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1 **Clinical outcomes in COVID-19 patients infected with different SARS-CoV-2 variants in**
2 **Marseille, France**

3

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16 **Abstract (250/250 words)**

17 *Objectives:* To compare the clinical and epidemiological aspects associated with different
18 predominant lineages circulating in Marseille from March 2020 to January 2021.

19 *Methods:* In this single-center retrospective cohort study, characteristics of patients infected
20 with four different SARS-CoV-2 variants were documented from medical files. The outcome
21 was the occurrence of clinical failure, defined as hospitalization (for outpatients), transfer to
22 the intensive-care unit (inpatients), and death (all).

23 *Results:* 254 patients were infected with clade 20A (20AS), 85 with Marseille-1 (M1V), 190
24 with Marseille-4 (M4V) and 211 with N501Y (N501YV) variants. 20AS presented a bell-
25 shaped epidemiological curve and nearly disappeared around May 2020. M1V reached a very
26 weak peak, then disappeared after a month-and-a-half. M4V appeared in July presented an
27 atypical wave form during seven months. N501YV has only recently appeared. As compared
28 to 20AS, patients infected with M1V were less likely to report dyspnoea (aOR=0.50, p=0.04),
29 rhinitis (aOR=0.57, p=0.04) and to be hospitalised (aOR=0.22, p=0.002). Patients infected
30 with M4V were more likely to report fever than those with 20AS and M1V (aOR=2.49,
31 p<0.0001 and aOR=2.30, p=0.007, respectively) and to be hospitalised than those with M1V
32 (aOR=4.81, p=0.003). Patients infected with N501YV reported lower rate of rhinitis
33 (aOR=0.50, p=0.001) and anosmia (aOR=0.57, p=0.02), as compared to those infected with
34 20AS. A lower rate of hospitalisation associated with N501YV infection as compared to
35 20AS and M4V (aOR=0.33, p<0.0001 and aOR=0.27, p<0.0001, respectively).

36 *Conclusions:* The four lineages have presentations which differ from one other,
37 epidemiologically and clinically. This supports SARS-CoV-2 genomic surveillance through
38 next-generation sequencing.

39

40 **Keywords:** COVID-19; SARS-CoV-2; variant; mutation; N501Y; Marseille

41 **Text (1914/2500 words)**

42 **Introduction**

43 Very little is known about viral factors underlying the clinical presentation and severity of
44 COVID-19. To date, most studies showed that the viral mutations, especially the D614G
45 mutation in the spike protein, correlated with a higher infectivity than the wild-type virus.
46 However, the evidence of an association between viral mutations and severity of the disease is
47 scant [1].

48 In Marseille, France, the first episode was predominantly due to clade 20A (20AS) strains
49 originating from Wuhan, China. The second episode was linked to Marseille-1 variant (M1V),
50 which had an African origin and specific clinical and epidemiological profiles [2]. Marseille-4
51 variant (M4V) likely originating from a mink farm in the North of France was observed soon
52 after [3], and became prevalent across most of Europe [4-7]. Finally, the third episode due to
53 N501Y variants (N501YV) previously identified in the UK, South Africa and Brazil [4-7]
54 started in early 2021.

55 We compared the clinical and epidemiological aspects of the diseases associated with four
56 different predominant lineages circulating in Marseille.

57

58 **Material and Methods**

59 **Data source and study design**

60 A single retrospective cohort study was conducted at Méditerranée Infection Institute (IHU)
61 in Marseille, Southern France. All available SARS-CoV-2 genome sequences obtained by our

62 institute between March 2020 and January 2021 were reviewed. Those selected were
63 sequences of 20AS obtained from respiratory samples collected before June 2020 (the
64 predominant variant of the first epidemic in Marseille), sequences of the M1V or M4V
65 (predominant variants during the second phase of the epidemic), and sequences harbouring
66 N501Y substitution within the spike which is the main variant circulating during the third
67 episode of the current epidemic in Marseille. A second filter was applied to include only
68 patients with available clinical status and follow-up.

69 **Patients**

70 Patients seen by our institute's medical team at the outpatient clinic or hospitalised in the
71 conventional infectious disease units were included, regardless of age and disease severity.
72 Demographic and clinical data including comorbidities were retrospectively retrieved from
73 medical files, including the main symptoms, in/outpatient status, transfer to an intensive care
74 unit (ICU) and death. At the time of study, all patients were discharged (recovered or died). In
75 addition, possible death occurring post-discharge (90 days for the last included patient) was
76 checked using the national data on mortality related to COVID-19 [8]. All patients with
77 available clinical data were included. Patients with missing clinical data were patients whose
78 samples were sent to our laboratory by external medical structures were excluded in further
79 analysis. Figure 1 shows the flow-chart of the study.

80 **Genome sequencing and assembling**

81 SARS-CoV-2-positive patients identified by real-time PCR with a Ct-value <30 [9] were
82 selected for next-generation sequencing. Whole genome sequencing was performed for 20S,
83 M1V and M4V, as previously described [2] from 200 µL of nasopharyngeal swab fluid after
84 viral RNA extraction with the EZ1 Virus Mini Kit v2.0, followed by reverse transcription by
85 SuperScript IV (ThermoFisher Scientific, Waltham, MA, USA), cDNA second strand

86 synthesis using Klenow Fragment DNA polymerase (New England Biolabs, Beverly, MA,
87 USA), and the generation of purified DNA with Agencourt AMPure XP beads (Beckman
88 Coulter, Villepinte, France). Genome next-generation sequencing used Illumina technology
89 on a MiSeq instrument and the Illumina Nextera XT Paired end strategy (Illumina Inc., San
90 Diego, CA, USA). Genome assemblies were performed with the CLC Genomics workbench
91 v.7 software by mapping on the SARS-CoV-2 genome GenBank Accession no. NC_045512.2
92 (Wuhan-Hu-1 isolate). Recovered genomes were compared to sequences from the GISAID
93 database (<https://www.gisaid.org/>). Phylogeny reconstructions were performed with the
94 GISAID TreeTool v2.0 ([https://www.gisaid.org/epiflu-applications/upcoming-features-in-](https://www.gisaid.org/epiflu-applications/upcoming-features-in-v20/treetool-app/)
95 [v20/treetool-app/](https://www.gisaid.org/epiflu-applications/upcoming-features-in-v20/treetool-app/)). N501YV were identified by specific qPCR [10].

96 **Statistics**

97 Statistical analyses were carried out using R [R Core Team. R: A language and environment
98 for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, 2020.
99 URL: <https://www.Rproject.org/>] and Stata version 15.1 [<http://www.stata.com>]. Qualitative
100 variables were presented by percentage. Univariate and multivariate analyses were conducted
101 to evaluate the different characteristics and clinical profiles of patients infected with different
102 lineages. We aim to evaluate the predictive factors associated with infection with different
103 SARS-CoV-2 variants. The dependent variables were the genetic characteristics of SARS-
104 CoV-2 lineages (20AS, M1V, M4V and N501YV). The primary outcome was the occurrence
105 of clinical failure, defined as hospitalization (for outpatients), transfer to the intensive-care
106 unit (inpatients), and death (all). Unadjusted associations between multiple covariate factors
107 and infection with different lineages were investigated using chi2 test. Crude Odds Ratio
108 (OR) and 95% confidence interval (95%CI) were calculated using a two-by-two frequency
109 table to evaluate the association of each predictive factor and infection with different SARS-
110 CoV-2 variants. Multivariate analysis was performed using logistical regression. Covariate

111 variables with general proportion <5% were excluded from statistical analysis, because of low
112 effective. Variables with a p-value <0.2 in the univariate analysis were included in the
113 multivariate analysis [11]. The ϕ coefficient was used to test for multicollinearity among the
114 independent variables. For pairs of variables that were highly correlated (absolute value of
115 correlation coefficient >0.7), only one variable was entered into the multivariate model.
116 Multivariable logistic regression (created by stepwise regression) was used to predictive
117 factors associated with infection with different SARS-CoV-2 variants. The results were
118 presented by adjusted Odds Ratio (aOR) with a 95%CI. A p-value < 0.05 was considered as
119 statistically significant.

120 **Ethics Statement**

121 Whole genome sequencing was performed on nasopharyngeal samples that were collected in
122 the context of routine diagnosis. No additional samples were collected for this study. Clinical
123 data were retrospectively retrieved from medical files and anonymised before analysis.
124 Ethical approval was obtained from the Marseille Institutional Review Board and Ethics
125 Committee (No. 2020-016-03).

126

127 **Results**

128 Between 29 February 2020 and 31 January 2021, 15 variants circulated in Marseille. We
129 identified 1,080 patients infected with four principal lineages: 20AS (N=339), M1V (N=98),
130 M4V (N=420) and N501YV (N=223). Figure 2 shows the extrapolated timeline of SARS-
131 CoV-2 variants identified in our institute. 20AS presented a bell-shaped epidemiological
132 curve characteristic of seasonal respiratory infections and nearly disappeared around May
133 2020. The M1V reached a very weak peak but represented up to 100% of infections during
134 part of the month of July, then disappeared after a month-and-a-half [2]. The M4V which

135 appeared in July presented an atypical wave form and continued to represent a significant
136 proportion of the cases in February, indicating a duration of seven months which is not
137 comparable to that of the other two epidemics. The N501YV has only recently appeared, and
138 conclusions cannot yet be reached as to the epidemic form it will take. Clinical data were
139 available from 740 patients whose virus genome was documented and who were treated at our
140 institute (Table 1). Twenty percent (148/740) of patients were aged ≥ 60 years and 49.5%
141 (366/740) were male. A total of 20.5% (152/740) patients were hospitalised, 3.2% (24/740)
142 were transferred to an intensive care unit (ICU) and 4.3% (32/704) died. It should be noted
143 that no patient infected with the M1V was transferred to an ICU or died.

144 In univariate analysis, significant differences were observed between patients infected with
145 different lineages of SARS-CoV-2 with regards to age, certain co-morbidities and symptoms
146 and disease severity (Table 2). In multivariate, some characteristics appeared to be
147 independent factors associated with infection with different virus lineages (Table 3). Notably,
148 lower rates of dyspnoea, rhinitis and hospitalisation were seen in patients infected with the
149 M1V as compared to those infected with 20AS. Compared to those infected with 20AS or the
150 M1V, patients infected with the M4V were older and more likely to present with fever. In
151 addition, lower rate of rhinitis was observed in M4V infection as compared to 20AS and a
152 higher hospitalisation rate was associated with M4V infection as compared to M1V. Higher
153 rate of cancer and fever, and lower rate of rhinitis and anosmia were seen N501YV infection
154 as compared to 20AS. Older age and fever associated with N501YV infection as compared to
155 M1V. Finally, a lower rate of hospitalisation associated with N501YV infection as compared
156 to 20AS and M4V.

157

158 **Discussion**

159 These four lineages have presentations which are quite different from each other on certain
160 points. These variants look completely different in the same location at different times.

161 Clinically, the age of the patients is different. Patients infected with the M1V are clearly
162 younger than those with the initial virus or those with the M4V and the N501YV. This is also
163 associated with lower disease severity. Differences in the frequency of fever, dyspnoea,
164 rhinitis and anosmia were observed according to lineages. Hospitalisation rates also varied
165 with lineages. The N501YV is known to associate with an increased infectivity, but the
166 correlation with the severity of the disease is unclear. Initially, it was described as associating
167 with increased hospitalization and mortality rates [12-14]. An analysis of syndromic
168 community testing and death records showed that this variant was associated with an increase
169 in deaths from 2.5 to 4.1 per 1000 detected cases. By contrast, in a recent clinical study, no
170 association of this variant with disease severity was observed [15]. The increase in severity of
171 N501YV was only found in studies based on a community-based testing dataset, while ours
172 and that of Frampton et al were conducted among patients seen at hospital. Although these
173 large community studies found a significant difference in mortality at a population level, the
174 absolute risk increase affecting individual patients is probably minimal.

175 This work has some limitations. Several biomarkers known to be associated with severity,
176 including lymphopenia, thrombopenia, D-dimer counts, troponin level, lactate dehydrogenase,
177 were not considered in this analysis. In addition, we cannot provide information on duration
178 of symptoms which could be different by variant. Furthermore, we analysed only patients
179 seen at our hospital, requiring medical care and that could introduce a major selection bias. A
180 large proportion of patients (not seen at our hospital) were excluded from our analysis
181 because of missing data. The patients being uncaptured here could be young and
182 asymptomatic or pauci-symptomatic and the real severity of variant may differ from our
183 results. Finally, the variants changed over time, as did our clinical understanding,

184 management, and treatment of COVID-19. There is a secular trend toward decreasing
185 hospitalization and mortality, such that the rates reported here by variant may be either over-
186 or underestimated. Nevertheless, these clinical and epidemiological nuances represent a
187 definite interest when considering the clinical and epidemiological specificity of the variants
188 which appeared extremely clear to us in the field. We must remember that all these patients
189 were admitted to the same institute and data was collected by doctors who observed the
190 patients directly. This underlines the fact that COVID-19 presents a variability from July
191 2020, which is associated with epidemiological modifications such as the source (the M1V
192 undoubtedly came from Africa, the 20AS from China, the N501YV from England and the
193 source of M4V is unknown but is believed to be of European origin) [2,3].

194 Thus, it is difficult to use the same name to qualify a disease, the variants of which present
195 epidemiological origins, epidemic curves and clinical manifestations which are distinct from
196 one other.

197 In practice, as for the influenza virus, SARS-CoV-2 seems to present mutants with a severity
198 and an epidemiological course that is specifically linked to these mutations. The severity is
199 also different since the M1V was less severe than other lineages, the N501YV appears to be
200 less severe than the M4V, which seems to have had the greatest severity compared to others.
201 This is despite the fact that patient care from diagnosis to discharge took place under the same
202 circumstances, in the same institute and under the same conditions, providing perfectly
203 comparable data, in contrast to most other studies, in particular multicentric studies.

204

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215

216 **Conflicts of Interest**

217 Thi-Loi Dao, Van-Thuan Hoang, Nhu Ngoc Nguyen, Jérémy Delerce, Hervé Chaudet,
218 Anthony Levasseur, Jean-Christophe Lagier, Didier Raoult, Philippe Colson and Philippe
219 Gautret declare that they have no conflicts of interest.

220 **Author Contributions Statement**

221 TLD, VTH and PG contributed to experimental design, data analysis, statistics, interpretation
222 and writing. TLD, VTH, NNN and JCL contributed to collecting the data of patients. JD
223 analyzed the sequencing results. PC and AL contributed to interpretation of sequencing
224 results. HC contributed to statistical analysis. DR, HC, PC, AL and JCL contributed to
225 critically reviewing the manuscript. PG coordinated the work.

226

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Table 1: Socio-demographic characteristics, comorbidities, clinical signs and disease severity of patients infected with clade 20A strains and with the Marseille-1, Marseille-4 and N501Y SARS-CoV-2 variants.

Table 2: Socio-demographic characteristics, comorbidities, clinical signs and disease severity of patients infected with different SARS-CoV-2 lineages, univariate analysis

Table 3: Socio-demographic characteristics, comorbidities, clinical signs and disease severity of patients infected with different SARS-CoV-2 lineages, multivariate analysis

Figure 1. Flow chart of the study

Legend to figure: 20AS: clade 20A strain, M1V: Marseille-1 variant, V: Marseille-4 variant, N501YV: N501Y variant

Figure 2. Weekly numbers of cases of infections with the different genotypes of SARS-CoV-2

Legend to figure: The weekly numbers of cases of infections with the different genotypes of SARS-CoV-2 were extrapolated from the actual numbers of detection of each of the genotypes by relating them to the weekly numbers of SARS-CoV-2 diagnoses. The grey zone corresponds to the extrapolated number of cases with other genotypes than clade 20A strain, Marseille-1, Marseille-4 and N501Y variants. These genotypes included clades 19, 20B, 20C, Marseille-2, -3, -5, -6, -7, -8, -9 and -10 variants. SARS-CoV-2 genotypes were determined by genomic sequencing and specific qPCR. The grey zone corresponds to the extrapolated number.

1080 patients seen at the outpatient clinic or hospitalised
(339 with 20AS, 98 with M1V, 420 with M4V and 223 with N501YV)



Inclusion

740 discharged patients with available clinical data
(254 with 20AS, 85 with M1V, 190 with M4V and 211 with N501YV)

Exclusion

340 patients with missing data or whose samples were send to laboratory by external medical structures

Demographic and clinical data were retrospectively retrieved from medical files

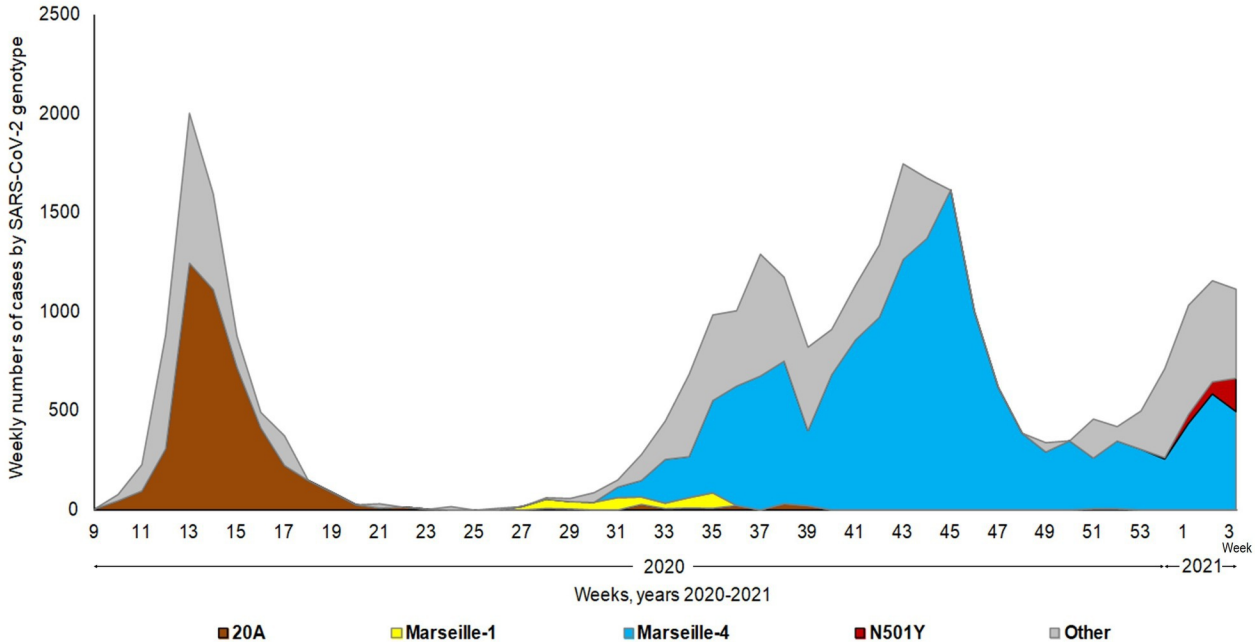


Table 1: Socio-demographic characteristics, comorbidities, clinical signs and disease severity of patients infected with clade 20A strains and with the Marseille-1, Marseille-4 and N501Y SARS-CoV-2 variants.

Variables	20A	Marseille-1	Marseille-4	N501Y	P-value
	N = 254	N = 85	N = 190	N = 211	
	n (%)	n (%)	n (%)	n (%)	
Age [¶]					
Median	45.5	34.0	54.0	49.0	<0.0001
Interquartile	32 - 59	24 - 48	36 - 70	35 - 61	
Range	0 - 95	13 - 90	11 - 97	13 - 100	
<45 years	125 (49.2)	59 (69.4)	63 (33.2)	91 (43.1)	<0.0001
45-64 years	81 (31.9)	20 (23.5)	69 (36.3)	84 (39.8)	
≥ 65 years	48 (18.9)	6 (7.1)	58 (30.5)	36 (17.1)	
Sex = Male	113 (44.5)	48 (56.5)	102 (53.7)	103 (48.8)	0.13
Hypertension	51 (20.1)	8 (9.4)	47 (24.7)	36 (17.1)	0.02
Diabetes	18 (7.1)	4 (4.7)	21 (11.1)	12 (5.7)	0.14
Cancer	10 (3.9)	2 (2.4)	15 (7.9)	15 (7.1)	0.13
Chronic respiratory diseases	23 (9.1)	7 (8.2)	20 (10.5)	27 (12.8)	0.53
Chronic heart diseases	27 (10.6)	4 (4.7)	29 (15.3)	20 (9.5)	0.06
Obesity	22 (8.7)	8 (9.4)	10 (5.3)	18 (8.5)	0.49
Fever	67 (26.4)	22 (25.9)	87 (45.8)	97 (46.0)	<0.0001
Cough	123 (48.4)	39 (45.9)	73 (38.4)	97 (46.0)	0.20
Dyspnoea	72 (28.3)	13 (15.3)	42 (22.1)	48 (22.8)	0.08
Rhinitis	106 (41.7)	26 (30.6)	37 (19.5)	56 (26.5)	<0.0001
Anosmia [‡]	76 (29.9)	26 (30.6)	35 (18.5)	43 (20.4)	0.01
Ageusia [‡]	71 (28.0)	23 (27.1)	34 (18.0)	44 (20.9)	0.06
Hospitalisation	53 (20.9)	5 (5.9)	67 (35.3)	27 (12.8)	<0.0001
Transfer to ICU*	5 (2.0)	0 (0)	10 (5.3)	9 (4.3)	0.06
Death*	10 (3.9)	0 (0)	15 (7.9)	7 (3.3)	0.02

*Transfer to ICU and death were not considered in later analyses, due to their low proportion (<5%)

‡ Data was not available for two children aged <11 years.

¶ 15 patients less than 18 year-old

Table 2: Socio-demographic characteristics, comorbidities, clinical signs and disease severity of patients infected with different SARS-CoV-2 lineages, univariate analysis

Variables	Marseille 1-vs. 20A (reference = 20A)	Marseille-4 vs. 20A (reference = 20A)	Marseille-4 vs. Marseille-1 (reference = Marseille-1)	N501Y vs 20A (reference = 20A)	N501Y vs. Marseille-1 (reference = Marseille-1)	N501Y vs. Marseille-4 (reference = Marseille-4)
	OR	OR	OR	OR	OR	OR
	[95%CI] P-value	[95%CI] P-value	[95%CI] P-value	[95%CI] P-value	[95%CI] P-value	[95%CI] P-value
Age						
<45 years	reference	reference	reference	reference	reference	reference
45-64 years	0.52 [0.29 – 0.93] 0.03	1.69 [1.09 – 2.63] 0.02	3.23 [1.75 – 5.95] <0.000	1.42 [0.95 – 2.14] 0.09	2.72 [1.51 – 4.90] 0.001	0.84 [0.54 – 1.32] 0.46
≥ 65 years	0.26 [0.11 – 0.65] 0.004	2.40 [1.47 – 3.90] <0.000	9.05 [3.64 – 22.55] <0.000	1.03 [0.62 – 1.71] 0.91	3.89 [1.54 – 9.80] 0.004	0.43 [0.25 – 0.73] 0.002
Sex = Male	1.62 [0.99 – 2.66] 0.06	1.45 [0.99 – 2.11] 0.06	0.89 [0.53 – 1.50] 0.67	1.19 [0.83 – 1.72] 0.35	0.74 [0.44 – 1.22] 0.23	0.82 [0.55 – 1.22] 0.33
Hypertension	0.41 [0.19 – 0.91]	1.31 [0.83 – 2.05]	3.16 [1.42 – 7.03]	0.82 [0.51 – 1.31]	1.98 [0.88 – 4.46]	0.62 [0.38 – 1.02]

	0.03	0.24	0.005	0.41	0.10	0.06
Diabetes	0.65	1.63	2.52	0.79	1.22	0.49
	[0.21 – 1.97]	[0.84 – 3.15]	[0.84 – 7.57]	[0.37 – 1.68]	[0.38 – 3.90]	[0.23 – 1.02]
Cancer	0.44	0.15	0.10	0.54	0.74	0.06
	0.59	2.09	3.56	1.87	3.18	0.89
Chronic respiratory diseases	[0.13 – 2.74]	[0.92 – 4.76]	[0.80 – 15.92]	[0.82 – 4.25]	[0.71 – 14.20]	[0.42 – 1.88]
	0.50	0.08	0.10	0.14	0.13	0.77
Chronic heart diseases	0.90	1.18	1.31	1.47	1.64	1.25
	[0.37 – 2.18]	[0.63 – 2.22]	[0.53 – 3.23]	[0.82 – 2.66]	[0.68 – 3.91]	[0.67 – 2.31]
Obesity	0.82	0.60	0.56	0.20	0.27	0.48
	0.42	1.51	3.65	0.88	2.12	0.58
Fever	[0.14 – 1.22]	[0.86 – 2.66]	[1.24 – 10.73]	[0.48 – 1.62]	[0.70 – 6.40]	[0.32 – 1.07]
	0.11	0.15	0.02	0.68	0.18	0.08
Cough	1.10	0.59	0.53	0.98	0.90	1.68
	[0.47 – 2.56]	[0.27 – 1.27]	[0.20 – 1.41]	[0.51 – 1.89]	[0.37 – 2.15]	[0.75 – 3.73]
Diabetes	0.83	0.18	0.21	0.96	0.81	0.20
	0.97	2.36	2.42	2.37	2.44	1.01
Cough	[0.56 – 1.71]	[1.58 – 3.51]	[1.38 – 4.25]	[1.61 – 3.50]	[1.40 – 4.25]	[0.68 – 1.49]
	0.93	<0.000	0.002	<0.000	0.002	0.97
Diabetes	0.90	0.66	0.74	0.91	1.01	1.36
	[0.55 – 1.48]	[0.45 – 0.97]	[0.44 – 1.23]	[0.63 – 1.31]	[0.61 – 1.66]	[0.92 – 2.03]
Cough	0.69	0.04	0.25	0.60	0.99	0.13

Dyspnoea	0.46 [0.24 – 0.87] 0.02	0.72 [0.46 – 1.11] 0.14	1.57 [0.79 – 3.11] 0.19	0.74 [0.49 – 1.14] 0.17	1.63 [0.83 – 3.20] 0.15	1.04 [0.65 – 1.66] 0.88
Rhinitis	0.62 [0.36 – 1.04] 0.07	0.34 [0.22 – 0.52] <0.000	0.55 [0.31 – 0.98] 0.04	0.50 [0.34 – 0.75] 0.001	0.82 [0.47 – 1.43] 0.48	1.49 [0.93 – 2.39] 0.10
Anosmia	1.03 [0.60 – 1.75] 0.92	0.53 [0.34 – 0.83] 0.006	0.52 [0.28 – 0.93] 0.03	0.60 [0.39 – 0.92] 0.02	0.58 [0.33 – 1.03] 0.06	1.13 [0.69 – 1.85] 0.64
Ageusia	0.95 [0.55 – 1.65] 0.86	0.56 [0.35 – 0.89] 0.01	0.59 [0.32 – 1.08] 0.09	0.68 [0.44 – 1.04] 0.07	0.71 [0.40 – 1.27] 0.25	1.20 [0.73 – 1.98] 0.47
Hospitalisation	0.24 [0.09 – 0.61] 0.003	2.07 [1.35 – 3.16] 0.001	8.72 [3.37 – 22.56] <0.000	0.56 [0.34 – 0.92] 0.02	2.35 [0.87 – 6.32] 0.09	0.27 [0.16 – 0.44] <0.000

Table 3: Socio-demographic characteristics, comorbidities, clinical signs and disease severity of patients infected with different SARS-CoV-2 lineages, multivariate analysis*

Variables	Marseille-1 vs. 20A (reference = 20A)	Marseille-4 vs. 20A (reference = 20A)	Marseille-4 vs. Marseille-1 (reference = Marseille-1)	N501Y vs 20A (reference = 20A)	N501Y vs. Marseille-1 (reference = Marseille-1)	N501Y vs. Marseille-4 (reference = Marseille-4)
	adjusted OR [95%CI] P-value	adjusted OR [95%CI] P-value	adjusted OR [95%CI] P-value	adjusted OR [95%CI] P-value	adjusted OR [95%CI] P-value	adjusted OR [95%CI] P-value
Age						
<45 years		reference			reference	
45-64 years	-	1.61 [1.01 – 2.56] 0.04	2.61 [1.38 – 4.92] 0.003	-	2.68 [1.48 – 4.87] 0.001	-
≥ 65 years	-	1.93 [1.15 – 3.23] 0.01	4.12 [1.49 – 11.38] 0.006	-	3.70 [1.45 – 9.42] 0.006	-
Cancer	-	-	-	2.73 [1.09 – 6.84] 0.03	-	-
Fever	-	2.49 [1.64 – 3.80]	2.30 [1.26 – 4.23]	2.58 [1.72 – 3.86]	2.35 [1.33 – 4.15]	-

		<0.000	0.007	<0.000	0.003	
Dyspnoea	0.50 [0.26 – 0.98] 0.04	-	-	-	-	-
Rhinitis	0.57 [0.33 – 0.97] 0.04	0.36 [0.23 – 0.57] <0.000	-	0.50 [0.33 – 0.76] 0.001	-	-
Anosmia	-	-	-	0.57 [0.36 – 0.90] 0.02	-	-
Hospitalisation	0.22 [0.09 – 0.58] 0.002	-	4.81 [1.69 – 13.69] 0.003	0.33 [0.18 – 0.60] <0.000	-	0.27 [0.17 – 0.45] <0.000

*All variables with p-value <0.20 in the univariate analysis were included in the logistical regression, but only significant variables (in multivariate) were presented.