

**Table S1: Laboratory results comparing patients who required any type of respiratory support with those who did not, and patients who required NIV and CMV with those who did not.** The results are expressed as median and interquartile range [25-75].

Parameter	Patients who required any type of respiratory support (n=37)	Patients who DID NOT required respiratory support (n=7)	p-value	Patients who required NIV (n=11)	Patients who DID NOT required NIV (n=33)	p-value	Patients who required CMV (n=4)	Patients who DID NOT required CMV (n=40)	p-value
Hemoglobin; minimum (g/dL)	12.4 [10.8 – 14.6]	<b>11.8 [10.8 – 13]</b>	0.572	<b>10.6 [9.4 – 12.2]</b>	13 [11.5 – 14.6]	<b>0.003</b>	<b>9.3 [9 – 10.3]</b>	12.7 [11.4 – 14.5]	<b>0.001</b>
Platelets; minimum (x10 <sup>3</sup> /μl)	181 [163 – 226]	147 [121 – 321]	0.961	182 [168 – 227]	181 [135 – 234]	0.808	182 [92 – 258]	179 [140 – 226]	0.750
Leucocyte count; maximum (/mm <sup>3</sup> )	9200 [6500 – 11400]	5600 [3800 – 8200]	<b>0.021</b>	10900 [7400 – 13000]	7700 [5500 – 10200]	0.118	11000 [4400 – 17000]	8050 [5800 – 10800]	0.547
Lymphocyte count; minimum (/mm <sup>3</sup> )	<b>800 [550 – 1400]</b>	1600 [600 – 2000]	<b>0.037</b>	<b>600 [400 – 900]</b>	<b>1100 [700 – 1600]</b>	<b>0.005</b>	<b>700 [150 – 1400]</b>	<b>850 [620 – 1500]</b>	0.188
Neutrophile count; maximum (/mm <sup>3</sup> )	<b>6100 [3900 – 8000]</b>	3000 [2200 – 5800]	<b>0.003</b>	<b>7800 [5200 – 8600]</b>	4800 [3050 – 6900]	0.110	<b>6500 [2500 – 10100]</b>	<b>5700 [3200 – 7500]</b>	0.841
C-reactive protein; maximum (mg/L)	<b>49 [16 – 112]</b>	<b>17 [2.8 – 69]</b>	<b>0.046</b>	<b>63 [31 – 178]</b>	<b>35 [13 – 71]</b>	0.192	<b>46 [16 – 148]</b>	<b>39 [14 – 94]</b>	0.988
Procalcitonin; maximum (ng/mL)	0.18 [0.06 – 0.57]	0.12 [0.05 – 0.62]	0.124	<b>0.52 [0.31 – 1.64]</b>	0.09 [0.06 – 0.38]	<b>0.008</b>	<b>0.72 [0.36 – 1.26]</b>	0.11 [0.06- 0.54]	0.731
Ferritin; maximum (ug/L)	<b>400 [190 – 1300]</b>	<b>263 [136 – 310]</b>	0.258	<b>819 [385 – 1952]</b>	<b>268 [189 – 742]</b>	0.112	<b>1990 [166 – 9400]</b>	<b>310 [190 – 1150]</b>	<b>0.002</b>
LDH; maximum (IU/L)	<b>840 [720 – 1090]</b>	<b>613 [589 – 949]</b>	0.074	<b>1086 [805 – 2123]</b>	<b>791 [589 – 1029]</b>	<b>0.006</b>	<b>1960 [1050 – 3100]</b>	<b>832 [612 – 1070]</b>	0.132
IL-6; maximum (pg/mL)	<b>32 [8.5 – 91]</b>	<b>20 [3 – 40]</b>	0.191	<b>43 [25 – 112]</b>	<b>11 [6 – 85]</b>	0.379	<b>71 [4.6 – 123]</b>	<b>28 [9 – 94]</b>	0.458
PT; minimum (%)	76 [71 – 91]	85 [76 – 98]	0.351	75 [69 – 82]	81 [72 – 93]	0.130	79 [74 – 94]	79 [71 – 92]	0.700
aPTT; maximum (seconds)	26 [23 – 29]	28 [25 – 29]	0.494	25 [22 – 31]	26 [24 – 28]	0.830	28 [18 – 32]	26 [24 – 29]	0.945
INR; maximum	1.13 [1.04 – 1.21]	1.11 [1.01 – 1.19]	0.443	1.18 [1.08 – 1.29]	1.11 [1.03 – 1.15]	0.113	1.10 [0.9 – 1.20]	1.13 [1.05 – 1.23]	0.381
Fibrinogen; maximum (g/L)	<b>5.3 [4.6 – 6.5]</b>	<b>4.5 [3.9 – 6]</b>	0.605	<b>5.1 [4.4 – 6.8]</b>	<b>4.9 [4.5 – 6.1]</b>	0.969	<b>4.3 [3.7 – 5.5]</b>	<b>5 [4.6 – 6.7]</b>	0.069
D-dimer;	<b>1 [0.6 – 2.1]</b>	0.42 [0.39 – 1.92]	0.162	<b>1.2 [0.8 – 2.4]</b>	<b>0.75 [0.42 – 1.8]</b>	0.687	<b>2.1 [1.1 – 3.4]</b>	<b>0.89 [0.58 – 1.86]</b>	0.750

maximum (mg/L)									
Troponin; maximum (ng/mL)	0.002 [0.001 – 0.007]	0.002 [0.0002 – 0.011]	0.234	0.007 [0.005 – 0.085]	0.001 [0.001 – 0.003]	<b>0.041</b>	0.007 [0.001 – 0.02]	0.002 [0.001 – 0.006]	<b>0.003</b>
NT-ProBNP; maximum (ng/L)	81 [16 – 196]	20 [14 – 90]	0.731	<b>160 [131 – 262]</b>	20 [15 – 81]	0.101	<b>162 [135 – 196]</b>	36 [15 – 87]	0.494
Creatin kinase; maximum (UI/L)	67 [45 – 161]	71 [13 – 180]	0.345	53 [25 -215]	75 [46 – 130]	0.238	140 [24 – 450]	67 [45 – 134]	<b>0.001</b>
Sodium; average (mmol/L)	140 [136 -143]	138 [137 – 141]	0.164	141 [139 – 146]	138 [136 – 141]	0.052	141 [139 – 148]	139 [136 – 141]	0.289
Potassium; average (mmol/L)	4 [3.8 – 4.2]	4.3 [3.6 – 4.5]	0.652	4 [3.6 – 4.2]	4.1 [3.8 – 4.3]	0.332	3.8 [3.5 – 4.6]	4.1 [3.8 – 4.3]	0.844
Ionic Calcium; average (mmol/L)	1.22 [1.15 – 1.26]	1.20 [1.17 – 1.26]	0.984	1.23 [1.14 – 1.29]	1.21 [1.18 – 1.25]	0.533	1.29 [1.14 – 1.32]	1.21 [1.15 – 1.25]	0.127
Phosphate; average (mg/dL)	3.7 [3.2 – 4.3]	3.7 [3.1 – 4]	0.915	3.7 [2.5 – 4.9]	3.7 [3.1 – 4.2]	0.776	5 [3.8 – 5.2]	3.7 [3.1 – 4.3]	0.456
Magnesium; average (mg/dL)	2.1 [1.8 – 2.2]	1.9 [1.8 – 2.1]	0.093	2.1 [1.8 – 2.6]	2 [1.8 – 2.1]	0.128	2.2 [2 – 2.3]	2.05 [1.8 – 2.1]	0.370
Creatinine; maximum (mg/dL)	0.62 [0.51 – 0.74]	0.46 [0.43 – 0.60]	<b>0.009</b>	0.58 [0.46 – 0.72]	0.59 [0.47 – 0.72]	0.148	0.59 [0.42 – 1.85]	0.59 [0.47 – 0.72]	0.053
AST; maximum (IU/L)	<b>53 [30 – 102]</b>	<b>39 [28 – 48]</b>	<b>0.009</b>	<b>91 [33 – 138]</b>	<b>44 [30 – 63]</b>	0.509	<b>72 [54 – 126]</b>	<b>45 [30 – 74]</b>	0.698
ALT; maximum (IU/L)	<b>46 [21 – 112]</b>	26 [21 – 77]	0.170	<b>81 [24 – 119]</b>	31 [20 – 104]	0.777	<b>76 [35 – 112]</b>	<b>34 [20 – 105]</b>	0.637
Total Bilirubin; maximum (mg/dL)	0.4 [0.3 – 0.6]	0.3 [0.2 – 0.4]	0.113	0.9 [0.3 – 1.2]	0.3 [0.3 – 0.5]	0.238	0.6 [0.3 – 1.3]	0.3 [0.3 – 0.5]	0.180
Conjugated Bilirubin, maximum (mg/dL)	0.2 [0.1 – 0.3]	0.1 [0.1 – 0.2]	0.186	0.2 [0.1 – 0.3]	0.2 [0.1 – 0.2]	0.332	0.2 [0.1 – 0.3]	0.2 [0.1 – 0.3]	0.504
Albumin; minimum (mg/dL)	<b>30 [28 – 36]</b>	<b>36 [35 – 40]</b>	0.113	<b>29 [28 – 32]</b>	37 [35 – 42]	<b>0.008</b>	<b>30 [28 – 32]</b>	<b>36 [29 – 38]</b>	0.180
Triglycerides; average (mg/dL)	125 [75 – 288]	124 [70 – 190]	0.399	<b>176 [75 – 345]</b>	115 [61 – 206]	0.149	<b>240 [201 – 381]</b>	113 [71 – 220]	<b>0.001</b>
Total cholesterol; average (mg/dL)	131 [91 – 164]	95 [77 – 140]	0.223	132 [92 – 166]	123 [86 – 156]	0.854	150 [123 – 183]	123 [87 – 149]	0.299
HDL cholesterol; average (mg/dL)	<b>26 [23 – 31]</b>	<b>27 [16 – 34]</b>	0.938	<b>23 [17 – 25]</b>	<b>29 [25 – 38]</b>	<b>0.012</b>	<b>22 [17 – 29]</b>	<b>26 [23 – 33]</b>	0.566

LDL cholesterol; average (mg/dL)	86 [64 – 101]	56 [44 – 120]	0.252	89 [65 – 105]	77 [52 – 95]	0.718	105 [90 – 132]	81 [56 – 91]	0.115
VLDL cholesterol; average (mg/dL)	23 [15 – 47]	15 [14 – 20]	<b>0.009</b>	<b>25 [15 – 55]</b>	19 [12 – 38]	0.585	<b>30 [28 – 52]</b>	19 [14 – 35]	0.478

*NIV : non-invasive ventilation, CMV : conventional mechanical ventilation, CRP : C-reactive protein, PCT : procalcitonin, LDH : lactate dehydrogenase, IL-6 : interleukin-6, PT : prothrombin time, aPTT : activated partial thromboplastin time, INR : international normalized ratio, NT-ProBNP: N-terminal pro brain natriuretic peptide, CK : creatin kinase, AST : aspartate aminotransferase, ALT : alanine aminotransferase, HDL cholesterol : high-density lipoprotein cholesterol, LDL cholesterol : low-density lipoprotein cholesterol, VLDL cholesterol : very low-density lipoprotein cholesterol.*

**Table S2: Evaluation of potential risk factors associated with greater severity: admission to the PICU, need for NIV and need for CMV.** The results are expressed as counts and percentages (in parenthesis).

Risk factor	Patients ADMITTED to the PICU (n=13)	Patients NOT admitted to the PICU (n=31)	Odds Ratio [95% CI]	p-value	Patients who required NIV (n=11)	Patients who DID NOT required NIV (n=33)	Odds Ratio [95% CI]	p-value	Patients who required CMV (n=4)	Patients who DID NOT required CMV (n=40)	Odds Ratio [95% CI]	p-value
Gender (males)	9 (69.2%)	17 (54.8%)	0.54 [0.13 – 2.13]	0.376	7 (63.6%)	19 (57.6%)	0.77 [0.18 – 3.17]	1	3 (75%)	23 (57.5%)	0.45 [0.04 – 4.72]	0.634
Gender (females)	4 (30.8%)	14 (45.2%)			4 (36.4%)	14 (42.4%)			1 (25%)	17 (42.5%)		
Age (<12 years old)	6 (46.2%)	10 (32.3%)	0.55 [0.14 – 2.09]	0.496	5 (45.5%)	11 (33.3%)	0.6 [0.14 – 2.4]	0.492	3 (75%)	13 (32.5%)	0.16 [0.01 – 1.69]	0.129
Age (≥12 years old)	7 (53.8%)	21 (67.7%)			6 (54.5%)	22 (66.7%)			1 (25%)	27 (67.5%)		
Presence of comorbidities	11 (84.6%)	25 (80.6%)	1.32 [0.22 – 7.59]	1	9 (81.8%)	27 (81.8%)	1 [0.17 – 5.86]	1	4 (100%)	32 (80%)		1
Obesity / Overweight	3 (23.1%)	10 (32.3%)	0.63 [0.14 – 2.8]	0.722	2 (18.2%)	11 (33.3%)	0.44 [0.08 – 2.4]	0.461	0	13 (32.5%)		
Recurrent wheezing / Asthma	1 (7.7%)	12 (38.7%)	0.13 [0.01 – 1.14]	0.068	1 (9.1%)	12 (36.4%)	0.17 [0.02 – 1.54]	0.132	0	13 (32.5%)		
Other pulmonary disease	4 (30.8%)	6 (19.4%)	1.85 [0.42 – 8.11]	0.449	4 (36.4%)	6 (18.2%)	2.57 [0.56 – 11.6]	0.237	2 (50%)	8 (20%)	4 [0.48 – 32.9]	0.218
Other neurological disorder	2 (15.4%)	7 (22.6%)	0.62 [0.11 – 3.5]	0.703	1 (9.1%)	8 (24.2%)	0.31 [0.03 – 2.83]	0.411	0	9 (22.5%)		
Prematurity ≤ 34 GA	4 (30.8%)	1 (3.2%)	<b>13.3 [1.3 – 134.9]</b>	<b>0.022</b>	4 (36.4%)	1 (3%)	<b>18.2 [1.7 – 189.6]</b>	<b>0.010</b>	3 (75%)	2 (5%)	<b>57 [3.9 – 825]</b>	<b>0.003</b>
Neuromuscular disorder	3 (23.1%)	1 (3.2%)	9 [0.83 – 96.6]	0.071	2 (18.2%)	2 (6.1%)	3.4 [0.42 – 28]	0.256	0	4 (10%)		
Immunodeficiency	2 (15.4%)	2 (6.5%)	2.6 [0.33 – 21.1]	0.570	1 (9.1%)	3 (9.1%)	1 [0.93 – 10.7]	1	1 (25%)	3 (7.5%)	4.1 [0.32 – 52.6]	0.327
Nephropathy	1 (7.7%)	2 (6.5%)	1.2 [0.1 – 14.6]	1	0	3 (9.1%)			0	3 (7.5%)		
Down syndrome	1 (7.7%)	2 (6.5%)	1.2 [0.1 – 14.6]	1	1 (9.1%)	2 (6.1%)	1.55 [0.1 – 18.9]	1	1 (25%)	2 (5%)	6.33 [0.43 – 91.7]	0.254
Cerebral palsy	1 (7.7%)	1 (3.2%)	2.5 [0.14 – 43.2]	0.508	1 (9.1%)	1 (3%)	3.2 [0.18 – 55.9]	0.442	0	2 (5%)		
Cardiopathy	1 (7.7%)	1 (3.2%)	2.5 [0.14 – 43.2]	0.508	1 (9.1%)	1 (3%)	3.2 [0.18 – 55.9]	0.442	0	2 (5%)		

Diabetes mellitus	2 (15.4%)	0			1 (9.1%)	1 (3%)	3.2 [0.18 – 55.9]	0.442	1 (25%)	1 (2.5%)	13 [0.64 – 263.8]	0.175
Other metabolic disorder	1 (7.7%)	1 (3.2%)	2.5 [0.14 – 43.2]	0.508	1 (9.1%)	1 (3%)	3.2 [0.18 – 55.9]	0.442	1 (25%)	1 (2.5%)	13 [0.64 – 263.8]	0.175
Other diseases	6 (46.2%)	12 (38.7%)	1.3 [0.36 – 5]	0.647	4 (36.4%)	14 (42.4%)	0.77 [0.18 – 3.17]	1	1 (25%)	17 (42.5%)	0.45 [0.43 – 4.7]	0.634
Time until diagnosis ≤2 days (n=30)	7 (23.3%)	23 (76.6%)	2.46 [0.63 – 9.55]	0.288	5 (16.7%)	25 (83.3%)	3.7 [0.89 – 15.6]	0.132	2 (6.7%)	28 (93.3%)	2.33 [0.29 – 18.5]	0.581
Time until diagnosis >2 days (n=14)	6 (42.9%)	8 (57.1%)			6 (42.9%)	8 (57.1%)			2 (14.3%)	12 (85.7%)		
Time until admission ≤6 days (n=25)	10 (40%)	15 (60%)	0.28 [0.06 – 1.22]	0.081	8 (32%)	17 (68%)	0.39 [0.09 – 1.77]	0.301	4 (16%)	21 (84%)		0.122
Time until admission >6 days (n=19)	3 (15.8%)	16 (84.2%)			3 (15.8%)	16 (84.2%)			0	0		
Viral coinfection	3 (23.1%)	2 (6.4%)	3 [0.37 – 24.17]	0.347	3 (27.2%)	2 (6.1%)	3 [0.37 – 24.17]	0.347	2 (50%)	3 (18.8%)	4.3 [0.4 – 44.4]	0.249
Bacterial coinfection	3 (23.1%)	1 (3.2%)		1	3 (27.2%)	1 (3%)	1 [0.4 – 24.5]	1	2 (50%)	2 (5%)	1 [0.63 – 15.9]	1

PICU : pediatric intensive care unit, NIV : non-invasive ventilation, CMV : conventional mechanical ventilation, GA : gestational age.

**Table S3: Differences of the patients regarding SARS-CoV-2 variant periods:** Wuhan period (March 2020-February 2021), Alpha period (B.1.1.7; February 2021-June 2021), Delta period (B.1.617.1; June 2021 - December 2021) and Omicron period (B.1.1.529; December 2021 - March 2022). The results are expressed as counts and percentages (in parenthesis).

Variable	Wuhan period (n=14)	Alpha period (n=7)	Delta period (n=11)	Omicron period (n=12)	p-value
Gender (males)	8 (57.1%)	5 (71.4%)	7 (63.6%)	6 (50%)	0.809
Gender (females)	6 (42.9%)	2 (28.6%)	4 (36.4%)	6 (50%)	
Age (<12 years old)	3 (21.4%)	2 (28.6%)	1 (9.1%)	10 (83.3%)	<b>0.001</b>
Age (≥12 years old)	11 (78.6%)	5 (71.4%)	10 (90.9%)	2 (16.7%)	
Presence of comorbidities	10 (71.4%)	7 (100%)	9 (81.8%)	10 (83.3%)	0.459
Obesity / Overweight	6 (42.9%)	2 (28.6%)	4 (36.4%)	1 (8.3%)	0.258
Recurrent wheezing / Asthma	3 (21.4%)	1 (14.3%)	4 (36.4%)	5 (41.7%)	0.509
Other pulmonary disease	3 (21.4%)	1 (14.3%)	2 (18.2%)	4 (33.3%)	0.754
Other neurological disorder	3 (21.4%)	3 (42.9%)	2 (18.2%)	1 (8.3%)	0.350
Prematurity ≤ 34 GA	1 (7.1%)	0	2 (18.2%)	2 (16.7%)	0.575
Neuromuscular disorder	2 (14.3%)	1 (14.3%)	1 (9.1%)	0	0.596
Immunodeficiency	3 (21.4%)	1 (14.3%)	0	0	0.164
Nephropathy	1 (7.1%)	1 (14.3%)	0	1 (8.3%)	0.690
Down syndrome	0	0	2 (18.2%)	1 (8.3%)	0.282
Cerebral palsy	0	0	1 (9.1%)	1 (8.3%)	0.589
Cardiopathy	0	0	0	2 (16.7%)	0.134
Diabetes mellitus	2 (14.3%)	0	0	0	0.213
Other metabolic disorder	0	1 (14.3%)	1 (9.1%)	0	0.349
Other diseases	6 (42.9%)	6 (85.7%)	1 (9.1%)	5 (41.7%)	<b>0.015</b>
Fever	14 (100%)	6 (85.7%)	9 (81.8%)	11 (91.7%)	0.434
Cough	9 (64.3%)	4 (57.1%)	9 (81.8%)	12 (100%)	0.085
Respiratory distress	10 (71.4%)	5 (71.4%)	10 (90.9%)	8 (66.7%)	0.558
Rhinorrhea	3 (21.4%)	2 (28.6%)	4 (36.4%)	10 (83.3%)	<b>0.010</b>
General malaise	5 (35.7%)	3 (42.9%)	7 (63.6%)	4 (33.3%)	0.446
Chest pain	4 (28.6%)	3 (42.9%)	4 (36.4%)	2 (16.7%)	0.614
Diarrhea	7 (50%)	3 (42.9%)	1 (9.1%)	1 (8.3%)	<b>0.037</b>
Headache	5 (35.7%)	2 (28.6%)	3 (27.3%)	0	0.162
Nausea/Vomiting	2 (14.3%)	1 (14.3%)	0	5 (41.7%)	0.069
Odynophagia	1 (7.1%)	0	5 (45.5%)	1 (8.3%)	<b>0.020</b>

Myalgia	3 (21.4%)	1 (14.3%)	2 (18.2%)	0	0.422
Abdominal pain	1 (7.1%)	1 (14.3%)	0	0	0.416
Anosmia / Ageusia	1 (7.1%)	0	0	0	0.533
CXR: Bilateral consolidation	6 (42.9%)	1 (14.3%)	8 (72.7%)	3 (25%)	<b>0.005</b>
CXR: Lobar consolidation	6 (42.9%)	2 (28.6%)	2 (18.2%)	7 (58.3%)	
CXR: Ground-glass opacities	2 (14.3%)	1 (14.3%)	1 (9.1%)	2 (16.7%)	
CXR: Interstitial opacities	0	3 (42.9%)	0	0	
Total hospital stay ≤5 days (n=22)	5 (22.7%)	4 (18.2%)	7 (31.8%)	6 (27.3%)	0.551
Total hospital stay >5 days (n=22)	9 (40.9%)	3 (13.6%)	4 (36.4%)	6 (27.3%)	
Admission to the PICU	4 (28.6%)	2 (28.6%)	4 (36.4%)	3 (25%)	0.945
Total PICU stay ≤5 days (n=9)	3 (33.3%)	2 (22.2%)	3 (44.4%)	1 (11.1%)	0.419
Total PICU stay >5 days (n=4)	1 (25%)	0	1 (25%)	2 (50%)	
Presenting complications	2 (14.3%)	1 (14.3%)	1 (9.1%)	4 (33.3%)	0.761
Need for respiratory support	11 (78.6%)	6 (85.7%)	10 (90.9%)	10 (83.3%)	0.868
Need for NIV	3 (21.4%)	1 (14.3%)	4 (36.4%)	3 (25%)	0.734
Need for CMV	1 (7.1%)	0	1 (9.1%)	2 (16.7%)	0.660
Treatment with steroids	8 (57.1%)	6 (85.7%)	9 (81.8%)	6 (50%)	0.232
Treatment with remdesivir	1 (7.1%)	1 (14.3%)	2 (18.2%)	3 (25%)	0.659
Treatment with immunomodulators	3 (21.4%)	0	1 (9.1%)	0	0.534

GA : gestational age, CXR : chest X-ray, PICU : pediatric intensive care unit, NIV : non-invasive ventilation, CMV : conventional mechanical ventilation.