decision-making and imaging practices. In addition, chest CT was not performed in all patients and was reserved for selected cases with clinical deterioration, potentially introducing selection bias in the assessment of radiological severity. Incomplete availability of D-dimer and troponin measurements limited the sample size available for exploratory multivariable analyses. Long-term clinical follow-up was not available; therefore, longer-term outcomes could not be evaluated. Furthermore, MIS-C was not evaluated separately because the study was conducted during the early phase of the pandemic, when the clinical recognition of MIS-C was still evolving. Therefore, the possibility of unrecognized early MIS-C in some severe cases cannot be completely excluded. Finally, the number of infected household contacts was obtained from patient or caregiver reports and may therefore be subject to recall bias. Despite these limitations, the study provides comprehensive real-world data from the early pandemic period and integrates demographic, clinical, laboratory, and radiological findings within a unified severity-based framework.

7. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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