

Supplementary Material

Clinical Features of COVID-19 in Italian Outpatient Children and Adolescents During Parental, Delta, and Omicron Waves: a prospective, observational, cohort study

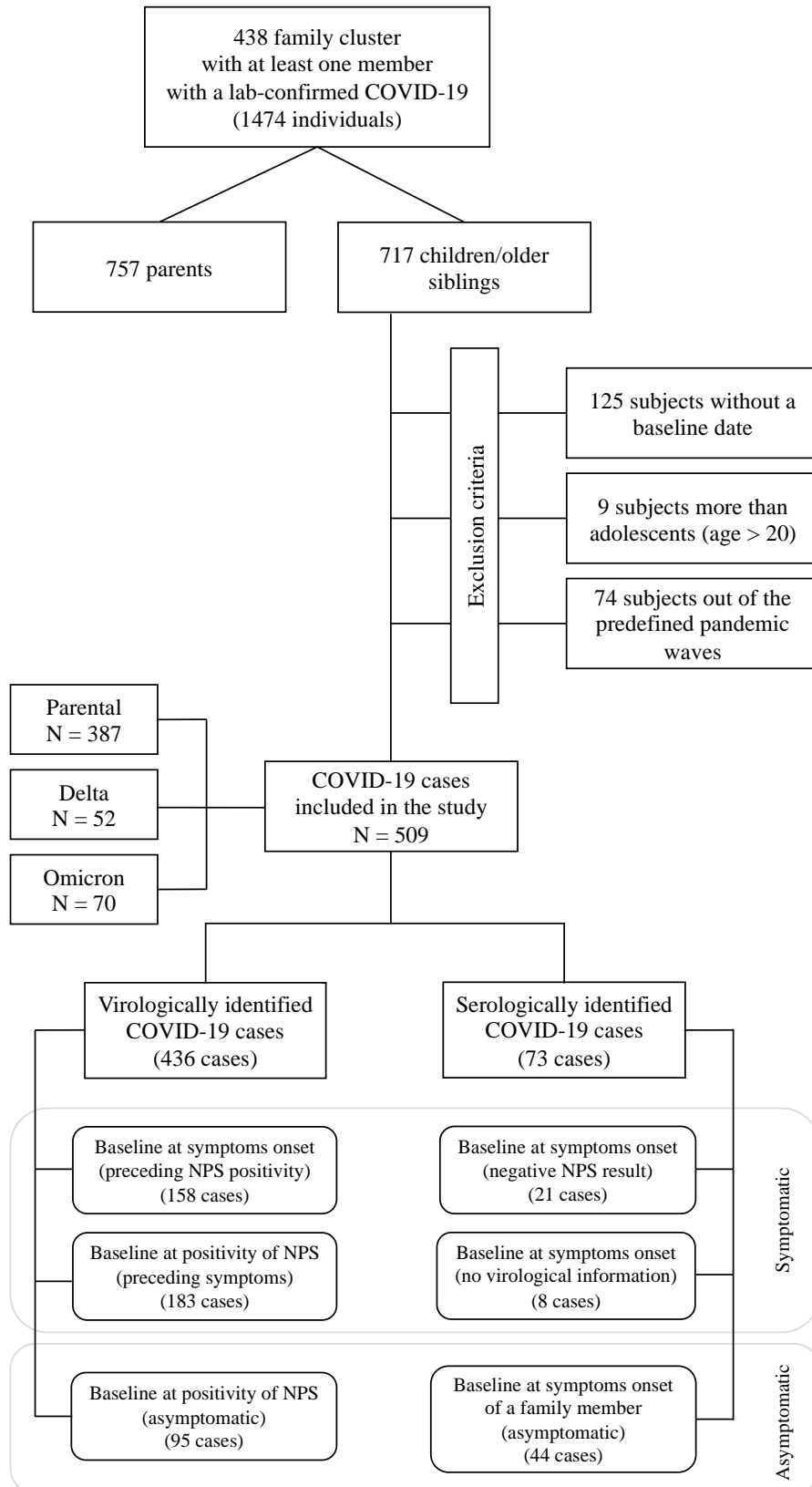
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1 Supplementary Figures

Supplementary Figure 1. Number of COVID-19 pediatric cases enrolled between April 2020 and December 2022 at the COVID-19 Family Cluster Follow-up Clinic (CovFC) of our institution. In gray boxes are presented the criteria for the definition of the baseline of infection for COVID-19 cases.



2 Supplementary Tables

Supplementary Table 1. Differences in clinical manifestations of SARS-CoV-2 infection between children who had previously received at least one dose of COVID-19 vaccine and those children who did not.

	Unvaccinated (N = 47)	Vaccinated (N = 23)	P - Value
<i>Symptoms, N (%)</i>			
Rhinitis	17 (36.17)	9 (39.13)	0.8097
Cough	17 (36.17)	7 (30.43)	0.6349
Dyspnea	1 (2.13)	1 (4.35)	0.4476
Fever	39 (82.98)	14 (60.87)	0.0427
Otalgia	0 (0)	0 (0)	-
Myalgia	3 (6.38)	2 (8.7)	0.339
Arthralgia	0 (0)	2 (8.7)	0.1048
Sore throat	6 (12.77)	4 (17.39)	0.2397
Hyposmia and/or ageusia	2 (4.26)	1 (4.35)	0.4542
Conjunctivitis	1 (2.13)	0 (0)	0.6714
Fatigue	10 (21.28)	5 (21.74)	0.2415
Headache	10 (21.28)	6 (26.09)	0.6526
Alteration of consciousness	0 (0)	0 (0)	-
Abdominal pain	1 (2.13)	0 (0)	0.6714
Nausea/vomiting	4 (8.51)	1 (4.35)	0.339
Diarrhea	4 (8.51)	0 (0)	0.1945
Poor feeding	3 (6.38)	1 (4.35)	0.4067
Lymphadenopathy	0 (0)	0 (0)	-
Skin rash	0 (0)	0 (0)	-
Pneumonia	1 (2.13)	0 (0)	0.6714
Other symptoms	5 (10.64)	0 (0)	0.1267
<i>Number of symptoms, N (%)</i>			
0	1 (2.13)	1 (4.35)	0.0175
1	9 (19.15)	5 (21.74)	
2	13 (27.66)	8 (34.78)	
≥ 3	24 (51.06)	9 (39.13)	
<i>Duration of symptoms</i>			
days	2 (1 - 4)	3 (1 - 4)	0.7403

Supplementary Table 2. Clinical features of SARS-CoV-2 infection among different age groups (0-2 months, 3-11 months, 1-4 years, 5-11 years, and 12-20 years).

		0 - 2 months (N=13)	3 - 11 months (N=36)	1 - 4 years (N=83)	5 - 11 years (N=248)	12 - 20 years (N=129)
Rhinitis		5 (38.46)	7 (19.44)	24 (28.92)	40 (16.13)	29 (22.48)
Fever		10 (76.92)	22 (61.11)	45 (54.22)	99 (39.92)	62 (48.06)
Myalgia		2 (15.38)	5 (13.89)	20 (24.1)	28 (11.29)	20 (15.5)
Arthralgia		0 (0)	0 (0)	2 (2.41)	6 (2.42)	7 (5.43)
Sore throat		N/A	N/A	2 (2.41)	13 (5.24)	13 (10.08)
Hyposmia and/or ageusia		N/A	N/A	0 (0)	20 (8.06)	26 (20.16)
Fatigue		1 (7.69)	1 (2.78)	8 (9.64)	43 (17.34)	26 (20.16)
Headache		N/A	N/A	2 (2.41)	49 (19.76)	29 (22.48)
Abdominal pain		0 (0)	0 (0)	3 (3.61)	10 (4.03)	2 (1.55)
Nausea/vomiting		0 (0)	1 (2.78)	2 (2.41)	12 (4.84)	8 (6.2)
Diarrhea		0 (0)	7 (19.44)	8 (9.64)	15 (6.05)	9 (6.98)
Poor feeding		2 (15.38)	4 (11.11)	5 (6.02)	7 (2.82)	2 (1.55)
Number of symptoms						
	0	1 (7.69)	8 (22.22)	20 (24.1)	82 (33.06)	28 (21.71)
	1	6 (46.15)	11 (30.56)	24 (28.92)	60 (24.19)	33 (25.58)
	2	3 (23.08)	10 (27.78)	16 (19.28)	46 (18.55)	29 (22.48)
	≥ 3	3 (23.08)	7 (19.44)	23 (27.71)	60 (24.19)	39 (30.23)
Duration of symptoms, days						
		2 (1 - 5)	3 (2 - 7)	3 (1 - 6)	3 (1 - 5)	3 (1 - 7)

N/A = not assessed.

Supplementary Table 3. Clinical features of COVID-19 among different age groups (0-2, 3-4, 5-11, and 12-20 years), overall (N=509) and stratified according to the variant of concern (VOC) (Parental=387, Delta=52, Omicron=70).

	0 - 2 years	3 - 4 years	5 - 11 years	12 - 20 years	P-value
Rhinitis – Overall, N (%)	25 (29.41)	15 (23.44)	36 (15.58)	29 (22.48)	0.0426
Parental	15 (22.39)	9 (19.15)	16 (9.7)	22 (20.37)	0.0323
Delta	3 (37.5)	4 (57.14)	8 (27.59)	2 (25)	0.0107
Omicron	7 (70)	2 (20)	12 (32.43)	5 (38.46)	0.0012
Cough - Overall, N (%)	17 (20)	12 (18.75)	26 (11.26)	20 (15.5)	0.173
Parental	9 (13.43)	7 (14.89)	9 (5.45)	12 (11.11)	0.1011
Delta	5 (62.5)	1 (14.29)	5 (17.24)	3 (37.5)	0.0015
Omicron	3 (30)	4 (40)	12 (32.43)	5 (38.46)	0.0171
Dyspnea - Overall, N (%)	2 (2.35)	0 (0)	2 (0.87)	3 (2.33)	0.0197
Parental	2 (2.99)	0 (0)	2 (1.21)	1 (0.93)	0.0458
Delta	0 (0)	0 (0)	0 (0)	0 (0)	-
Omicron	0 (0)	0 (0)	0 (0)	2 (15.38)	0.0323
Fever - Overall, N (%)	54 (63.53)	31 (48.44)	91 (39.39)	62 (48.06)	0.002
Parental	41 (61.19)	18 (38.3)	51 (30.91)	48 (44.44)	0.0003
Delta	4 (50)	5 (71.43)	13 (44.83)	5 (62.5)	0.0117
Omicron	9 (90)	8 (80)	27 (72.97)	9 (69.23)	0.0142
Otalgia - Overall, N (%)	1 (1.18)	1 (1.56)	0 (0)	0 (0)	0.0421
Parental	1 (1.49)	0 (0)	0 (0)	0 (0)	0.1731
Delta	0 (0)	1 (14.29)	0 (0)	0 (0)	0.1346
Omicron	0 (0)	0 (0)	0 (0)	0 (0)	-
Myalgia - Overall, N (%)	0 (0)	1 (1.56)	10 (4.33)	10 (7.75)	0.0002
Parental	0 (0)	1 (2.13)	6 (3.64)	7 (6.48)	0.0022
Delta	0 (0)	0 (0)	1 (3.45)	1 (12.5)	0.175
Omicron	0 (0)	0 (0)	3 (8.11)	2 (15.38)	0.0501
Arthralgia - Overall, N (%)	0 (0)	3 (4.69)	5 (2.16)	7 (5.43)	0.0009
Parental	0 (0)	3 (6.38)	5 (3.03)	5 (4.63)	0.0030
Delta	0 (0)	0 (0)	0 (0)	0 (0)	-
Omicron	0 (0)	0 (0)	0 (0)	2 (15.38)	0.0323
Sore throat - Overall, N (%)	1 (1.18)	1 (1.56)	13 (5.63)	13 (10.08)	< 0.0001
Parental	1 (1.49)	0 (0)	6 (3.64)	10 (9.26)	0.0003
Delta	0 (0)	0 (0)	0 (0)	1 (12.5)	0.1538
Omicron	0 (0)	1 (10)	7 (18.92)	2 (15.38)	0.0202
Hyposmia and/or ageusia - Overall, N (%)	0 (0)	1 (1.56)	19 (8.23)	26 (20.16)	< 0.0001
Parental	0 (0)	1 (2.13)	16 (9.7)	21 (19.44)	< 0.0001
Delta	0 (0)	0 (0)	2 (6.9)	3 (37.5)	0.0087
Omicron	0 (0)	0 (0)	1 (2.7)	2 (15.38)	0.0527
Conjunctivitis - Overall, N (%)	2 (2.35)	2 (3.13)	5 (2.16)	3 (2.33)	0.0238
Parental	2 (2.99)	1 (2.13)	4 (2.42)	3 (2.78)	0.0342
Delta	0 (0)	0 (0)	1 (3.45)	0 (0)	0.5577
Omicron	0 (0)	1 (10)	0 (0)	0 (0)	0.1429
Fatigue - Overall, N (%)	5 (5.88)	8 (12.5)	40 (17.32)	26 (20.16)	0.0274
Parental	4 (5.97)	3 (6.38)	27 (16.36)	21 (19.44)	0.0274

	Delta	0 (0)	2 (28.57)	5 (17.24)	2 (25)	0.019
	Omicron	1 (10)	3 (30)	8 (21.62)	3 (23.08)	0.0184
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Headache - Overall, N (%)		0 (0)	3 (4.69)	48 (20.78)	29 (22.48)	< 0.0001
	Parental	0 (0)	3 (6.38)	29 (17.58)	24 (22.22)	0.0001
	Delta	0 (0)	0 (0)	6 (20.69)	2 (25)	0.0177
	Omicron	0 (0)	0 (0)	13 (35.14)	3 (23.08)	0.0004
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Alteration of consciousness - Overall, N (%)		0 (0)	0 (0)	0 (0)	0 (0)	-
	Parental	0 (0)	0 (0)	0 (0)	0 (0)	-
	Delta	0 (0)	0 (0)	0 (0)	0 (0)	-
	Omicron	0 (0)	0 (0)	0 (0)	0 (0)	-
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Abdominal pain - Overall, N (%)		0 (0)	4 (6.25)	9 (3.9)	2 (1.55)	0.0009
	Parental	0 (0)	3 (6.38)	8 (4.85)	2 (1.85)	0.0019
	Delta	0 (0)	0 (0)	1 (3.45)	0 (0)	0.5577
	Omicron	0 (0)	1 (10)	0 (0)	0 (0)	0.1429
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Nausea/vomiting - Overall, N (%)		3 (3.53)	1 (1.56)	11 (4.76)	8 (6.2)	0.0045
	Parental	3 (4.48)	0 (0)	6 (3.64)	7 (6.48)	0.0039
	Delta	0 (0)	0 (0)	2 (6.9)	0 (0)	0.3062
	Omicron	0 (0)	1 (10)	3 (8.11)	1 (7.69)	0.0835
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Diarrhea - Overall, N (%)		12 (14.12)	5 (7.81)	13 (5.63)	9 (6.98)	0.0918
	Parental	9 (13.43)	4 (8.51)	11 (6.67)	7 (6.48)	0.3291
	Delta	0 (0)	1 (14.29)	2 (6.9)	1 (12.5)	0.084
	Omicron	3 (30)	0 (0)	0 (0)	1 (7.69)	0.0017
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Poor feeding - Overall, N (%)		7 (8.24)	5 (7.81)	6 (2.6)	2 (1.55)	0.0002
	Parental	6 (8.96)	4 (8.51)	3 (1.82)	2 (1.85)	0.0002
	Delta	0 (0)	0 (0)	1 (3.45)	0 (0)	0.5577
	Omicron	1 (10)	1 (10)	2 (5.41)	0 (0)	0.0726
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Lymphadenopathy - Overall, N (%)		0 (0)	0 (0)	1 (0.43)	0 (0)	0.4538
	Parental	0 (0)	0 (0)	1 (0.61)	0 (0)	0.4264
	Delta	0 (0)	0 (0)	0 (0)	0 (0)	-
	Omicron	0 (0)	0 (0)	0 (0)	0 (0)	-
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Skin rash - Overall, N (%)		1 (1.18)	3 (4.69)	4 (1.73)	4 (3.1)	0.0081
	Parental	1 (1.49)	2 (4.26)	4 (2.42)	4 (3.7)	0.0183
	Delta	0 (0)	1 (14.29)	0 (0)	0 (0)	0.1346
	Omicron	0 (0)	0 (0)	0 (0)	0 (0)	-
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Pneumonia - Overall, N (%)		0 (0)	0 (0)	2 (0.87)	1 (0.78)	0.1568
	Parental	0 (0)	0 (0)	2 (1.21)	0 (0)	0.1811
	Delta	0 (0)	0 (0)	0 (0)	0 (0)	-
	Omicron	0 (0)	0 (0)	0 (0)	1 (7.69)	0.1857
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Other symptoms - Overall, N (%)		7 (8.24)	5 (7.81)	10 (4.33)	13 (10.08)	0.192
	Parental	4 (5.97)	4 (8.51)	9 (5.45)	11 (10.19)	0.0027
	Delta	1 (12.5)	0 (0)	0 (0)	1 (12.5)	0.0483
	Omicron	2 (20)	1 (10)	1 (2.7)	1 (7.69)	0.0179
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Number of symptoms - Overall, N (%)						
	0	15 (17.65)	20 (31.25)	76 (32.9)	28 (21.71)	
	1	30 (35.29)	13 (20.31)	58 (25.11)	33 (25.58)	
	2	19 (22.35)	14 (21.88)	42 (18.18)	29 (22.48)	0.1426
	≥ 3	21 (24.71)	17 (26.56)	55 (23.81)	39 (30.23)	

Parental						
	0	12 (17.91)	19 (40.43)	67 (40.61)	26 (24.07)	
	1	27 (40.3)	8 (17.02)	43 (26.06)	32 (29.63)	
	2	16 (23.88)	9 (19.15)	22 (13.33)	22 (20.37)	0.008
	≥ 3	12 (17.91)	11 (23.4)	33 (20)	28 (25.93)	
Delta						
	0	3 (37.5)	0 (0)	8 (27.59)	2 (25)	
	1	1 (12.5)	3 (42.86)	6 (20.69)	0 (0)	
	2	1 (12.5)	2 (28.57)	9 (31.03)	2 (25)	< 0.0001
	≥ 3	3 (37.5)	2 (28.57)	6 (20.69)	4 (50)	
Omicron						
	0	0 (0)	1 (10)	1 (2.7)	0 (0)	
	1	2 (20)	2 (20)	9 (24.32)	1 (7.69)	
	2	2 (20)	3 (30)	11 (29.73)	5 (38.46)	< 0.0001
	≥ 3	6 (60)	4 (40)	16 (43.24)	7 (53.85)	
Duration of symptoms, days						
	Overall	3 (1 - 6)	3 (1 - 7)	2.5 (1 - 5)	3 (1 - 7)	0.4714
	parental	3 (1 - 7)	3 (1 - 5)	3 (1 - 5)	3 (1 - 7)	0.9248
	Delta	5 (3 - 7)	7 (7 - 19)	2 (1 - 2)	7 (2 - 13)	0.1442
	Omicron	2 (0 - 3.5)	2 (1 - 3)	2 (1 - 4)	6 (1 - 9)	0.3136

Supplementary Table 4. Clinical features of SARS-CoV-2 infection in children with at least one underlying disease compare with healthy subjects, overall, and stratified according to the variant of concern (VOC).

Comorbidities	Overall (N=509)		P-value	Parental (N = 387)		Delta (N = 52)		Omicron (N = 70)	
	0	At least 1		0	At least 1	0	At least 1	0	At least 1
Symptoms, N (%)									
Rhinitis	73 (18.72)	32 (26.89)	0.0538	47 (15.51)	15 (17.86)	10 (24.39)	7 (63.64)	16 (34.78)	10 (41.67)
Cough	48 (12.31)	27 (22.69)	0.0052	24 (7.92)	13 (15.48)	11 (26.83)	3 (27.27)	13 (28.26)	11 (45.83)
Dyspnea	3 (0.77)	4 (3.36)	0.0462	3 (0.99)	2 (2.38)	0 (0)	0 (0)	0 (0)	2 (8.33)
Fever	174 (44.62)	64 (53.78)	0.0794	121 (39.93)	37 (44.05)	20 (48.78)	7 (63.64)	33 (71.74)	20 (83.33)
Otalgia	2 (0.51)	0 (0)	0.5867	1 (0.33)	0 (0)	1 (2.44)	0 (0)	0 (0)	0 (0)
Myalgia	14 (3.59)	7 (5.88)	0.107	11 (3.63)	3 (3.57)	2 (4.88)	0 (0)	1 (2.17)	4 (16.67)
Arthralgia	11 (2.82)	4 (3.36)	0.2212	10 (3.3)	3 (3.57)	0 (0)	0 (0)	1 (2.17)	1 (4.17)
Sore throat	22 (5.64)	6 (5.04)	0.8019	14 (4.62)	3 (3.57)	1 (2.44)	0 (0)	7 (15.22)	3 (12.5)
Hyposmia and/or ageusia	33 (8.46)	13 (10.92)	0.4121	29 (9.57)	9 (10.71)	4 (9.76)	1 (9.09)	0 (0)	3 (12.5)
Conjunctivitis	9 (2.31)	3 (2.52)	0.259	8 (2.64)	2 (2.38)	0 (0)	1 (9.09)	1 (2.17)	0 (0)
Fatigue	65 (16.67)	14 (11.76)	0.1961	46 (15.18)	9 (10.71)	7 (17.07)	2 (18.18)	12 (26.09)	3 (12.5)
Headache	62 (15.9)	18 (15.13)	0.8396	44 (14.52)	12 (14.29)	5 (12.2)	3 (27.27)	13 (28.26)	3 (12.5)
Alteration of consciousness	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Abdominal pain	11 (2.82)	4 (3.36)	0.2212	9 (2.97)	4 (4.76)	1 (2.44)	0 (0)	1 (2.17)	0 (0)
Nausea/vomiting	15 (3.85)	8 (6.72)	0.186	11 (3.63)	5 (5.95)	2 (4.88)	0 (0)	2 (4.35)	3 (12.5)
Diarrhea	28 (7.18)	11 (9.24)	0.4587	22 (7.26)	9 (10.71)	3 (7.32)	1 (9.09)	3 (6.52)	1 (4.17)
Poor feeding	16 (4.1)	4 (3.36)	0.2074	12 (3.96)	3 (3.57)	1 (2.44)	0 (0)	3 (6.52)	1 (4.17)
Lymphadenopathy	1 (0.26)	0 (0)	0.7662	1 (0.33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Skin rash	9 (2.31)	3 (2.52)	0.2590	8 (2.64)	3 (3.57)	1 (2.44)	0 (0)	0 (0)	0 (0)
Pneumonia	0 (0)	3 (2.52)	0.0125	0 (0)	2 (2.38)	0 (0)	0 (0)	0 (0)	1 (4.17)
Other symptoms	23 (5.9)	12 (10.08)	0.1142	20 (6.6)	8 (9.52)	1 (2.44)	1 (9.09)	2 (4.35)	3 (12.5)
Number of symptoms, N (%)									
0	117 (30)	22 (18.49)		102 (33.66)	22 (26.19)	13 (31.71)	0 (0)	2 (4.35)	0 (0)
1	98 (25.13)	36 (30.25)	0.0906	83 (27.39)	27 (32.14)	7 (17.07)	3 (27.27)	8 (17.39)	6 (25)
2	79 (20.26)	25 (21.01)		53 (17.49)	16 (19.05)	10 (24.39)	4 (36.36)	16 (34.78)	5 (20.83)
≥ 3	96 (24.62)	36 (30.25)		65 (21.45)	19 (22.62)	11 (26.83)	4 (36.36)	20 (43.48)	13 (54.17)
Duration of symptoms									
days	3 (1 - 5)	3 (1 - 7)	0.3302	3 (1 - 5)	2 (1 - 6.5)	2 (1.5 - 7)	7 (2 - 12)	1.5 (0.5 - 3)	4 (2 - 7)

Supplementary Table 5. Impact on COVID-19 clinical manifestations of influenza and rotavirus immunization status.

	Flu Vaccine*			Rotavirus**		
	No (N = 327)	Yes (N = 59)	P-value	No (N = 148)	Yes (N = 353)	P-value
Symptoms, N (%)						
Rhinitis	58 (17.74)	10 (16.95)	0.8838	22 (14.86)	80 (22.66)	0.048
Cough	35 (10.7)	10 (16.95)	0.1688	23 (15.54)	51 (14.45)	0.7531
Dyspnea	5 (1.53)	0 (0)	0.4343	2 (1.35)	4 (1.13)	0.3246
Fever	144 (44.04)	24 (40.68)	0.632	69 (46.62)	164 (46.46)	0.9734
Otalgia	2 (0.61)	0 (0)	0.7173	1 (0.68)	1 (0.28)	0.4171
Myalgia	14 (4.28)	3 (5.08)	0.2438	3 (2.03)	18 (5.1)	0.1175
Arthralgia	11 (3.36)	0 (0)	0.1571	2 (1.35)	13 (3.68)	0.0949
Sore throat	15 (4.59)	4 (6.78)	0.1794	7 (4.73)	21 (5.95)	0.5878
Hyposmia and/or ageusia	33 (10.09)	6 (10.17)	0.9854	11 (7.43)	35 (9.92)	0.38
Conjunctivitis	9 (2.75)	0 (0)	0.2209	3 (2.03)	8 (2.27)	0.261
Fatigue	48 (14.68)	9 (15.25)	0.9087	18 (12.16)	61 (17.28)	0.1515
Headache	45 (13.76)	8 (13.56)	0.9669	20 (13.51)	60 (17)	0.3315
Alteration of consciousness	0 (0)	0 (0)	-	0 (0)	0 (0)	-
Abdominal pain	11 (3.36)	1 (1.69)	0.2966	5 (3.38)	10 (2.83)	0.2067
Nausea/vomiting	13 (3.98)	2 (3.39)	0.2887	8 (5.41)	15 (4.25)	0.5727
Diarrhea	25 (7.65)	2 (3.39)	0.1262	15 (10.14)	24 (6.8)	0.2035
Poor feeding	10 (3.06)	3 (5.08)	0.1971	4 (2.7)	15 (4.25)	0.4083
Lymphadenopathy	1 (0.31)	0 (0)	0.8472	0 (0)	1 (0.28)	0.7046
Skin rash	9 (2.75)	3 (5.08)	0.1783	7 (4.73)	5 (1.42)	0.0259
Pneumonia	1 (0.31)	0 (0)	0.8472	2 (1.35)	1 (0.28)	0.1843
Other symptoms	17 (5.2)	5 (8.47)	0.1327	12 (8.11)	22 (6.23)	0.4463
Number of symptoms, N (%)						
0	104 (31.80)	18 (30.51)	0.2463	45 (30.41)	93 (26.35)	0.7144
1	86 (26.30)	14 (23.73)		39 (26.35)	91 (25.78)	
2	59 (18.04)	17 (28.81)		30 (20.27)	73 (20.68)	
≥ 3	78 (23.85)	10 (16.95)		34 (22.97)	96 (27.20)	
Duration of symptoms						
days	3 (1 - 7)	2 (0 - 4)	0.0955	3 (1 - 7)	3 (1 - 6)	0.9879

* Patients aged at least 6 months, 96 missing values are handled in the analysis; **Patients aged more than 61 days