

## Supplementary Data

**Table S1.** Demographic, Clinical and Laboratory data of patients with non-severe outcome grouped by period of hospitalization.

	Non-severe COVID 19 First wave	Non-severe COVID 19 Second wave	Non-severe COVID 19 Third wave	P value
<b>Nº of subjects</b>	<b>287</b>	<b>599</b>	<b>503</b>	
<b>Nº (%) of males</b>	175(61)	362(60.4)	311(61.3)	0.953 <sup>a</sup>
<b>Age, years, median (Q1-Q3)</b>	57(45-66)	62(49-72)	60(51-71)	0.0001 <sup>b</sup>
<b>Days of enrolment after onset of symptoms, median (Q1-Q3)</b>	5(3-8)	6(2-10)	8(5-10)	0.0001 <sup>b</sup>
<b>Charlson comorbidity index, median (Q1-Q3)</b>	2(0-3)	3(1-4)	2(1-4)	0.0001 <sup>c</sup>
<b>Nº (%) of subjects with underlying chronic disease</b>				
- <b>With hypertension</b>	108(37.8)	263(44.3)	239(47.2)	0.35 <sup>a</sup>
- <b>With cardio-vascular disease</b>	49(17.1)	167(28.1)	120(23.7)	0.002 <sup>a</sup>
- <b>With diabetes</b>	39(13.6)	125(21)	90(17.8)	0.027 <sup>a</sup>
- <b>With malignancy</b>	17(5.9)	42(7.1)	27(5.3)	0.483 <sup>a</sup>
- <b>With chronic kidney disease</b>	19(6.6)	64(10.8)	22(4.4)	0.0001 <sup>a</sup>
- <b>With chronic obstructive pulmonary disease</b>	37(12.9)	50(8.4)	37(7.3)	0.024 <sup>a</sup>
- <b>With hepatopathy</b>	5(1.8)	20(3.4)	25(5)	0.059 <sup>a</sup>
<b>Nº (%) of asymptomatic subjects</b>	28(10.4)	120(20)	53(10.5)	0.0001 <sup>a</sup>
<b>Nº (%) of symptomatic patients</b>	240(89.6)	479(80)	454(89.5)	
<b>Nº (%) of symptomatic subjects with</b>				
- <b>fever</b>	189(68.7)	325(54.8)	305(60.4)	0.0001 <sup>a</sup>
- <b>cough</b>	109(39.5)	193(32.6)	161(32)	0.078 <sup>a</sup>
- <b>dyspnea</b>	103(37.1)	317(53.5)	356(70.6)	0.0001 <sup>a</sup>
- <b>hypo ageusia</b>	46(21.5)	27(4.6)	15(3)	0.0001 <sup>a</sup>
- <b>hypo-anosmia</b>	42(19.3)	29(4.9)	10(2.0)	0.0001 <sup>a</sup>
- <b>diarrhea</b>	19(8.1)	30(5.1)	22(4.4)	0.100 <sup>a</sup>
- <b>cutaneous lesions</b>	3(1.7)	2(0.3)	3(0.6)	0.138 <sup>a</sup>
<b>Length of hospitalization expressed in days, median (Q1-Q3)</b>	17(13-25)	13(8.5-20)	14(9.5-19)	0.0001 <sup>c</sup>

a, Chi-square test; b, non-way ANOVA; c, Kruskal-Wallis test.

**Table S2.** Demographic, Clinical and Laboratory data of patients with severe outcome grouped by period of hospitalization.

	severe COVID 19 First wave	severe COVID 19 Second wave	severe COVID 19 Third wave	P value
<b>Nº of subjects</b>	<b>105</b>	<b>318</b>	<b>199</b>	
<b>Nº (%) of males</b>	74(70.5)	199(62.6)	120(60.3)	0.206 <sup>a</sup>
<b>Age, years, median (Q1-Q3)</b>	73(58-80)	68(57-80)	70(58-81)	0.602 <sup>b</sup>
<b>Days of enrolment after onset of symptoms, Median (Q1-Q3)</b>	6(3-9.5)	6(2-9)	6.5(3-10)	0.760 <sup>b</sup>
<b>Charlson comorbidity index, median (Q1-Q3)</b>	3(1-5)	4(2-5)	3(1-5)	0.070 <sup>c</sup>
<b>Nº (%) of subjects with underlying chronic disease</b>				
- <b>With hypertension</b>	55(53.9)	157(49.8)	113(56.8)	0.297 <sup>a</sup>
- <b>With cardio-vascular disease</b>	40(39.2)	114(36.2)	71(35.7)	0.821 <sup>a</sup>
- <b>With diabetes</b>	24(23.5)	87(27.6)	41(20.6)	0.190 <sup>a</sup>
- <b>With malignancy</b>	19(18.6)	26(8.3)	12(6)	0.001 <sup>a</sup>
- <b>With chronic kidney disease</b>	13(12.7)	36(11.5)	19(9.5)	0.667 <sup>a</sup>
- <b>With chronic obstructive pulmonary disease</b>	19(18.6)	48(15.2)	19(9.5)	0.064 <sup>a</sup>
- <b>With hepatopathy</b>	3(2.9)	11(3.5)	4(2.0)	0.616 <sup>a</sup>
<b>Nº (%) of asymptomatic subjects</b>	3(3)	29(9.1)	6(3.0)	0.007 <sup>a</sup>
<b>Nº (%) of symptomatic patients</b>	97(97)	289(90.9)	193(97)	
<b>Nº (%) of symptomatic subjects with</b>				
- <b>fever</b>	48(78.7)	186(58.7)	117(59.1)	0.011 <sup>a</sup>
- <b>cough</b>	32(52.5)	114(36.2)	72(36.4)	0.048 <sup>a</sup>
- <b>dyspnea</b>	37(61.7)	241(178)	178(89.9)	0.000 <sup>a</sup>
- <b>hypo ageusia</b>	4(11.1)	10(3.2)	6(3.0)	0.046 <sup>a</sup>
- <b>hypo-anosmia</b>	1(2.8)	8(2.5)	2(1)	0.459 <sup>a</sup>
- <b>diarrhea</b>	5(11.1)	11(3.5)	3(1.5)	0.006 <sup>a</sup>
- <b>cutaneous lesions</b>	0(0)	1(0.3)	1(0.5)	0.894 <sup>a</sup>
<b>Length of hospitalization expressed in days, median (Q1-Q3)</b>	18(10-28)	16(10-24)	14(8-20)	0.006 <sup>c</sup>
<b>Number of patients who died during hospitalization, N°(%)</b>	65(61.9)	104(32.7)	46(23.1)	0.000 <sup>a</sup>

a, Chi- square test; b, non-way ANOVA; c, Kruskal-Wallis test.