

**Table S1.** Demographic and clinical characteristics of the patients segregated with respect to the predominant viral variant

Time window	Alpha			Delta			Omicron		
Vaccination status	Not vaccinated <i>n</i> = 502	Partially vaccinated <i>n</i> = 67	Completely vaccinated <i>n</i> = 19	Not vaccinated <i>n</i> = 227	Partially vaccinated <i>n</i> = 247	Completely vaccinated <i>n</i> = 24	Not vaccinated <i>n</i> = 70	Partially vaccinated <i>n</i> = 135	Completely vaccinated <i>n</i> = 4
<b>Demography</b>									
Age	53.1 (23.1)	63.7 (17.8) <sup>c</sup>	77.4 (14.1) <sup>c</sup>	42.9 (25.5) <sup>i</sup>	65.7 (20.2) <sup>c</sup>	63.9 (15.8) <sup>c,h</sup>	34.7 (27.9) <sup>l,j</sup>	57.3 (20.8) <sup>c,g,l</sup>	64.0 (27.0) <sup>a</sup>
Sex, female	275 (54.8)	34 (50.7)	11 (57.9)	129 (56.8)	132 (53.4)	17 (70.8)	37 (52.9)	72 (53.3)	0 <sup>i</sup>
Smoking habit	87 (17.3)	16 (23.9)	7 (36.8) <sup>a</sup>	29 (12.8)	48 (19.4) <sup>a</sup>	11 (45.8) <sup>c,e</sup>	2 (2.9) <sup>h,j</sup>	31 (23.0) <sup>c,h,j</sup>	0
Alcohol intake	34 (6.8)	5 (7.5)	2 (10.5)	11 (4.8)	17 (6.9)	7 (29.2) <sup>c,f</sup>	1 (1.4)	14 (10.4) <sup>a</sup>	0
<b>Symptoms</b>									
Pneumonia	260 (51.8)	38 (56.7)	3 (15.8) <sup>b,e</sup>	135 (59.5) <sup>g</sup>	112 (45.3) <sup>b,g</sup>	12 (50.0) <sup>g</sup>	18 (25.7) <sup>i,l</sup>	30 (22.2) <sup>i,k</sup>	0
Rhinorrhea	71 (14.1)	15 (22.4)	1 (5.3)	59 (26.0) <sup>i</sup>	28 (11.3) <sup>c,g</sup>	5 (20.8)	31 (44.3) <sup>i,k</sup>	37 (27.4) <sup>a,l</sup>	1 (0.25)
Cough	180 (35.9)	21 (31.3)	2 (10.5)	122 (53.7) <sup>i</sup>	84 (34.0) <sup>c,i</sup>	7 (29.2) <sup>a</sup>	35 (50.0) <sup>i</sup>	62 (45.9) <sup>g</sup>	2 (0.50)
Fever	279 (55.6)	38 (56.7)	6 (31.6) <sup>d</sup>	147 (64.8) <sup>g</sup>	127 (51.4) <sup>b,g</sup>	10 (41.7) <sup>a</sup>	35 (50.0)	47 (34.8) <sup>a,h,j</sup>	1 (0.25)
Chills	11 (2.2)	3 (4.5)	1 (5.3)	5 (2.2)	6 (2.4)	0	11 (15.7)	17 (12.6) <sup>k,l</sup>	0
Dyspnea	267 (53.2)	40 (59.7)	7 (36.8)	130 (57.3)	136 (55.1)	11 (45.8)	21 (30.0)	48 (35.6) <sup>h,l</sup>	0
General discomfort	207 (41.2)	33 (49.3)	3 (15.8) <sup>a,e</sup>	112 (49.3) <sup>g</sup>	101 (40.9) <sup>g</sup>	13 (54.2) <sup>g</sup>	36 (51.4)	66 (48.9)	3 (0.75) <sup>g</sup>
Vomiting	36 (7.2)	2 (3.0)	0	24 (10.6)	14 (5.7)	3 (12.5)	7 (10.0)	6 (4.4)	0
Diarrhea	59 (11.8)	8 (11.9)	1 (5.3)	30 (13.2)	22 (8.9)	4 (16.7)	7 (10.0)	7 (5.2)	0
Anosomia	31 (61.8)	7 (10.4)	1 (5.3)	25 (11.0) <sup>g</sup>	5 (2.0) <sup>c,h</sup>	1 (4.2)	1 (1.4)	5 (3.7)	0
Ageusia or dysgeusia	28 (5.6)	5 (7.5)	1 (5.3)	26 (11.5) <sup>h</sup>	4 (1.6) <sup>c,g</sup>	1 (4.2)	3 (4.3)	1 (0.7) <sup>g</sup>	0
Odynophagia	40 (8.0)	7 (10.4)	0	27 (11.9)	22 (8.9)	0	5 (7.1)	19 (14.1)	1 (0.25)
Headache	96 (19.1)	14 (20.9)	1 (5.3)	48 (21.1)	29 (11.7) <sup>b</sup>	1 (4.2)	9 (12.9)	18 (13.3)	1 (0.25)
Anorexia or hyporexia	25 (5.0)	4 (6.0)	1 (5.3)	19 (8.4)	8 (3.2) <sup>a</sup>	2 (8.4)	4 (5.7)	5 (3.7)	0
Myalgia	79 (15.7)	12 (17.9)	0	39 (17.2)	30 (12.1)	1 (4.2)	6 (8.6)	12 (8.9)	2 (0.50) <sup>g,i</sup>
Arthralgia	50 (10.0)	8 (11.9)	0	24 (10.6)	11 (4.4)	1 (4.2)	6 (8.6)	3 (2.2) <sup>h,j</sup>	1 (0.25)
Respiratory insufficiency	203 (40.4)	27 (40.3)	4 (21.1)	113 (49.8) <sup>g</sup>	86 (34.8) <sup>b</sup>	10 (41.7) <sup>i</sup>	11 (15.7)	20 (14.8) <sup>i,l</sup>	0
Pulmonary embolism	18 (3.6)	1 (1.5)	0	6 (2.6)	4 (1.6)	0	2 (2.9)	1 (0.7)	0
ARDS	19 (3.8)	2 (3.0)	0	17 (7.5) <sup>g</sup>	7 (2.8) <sup>a</sup>	1 (4.2)	5 (7.1)	2 (1.5) <sup>a</sup>	0
Dysuria	0	0	0	1 (0.4)	0	0	0	2 (1.5)	0
Acute kidney failure	25 (5.0)	3 (4.5)	1 (5.3)	12 (5.3)	20 (8.1)	2 (8.4)	0	4 (3.0) <sup>j</sup>	0
Other symptoms	138 (27.5)	18 (26.9)	0 <sup>e</sup>	32 (14.1) <sup>i</sup>	35 (14.2) <sup>g</sup>	2 (8.4)	13 (18.6)	26 (19.3)	1 (0.25)
<b>Comorbidities</b>									
Type 2 diabetes mellitus	94 (18.7)	16 (23.9)	8 (42.2) <sup>a</sup>	23 (10.1) <sup>h</sup>	65 (26.3) <sup>c</sup>	5 (20.8)	5 (7.1)	24 (17.8) <sup>a</sup>	0
Cardiovascular disease	243 (48.4)	38 (56.7)	17 (89.5) <sup>c,e</sup>	66 (29.1) <sup>h</sup>	156 (63.2) <sup>c</sup>	17 (70.8) <sup>c</sup>	17 (24.3)	68 (50.4) <sup>c,i</sup>	2 (0.50)
Chronic liver disease	24 (4.8)	4 (6.0)	1 (5.3)	9 (4.0)	17 (6.9)	5 (20.8) <sup>b,d</sup>	4 (5.7)	7 (5.2)	1 (0.25)
Chronic lung disease	64 (12.7)	13 (19.4)	3 (15.8)	31 (13.7)	63 (25.5) <sup>b</sup>	6 (25.0)	2 (2.9)	19 (14.1) <sup>c</sup>	0
Chronic kidney disease	40 (8.0)	8 (11.9)	4 (21.1)	11 (4.8)	44 (17.8) <sup>c</sup>	5 (20.8) <sup>a</sup>	4 (5.7)	12(8.9) <sup>i</sup>	2 (0.50)
CNMD	42 (8.4)	11(16.4) <sup>a</sup>	6 (31.6) <sup>b</sup>	9 (4.0) <sup>g</sup>	5 (2.0) <sup>b,c</sup>	2 (8.4)	0	16 (11.9) <sup>b,i</sup>	0

Immunosuppressed	13 (2.6)	1 (1.5)	0	2 (0.8)	4 (1.6)	0	1 (1.4)	4 (3.0)	0
Cancer	52 (10.4)	11 (16.4)	6 (31.6) <sup>b</sup>	13 (5.7) <sup>g</sup>	44 (17.8) <sup>c</sup>	10 (41.7) <sup>c,d</sup>	7 (10.0)	17 (12.6)	1 (0.25)
Obesity	104 (20.7)	19 (28.4)	2 (10.5)	34 (15.0)	34 (13.8) <sup>h</sup>	5 (20.8)	9 (12.9)	22 (16.3)	1 (0.25)
Pregnancy	0	0	0	8 (3.5) <sup>i</sup>	1 (0.4) <sup>a</sup>	0	1 (1.4)	0	0
Postpartum	0	0	0	4 (1.8) <sup>h</sup>	0	0	1 (1.4)	2 (1.5)	0
Concomitant infection	77 (15.3)	11 (16.4)	2 (10.5)	29 (12.8)	41 (16.6)	3 (12.5)	3 (4.3)	12 (8.9) <sup>j</sup>	0
Charlson index									
0	304 (60.6)	30 (44.8)	3 (15.8) <sup>c</sup>	174 (76.7) <sup>h</sup>	99 (40.1) <sup>c</sup>	7 (29.2) <sup>c</sup>	56 (80.0)	71 (53.4) <sup>a,j,*</sup>	2 (0.50)
1	72 (14.3)	12 (17.9)	3 (15.8)	26 (11.5)	35 (14.2)	3 (12.5)	7 (10.0)	27 (20.3)	0
2	60 (12.0)	11 (16.4)	4 (21.1)	15 (6.6)	35 (14.2)	5 (20.8)	4 (5.7)	18 (13.5)	1 (0.25)
3	39 (7.8)	5 (7.5)	2 (10.5)	6 (2.6)	37 (15.0)	4 (16.7)	0	7 (5.3)	0
4	17 (3.4)	5 (7.5)	7 (36.8)	3 (1.3)	24 (9.7)	4 (16.7)	2 (2.9)	8 (6.0)	1 (0.25)
5	6 (1.2)	2 (3.0)	0	2 (0.8)	8 (3.2)	1 (4.2)	0	2 (1.5)	2 (0.50)
6	2 (0.4)	1 (1.5)	0	1 (0.4)	5 (2.0)	0	1 (1.4)	0	1 (0.25)
7	2 (0.4)	1 (1.5)	0	0	4 (1.6)	0	0	0	0
9	0	0	0	0	0	0	0	0	0
McCabe score									
NFD	454 (90.4)	51 (76.1) <sup>b</sup>	12 (63.2) <sup>c</sup>	215 (94.7)	174 (70.4) <sup>c</sup>	17 (70.8) <sup>c</sup>	68 (97.1)	116 (85.9) <sup>j</sup>	4 (1.00)
UFD	48 (9.6)	16 (23.9)	7 (36.8)	11 (4.8)	73 (29.6)	7 (29.2)	2 (2.9)	17 (12.6)	0
RFD	0	0	0	1 (0.4)	0	0	0	2 (1.5)	0
COVID-19-related death	20 (4.0)	8 (11.9) <sup>a</sup>	2 (10.5) <sup>b</sup>	9 (4.0)	19 (3.4)	2 (8.4)	2 (2.9)	3 (2.2) <sup>g,i</sup>	1 (0.25)
Treatments									
NIMV	10 (2.0)	1 (1.5) <sup>a</sup>	1 (5.3)	1 (0.4)	2 (0.8)	0	3 (4.3) <sup>g</sup>	5 (3.7)	0
IMV	34 (6.8)	6 (9.0)	0 <sup>c</sup>	23 (10.1)	8 (3.2) <sup>b</sup>	1 (4.2)	2 (2.9)	3 (2.2)	0
HFOT	46 (9.2)	5 (7.5)	0	36 (15.9) <sup>g</sup>	11 (4.5) <sup>c</sup>	1 (4.2)	5 (7.1)	4 (3.0)	0
COT	256 (51.0)	38 (56.7)	8 (42.1) <sup>c</sup>	130 (57.3)	132 (53.4)	12 (50.0)	13 (18.6) <sup>i,l</sup>	37 (27.4) <sup>i,l</sup>	1 (0.25)
Anticoagulants	275 (54.8)	42 (62.7)	9 (47.4)	135 (59.5)	147 (59.5)	18 (75%)	13 (18.6) <sup>i,l</sup>	47 (34.8) <sup>a,l,i</sup>	1 (0.25)
Corticoids	282 (56.2)	45 (67.2)	11 (57.9)	137 (59.5)	131 (53.0)	14 (58.3)	19 (27.1) <sup>i,l</sup>	43 (31.9) <sup>i,l</sup>	1 (0.25)
Remdesivir	28 (5.6)	6 (9.0)	3 (15.8)	13 (5.7)	5 (2.0) <sup>a</sup>	0	2 (2.9)	6 (4.4)	0
Days of hospitalization	9.0 (16.1)	13.3 (23.0) <sup>c</sup>	10.8 (10.0) <sup>c</sup>	8.6 (14.5)	10.9 (18.1) <sup>c</sup>	8.5 (8.7)	4.3 (12.4) <sup>g</sup>	7.0 (17.2) <sup>g,i</sup>	12.7 (20.0)
Hospitalization site									
Internal Medicine	219 (43.6)	35 (52.2) <sup>a</sup>	3 (15.8) <sup>c,e</sup>	102 (44.9) <sup>c,i</sup>	103 (41.7) <sup>c</sup>	13 (54.2) <sup>b,d</sup>	5 (7.1) <sup>i,l</sup>	23 (17.0) <sup>c,l,i</sup>	0 <sup>i</sup>
Surgery	3 (0.6)	3 (4.5)	0	1 (0.4)	1 (0.4)	1 (4.2)	0	1 (0.7)	0
Emergency	129 (25.7)	14 (20.9)	4 (21.1)	36 (15.9)	60 (24.3)	3 (12.5)	32 (45.7)	57 (42.2)	2 (0.50)
Geriatrics	34 (6.8)	7 (10.4)	8 (42.1)	5 (2.2)	36 (14.6)	1 (4.2)	2 (2.9)	17 (12.6)	2 (0.50)
Oncology	7 (1.4)	1 (1.5)	1 (5.3)	2 (0.9)	7 (2.8)	3 (12.5)	0	2 (1.5)	0
Outpatient clinics	48 (9.6)	2 (3.0)	3 (15.8)	11 (4.8)	22 (8.9)	0	7 (10.0)	25 (18.5)	0
ICU	42 (8.4)	4 (6.0)	0	31 (13.7)	14 (5.7)	2 (8.4)	0	1 (0.7)	0
Pediatric emergencies	17 (3.4)	0	0	35 (15.4)	1 (0.4)	0	22 (31.4)	1 (0.7)	0
Traumatology	3 (0.6)	1 (1.5)	0	0	1 (0.4)	1 (4.2)	0	4 (3.0)	0

Data are presented as number of cases and percentages, or as means and SD. Statistical significance calculated by the  $\chi^2$  test (qualitative data) or the Student's *t*-test (quantitative data). ARDS: Acute respiratory distress syndrome; CNMD: Chronic neurological or neuromuscular disease; COT: Conventional oxygen therapy; HFOT: High-flow oxygen therapy; ICU: Intensive Care Unit; IMV: Invasive mechanical ventilation; NFD: Non-fatal disease; NIMV: Non-invasive mechanical ventilation; RFD: Rapidly fatal disease; UFD: Ultimately fatal disease. <sup>a</sup> *p* < 0.05, <sup>b</sup> *p* < 0.01, <sup>c</sup> *p* < 0.001, with respect to non- vaccinated patients; <sup>d</sup> *p* < 0.05, <sup>e</sup> *p* < 0.01, <sup>f</sup> *p* < 0.001, with respect to patients with incomplete vaccination; <sup>g</sup> *p* < 0.05, <sup>h</sup> *p* < 0.01, <sup>i</sup> *p* < 0.001, with respect to patients from the alpha time window; <sup>j</sup> *p* < 0.05, <sup>k</sup> *p* < 0.01, <sup>l</sup> *p* < 0.001, with respect to patients from the delta time window. \* *n* =133.