

Table S1. Clinical features of enrolled patients and study cohorts

	Prototype-infected cohort (n=963) (Tan Y. et.al., study 2020)	BA.2.2-infected cohort (n=9,911) (This study)	P value
Age			
Median (range) ~year	36 (25-51)	39 (27-63)	P<0.0001 ^a
<10 --no. (%)	8 (0.83%)	592 (5.97%)	P<0.0001 ^b
10-19 --no. (%)	90 (9.35%)	580 (5.85%)	
20-29 --no. (%)	248 (25.75%)	1,923 (19.40%)	
30-39 --no. (%)	233 (24.20%)	1,918 (19.35%)	
40-49 --no. (%)	135 (14.02%)	989 (9.98%)	
50-59 --no. (%)	126 (13.08%)	1,135 (11.45%)	
60-69 --no. (%)	90 (9.35%)	967 (9.76%)	
70-79 --no. (%)	30 (3.12%)	736 (7.43%)	
80-89 --no. (%)	3 (0.31%)	705 (7.11%)	
≥90 --no. (%)	0 (0.00%)	366 (3.69%)	
Gender			
Female --no. (%)	387 (40.19%)	4,543 (45.83%)	P=0.0008 ^b
Male --no. (%)	576 (59.81%)	5,368 (54.16%)	
Disease severity			
Mild/Moderate--no. (%)	930 (96.57%)	9,638 (97.25%)	P=0.22 ^b
Severe/Critical--no. (%)	33 (3.43%)	273 (2.76%)	
Vaccination			
Unvaccinated	-	1,545 (31.83%) [#]	
Vaccinated		3,309 (68.17%)	
Dose 1	-	148 (3.05%)	
Dose 2	-	1,608 (33.13%)	
Dose 3	-	1,553 (31.99%)	

[#]Vaccination data available only in 4,854 cases, or 48.98% of the total cases in this study

^at-test; ^bFisher exact test.

Table S2. Immunological and biochemical parameters associated with disease severity in BA.2.2 infected COVID-19 cases

	Mild/Moderate (n=9638)	Severe/Critical (n=273)	P value ^a
Albumin (Normal range 40-55 g/L)	41.775 (38-44)	33.00 (29-37)	<0.0001
Prealbumin (Normal range 180-400 mg/L)	224 (191-262)	151.5 (121.75-190.25)	<0.0001
Total Protein (Normal range 65-85 g/L)	70.24 (65.88-75)	63 (57.2-68)	<0.0001

Aspartate Aminotransferase (Normal range 13-35 U/L)	20 (16-26)	26 (19-38)	0.019
Alanine Aminotransferase (Normal range 7-40 U/L)	17 (12-26)	17 (11-31)	0.0015
Alkaline phosphatase (Normal range 50-135 U/L)	72 (58-94)	80 (65-103)	0.0082
Creatinine (Normal range 41-73 mmol/L)	62.9 (51-78.5)	77 (59.675-112.6)	<0.0001
Blood urea nitrogen (Normal range 2.6-7.5 mmol/L)	4.3 (3.4-5.5)	7.5 (5.345-10.925)	<0.0001
Total Bilirubin (Normal range 3.4-20.5 umol/L)	8.4 (6-11.8)	10.4 (7.3-14.8)	<0.0001
Direct Bilirubin (Normal range 0-8.6 umol/L)	3.9 (3-5.2)	6.2 (4.4-9.5)	<0.0001
Indirect Bilirubin (Normal range 1.7-10.2 g/L)	4.3 (2.6-6.7)	3.7 (2.3-6.4)	0.0074
Lactic acid dehydrogenase (Normal range 120-250 U/L)	197 (171-232.25)	254 (201-333)	<0.0001
Total Cholesterol (Normal range 0-5.17 mmol/L)	4.09 (3.24-4.79)	2.705 (0.9625-3.96)	<0.0001
Triacylglycerol (Normal range 0-1.69 mmol/L)	1.16 (0.84-1.7)	1.09 (0.81-1.5)	0.0024
High-sensitivity C-reactive Protein (Normal range 0-10 mg/L)	1.61 (0.50-4.56)	27.685 (5.07-76.66)	<0.0001
Lymphocyte Counts (Normal range 1.1-3.2 10e9/L)	1.49 (1.08-2)	0.85 (0.59-1.22)	<0.0001
Neutrophil Counts (Normal range 1.8-6.3 10e9/L)	3.14 (2.15-4.53)	4.79 (3.01-8.33)	<0.0001
Neutrophil Percent (Normal range 40-75 %)	59 (49.1-68.7)	76.4 (65.4-86.8)	<0.0001
Lymphocyte Percent (Normal range 20-50 %)	28.4 (20-37.6)	14 (7-23)	<0.0001
Monocyte Counts (Normal range 0.1-0.6 10e9/L)	0.51 (0.39-0.67)	0.5 (0.34-0.7125)	0.5999
Monocyte Percent (Normal range 3-10 %)	9.2 (7.1-12.1)	7.2 (4.8-10.5)	<0.0001
CD3+Counts (Normal range 690-2540 cell/uL)	1045 (745-1447)	512 (333-801)	<0.0001
CD3+Percent (Normal range 53-84 %)	69.79 (62.98-75.33)	66.03 (55.29-73.68)	<0.0001
CD8+Counts (Normal range 190-1140 cell/uL)	382 (250-547)	171 (98-311)	<0.0001
CD8+Percent (Normal range 13-41 %)	24.99 (19.86-30.59)	22.29 (15.25-30.68)	0.0197
CD4+Counts (Normal range 410-1590 cell/uL)	596 (413-832)	299 (189-468)	<0.0001
CD4+Percent (Normal range 31-60 %)	39.46 (33.78-45)	38.155 (28.55-46.27)	0.004
Hemoglobin (Normal range 130-175 g/L)	132 (119-146)	114 (98-130)	<0.0001
Platelet counts (Normal range 125-350 10e9/L)	207 (167-254)	168 (132-229)	<0.0001
Mean Platelet Volume (Normal range 9-13 fl)	10.6 (10-11.3)	10.6 (10.1-11.4)	0.0321
Mean corpuscular volume (Normal range 82-100 fl)	88.6 (85.4-91.8)	90.3 (86.2-93.9)	<0.0001
Red Blood Cell Count (Normal range 4.3-5.8 10e12/L)	4.44 (4-4.9)	3.79 (3.24-4.27)	<0.0001
Meant Corpuscular Hemoglobin (Normal range 27-34 pg)	30.1 (28.9-31.2)	30.5 (29.1-31.7)	0.0035
Mean Corpuscular Hemoglobin concentration (Normal range 316-354 g/L)	339 (331-347)	336 (326-346)	0.0515
Hematocrit (Normal range 40-50 %)	39.1 (35.3-42.9)	33.85 (29.175-38.5)	<0.0001
IL-4 (Normal range 0-8.56 pg/mL)	0.65 (0.55-0.78)	0.6 (0.5-0.75)	0.0017
IL-12P70 (Normal range 0-3.4 pg/mL)	1.01 (0.81-1.31)	0.92 (0.76-1.17)	0.017

IL-2 (Normal range 0-7.5 pg/mL)	0.805 (0.48-1.45)	0.76 (0.32-1.48)	0.2445
IL-1B (Normal range 0-12.4 pg/mL)	3.34 (1.44-6.92)	2.58 (0.98-7)	0.2592
IL-10 (Normal range 0-12.9 pg/mL)	1.39 (1.11-1.88)	1.46 (1.0975-2.445)	0.0014
IL-5 (Normal range 0-3.1 pg/mL)	1.63 (1.15-2.37)	1.5 (0.98-2.3775)	0.59
IL-17 (Normal range 0-21.4 pg/mL)	2.91 (1.75-4.39)	2.73 (1.73-4.2175)	0.8596
IL-8 (Normal range 0-20.6 pg/mL)	0.33 (0-15.7025)	1.075 (0-22.8275)	0.0734
IL-6 (Normal range 0-5.4 pg/mL)	1.7 (0.89-3.17)	7.62 (2.28-24.06)	0.0009
IFN-a (Normal range 0-8.5 pg/mL)	0.89 (0.44-1.97)	0.805 (0.39-2.15)	0.5495
IFN-g (Normal range 0-23.1 pg/mL)	2.76 (1.51-5.48)	1.59 (0.8825-2.835)	0.0383
TNF (Normal range 0-16.5 pg/mL)	0.67 (0.23-1.47)	0.34 (0.06-1.06)	0.0101
D-Dimer (Normal range 0-0.5 ug/mL)	0.29 (0.19-0.63)	1.37 (0.6525-2.84)	<0.0001
Fibrin and fibrinogen degradation product (Normal range 0-5 ug/mL)	1.7 (1.28-2.6)	4.62 (2.68-9.86)	<0.0001
INR	0.97 (0.93-1.03)	1.06 (0.98-1.16)	<0.0001
Fibrinogen (Normal range 2-4 g/L)	3.34 (2.83-4.02)	4.26 (3.12-5.46)	0.81
Activated partial thromboplastin time (Normal range 31.5-43.5 s)	37.4 (34.4-40.7)	40.4 (36.3-46.25)	<0.0001

Data are presented as median (IQR). ^aunivariate logistic regression analysis.

Table S3. Protection rate of vaccination against severe/critical COVID-19

	Protection rate against severe/critical COVID-19 ^a			
	1 dose	2 doses	3 doses	2 doses and 3 doses
Overall	33.24%	96.09%	95.95%	96.02%
>60	33.27%	86.16%	93.35%	90.15%

$$^a \text{Protection of vaccination against severe/critical COVID-19} = \left(1 - \frac{\text{fraction of severe/critical cases in vaccinated individuals}}{\text{fraction of severe/critical cases in unvaccinated individuals}}\right) * 100\%$$