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Research Letter

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Epidemiological, clinical and genomic snapshot of the first 100 B.1.1.7 SARS-CoV-2 cases in Madrid

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A new SARS-CoV-2 variant, B.1.1.7, emerged in September in the UK, and is responsible for 76.6% of COVID-19 cases.[1] This variant has also been reported in another 45 countries, 17 of them European.[2,3] B.1.1.7 is considered to have higher transmissibility.[4] It carries an unusually high number of specific mutations/deletions, 18, mostly non-synonymous and eight concentrate in the S gene,[5] including several which might have relevant functional roles. The 69/70 deletion may be associated to immune response evasion[6] and the N501Y substitution increases the affinity to the ACE2 receptor.[7] These findings have raised the alarm of having to face a new variant with the potential to accelerate the spread of the pandemic. A recent report finds a realistic possibility that B.1.1.7 is associated with an increased risk of death.[8]

More data on the behaviour of the B.1.1.7 variant once imported are needed to further understand its potential risks at a wider context. The aim of this study was to analyse the first 106 incident COVID-19 cases in Madrid (650 000 inhabitants covered by our tertiary hospital) infected by the B.1.1.7 variant.

We based our initial screening on the S gene signal dropout in the TaqPath assay (ThermoFisher, Waltham, USA) caused by the 69/70 deletion.[9] This screening criterion, based on the S signal dropout, has been accepted as a suitable proxy to identify the B.1.1.7 variant, with 100% specificity over the past weeks in the UK.[1]

Our first B.1.1.7 case was diagnosed at week 52 (21 December 2020). The patient had a previous positive RT-PCR on December 15. In the month preceding this first B.1.1.7 case, the lineage B.1.177 represented 91% of the SARS-CoV-2 strains in our population and the remaining sequences were distributed among minority lineages (B.2, B.1.1.305, B.1.1.130, B.1.1.29, A.2, B.1.1.1 and B.1.88). Since December 15, and until February 1 (week 2, 2021), we diagnosed 106 COVID-19 cases candidates to be infected by B.1.1.7, and at the time of the writing of this manuscript; B.1.1.7 represents 62% of the total newly diagnosed COVID-19 cases (average value for week 10 [2021]).

Among the B.1.1.7 cases in our study, 51.9% were women and the average age of all study subjects was 40 years (range

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Table 1. demographic and clinical features for the B.1.1.7 cases.

Demographics		
	Average	*Range*
Age	39.63	1–92
	Total	*Percentage (%)*
Sex		
Male	51	48.11
Female	55	51.88
COVID-19 symptoms		
Bilateral pneumonia	10	10.31
Dyspnea	15	15.46
Asthenia	28	28.87
Fever	23	23.71
General unrest	18	18.55
Diarrhoea	6	6.19
Cephalea	20	20.61
Odinophagia	5	5.15
Anosmia	16	16.50
Cough	18	18.55
Rhinorrhea	10	10.31
Myalgias	16	16.50
Severity		
Asymptomatic	9	9.28
Mild	66	68.04
Intermediate	13	13.40
Severe	9	9.28
Health care requirement		
Emergency	24	24.74
Hospital admission	14	14.43
ICU	4	4.12
Antecedents		
None of interest	75	77.32
High blood pressure	6	6.18
COPD	1	1.03
Asthma	5	5.15
Diabetes	2	2.06
Ictus	1	1.03
Overweight/obesity	2	2.06
Heart disease	2	2.06
Autoimmune	1	1.03
Oncological	2	2.06

1–92). A telephonic survey was performed to collect epidemiological and clinical information from 97 cases (approved by the ethical research committee of Gregorio Marañón Hospital; REF: MICRO.HGUGM.2020-042). Nine cases were asymptomatic, 79 had soft/moderate symptoms, and 14 were hospitalized (10 presented pneumonia, four were admitted to the intensive care unit and two deaths). Most cases (77.3%) had no comorbidities (Table 1).

Regarding the potential links to the UK, six cases (6.19%) had recently arrived from the UK and all had been diagnosed at the end of December; 12 cases (12.37%) had had contact with people coming from the UK; the remaining 79 cases (81.44%) did not have any direct or indirect links with the UK, indicating a wide community transmission. Moreover, the first case in our study was among those without links to the UK; the partner of this patient, diagnosed the same day, worked in the district tribunal and was in high contact with the general public. This suggests that B.1.1.7 community transmission in Madrid may have started before December 15. The average number of additional cases (either preceding or subsequent) communicated by each B.1.1.7 carrier possibly linked to them was 3.07 [range 0–10].

Whole genome sequencing (WGS, Supplementary Methods) characterization of B.1.1.7 positive specimens could be carried out from 88 cases and in all, the B.1.1.7 variant was confirmed. The phylogenetic analysis (Figure 1a) shows the diversity among the sequences, consistent with the circulating time of this lineage in the UK,[10] before being imported to Spain. Moreover, the integration of our WGS data with those from the B.1.1.7 sequences available from the UK in GISAID shows that the cases in Madrid correspond to sequences distributed throughout the tree (Figure 1b). To estimate the most recent common ancestor (MRCA) a multi-sequence alignment was performed, including the 88 B.1.1.7 sequences from Madrid and 67 additional sequences belonging to global SARS-CoV-2 diversity (Supplementary Methods). Before phylogenetic dating, root-to-tip regression of genetic divergence against sampling dates was performed to investigate the molecular clock signal using TempEst v 1.5.3. A strong temporal signal was observed ($R^2 = 0.83$; $P > 0.001$, slope $= 9.83 \times 10^{-4}$) in root-to-tip analysis, suggesting a strict clock model. The time of most recent common ancestor (MRCA) of Madrid B1.1.7 representatives was estimated in 10 December 2020 [95% HPD 25 November 2020; 24 December 2020]. In this analysis we also estimated the origin of the SARS-CoV-2 pandemic in 8 December 2019 [95% HPD 7 November 2019; 1 January 2020].

Focusing on Madrid sequences, 55 cases (61%) are involved in 14 clusters (0 SNPs between the cases sharing cluster, size 2–14; Figure 1a), suggesting post-importation transmission chains. Four out of the six cases who had arrived from the UK and 10 of the 11 individuals who had links with people recently arrived from that country were involved in some of these clusters (Figure 1a, Supplementary Table 1).

One large cluster (cluster 1), involving 14 cases, was identified, while the remaining clusters were smaller (2–5 cases; Figure 1a). Cluster 1 involved members of four different households (2, 2, 3 and 3 individuals); two of these family units were acquaintances and another two clustered cases knew one individual of one these families (Figure 1a, Supplementary Table 1). The next two largest clusters were number 9 and 16, which included five and six cases. Cluster 9 involved one household (five members) and a 2-year-old case without relationships with those in the cluster. Similarly, cluster 16 included five members from the same household and one unrelated case (Figure 1a). These data exemplify community transmissions in which the same strain is transmitted in different close circles and extends beyond them. Links were also found between the cases included in eight of the smaller clusters (all household-related except two involving close contact between partners or friends, Figure 1a, Supplementary Table 1).

We present valuable clinical and epidemiological data on the first 106 cases diagnosed with the new SARS-CoV-2 B.1.1.7 variant in Madrid that will help understand its dynamics once introduced into a new population. In our context, 16.3% of all newly diagnosed cases carry the B.1.1.7 variant 1 month after its first detection and most developed non-severe disease. The great

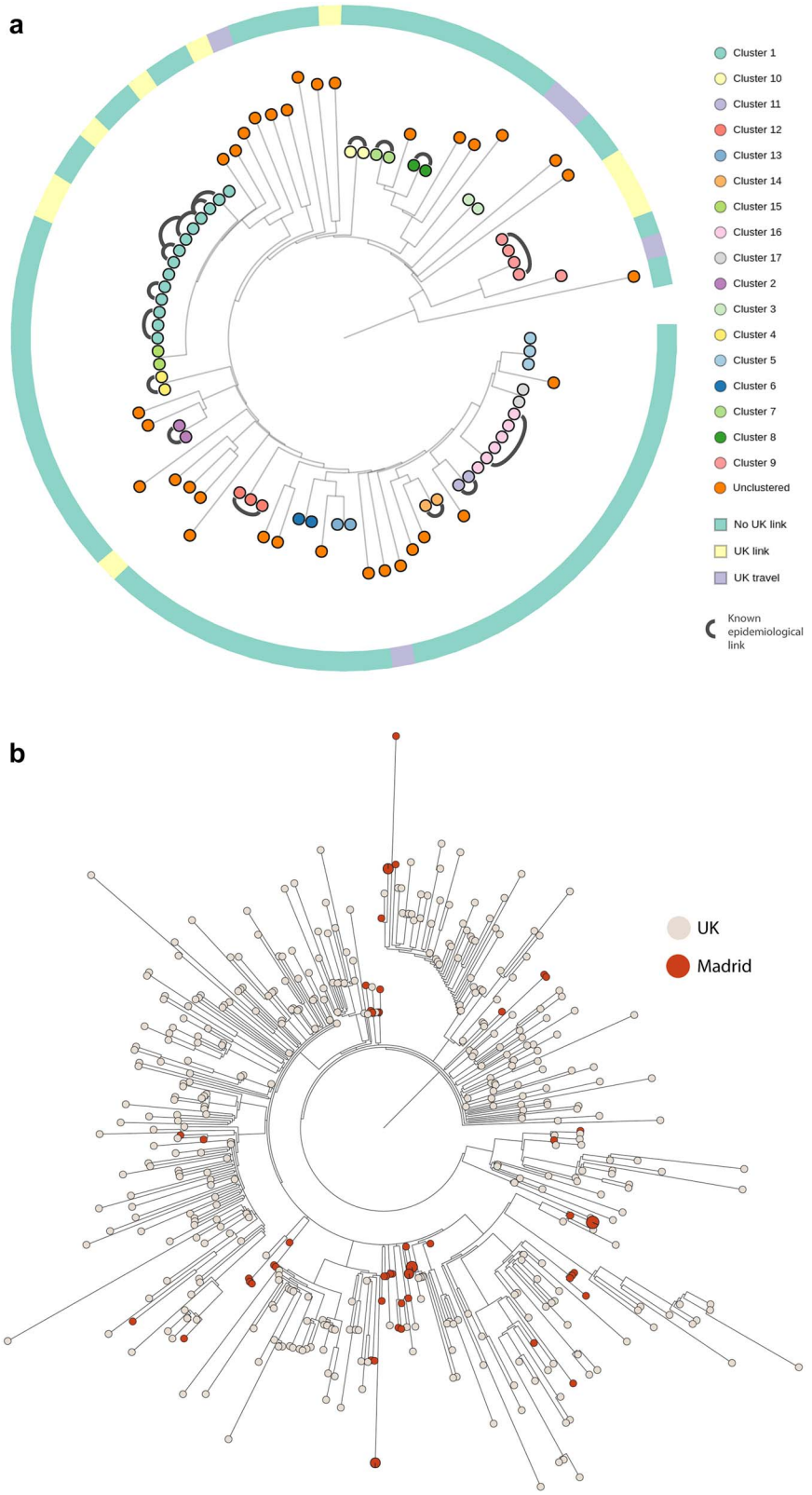

Figure 1. (a) Phylogenetic tree including the 88 sequences from specimens with the B.1.1.7 variant. Clustered cases are indicated with a colour code. Cases with epidemiological relationships are shown with a graphic link between them. The ring surrounding the tree indicates whether the cases had travelled from the UK, showed links to the UK or had no links to the UK. All Madrid sequences were uploaded to GISAID. Supplementary Methods. (b) Integration of the Madrid B.1.1.7 sequences from this study (circles sizes are proportional to the number of cases sharing each genotype) with a random subselection of 394 B.1.1.7 sequences among the 25 624 sequences deposited from the UK in GISAID between 1 December 2020 and 28 January 2021.

majority of the cases infected with B.1.1.7, including the first identified case, had no direct or indirect links to the UK. Thus, even from the start, the increase of this variant in our context is mostly due to post-importation transmission events within the community rather than further imports. One of the transmission clusters identified by genomic viral analysis was very large and alerts on the need of more efficient control measures to minimize a rapid transmission of the B.1.1.7 variant.

Supplementary data

Supplementary data are available at *JTM* online.

Author's contributions

Laboratory experimental tasks: P.C., M.H., V.M.D.C. Bioinformatic analysis: P.J.S.C., S.B.S., L.P.L., M.G.L. Sequencing: J.S.G. Microbiological data and databases: L.A. Clinical/epidemiological research: A.E. Data analysis: D.G.V., L.P.L. Analytical strategies, protocols, pipelines and funding: I.C., F.G.C. MS writing and revisions: D.G.V., L.P.L., P.M.

Conflict of interest

The authors declare no conflict of interest.

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