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# Molecular epidemiology of COVID-19 in Oman: A molecular and surveillance study for the early transmission of COVID-19 in the country

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ABSTRACT

*Background:* Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been proven to be lethal to human health, which affects almost every corner of the world. The objectives of this study were to add context to the global data and international genomic consortiums, and to give insight into the efficiency of the contact tracing system in Oman.
*Methods:* We combined epidemiological data and whole-genome sequence data from 94 samples of SARS-CoV-2 in Oman to understand the origins, genetic variation, and transmissibility. The whole-genome size of sequence data was obtained through a customized SARS-COV-2 research panel. Amplifier methods ranged from 26 Kbp to 30 Kbp and were submitted to GISAID.
*Findings:* The study found that P323L (94.7%) is the most common mutation, followed by D614G (92.6%) Spike protein mutation. A unique mutation, I280V, was first reported in Oman and was associated with a rare lineage, B.1.113 (10.6%). In addition, the study revealed a good agreement between genetic and epidemiological data.
*Interpretation:* Oman's robust surveillance system was very efficient in guiding the outbreak investigation processes in the country, the study illustrates the future importance of molecular epidemiology in leading the national response to outbreaks and pandemics.


## Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (Paules et al., 2020; Wu et al., 2020) outbreak began in Wuhan, Hubei province, China in late December 2019 and spread globally with extraordinarily high rates of morbidity and mortality. As of December 9, 2020, more than 67.5 million confirmed cases of coronavirus disease-2019 (COVID-19) have been reported, which caused more than 1.5 million deaths (WHO 2020). Coronavirus, subfamily Coronavirinae from family *Coronaviridae*, comprises a large group of viruses that have been mainly associated with birds and mammals (Khan and McIntosh, 2005; Fehr and Perlman, 2015; Paules et al., 2020). The subfamily includes four genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*.

The coronaviruses were first identified and characterized before the 1960s and were attributed to cause a disease of the respiratory system (Khan and McIntosh, 2005; Paules et al., 2020). SARS-CoV-2 has spread among humans to cause catastrophic devastation in health systems and economies. Given the possible high mutation rate of RNA viruses as compared to DNA viruses, it was not unexpected that the viral genome of SARS-CoV-2 would mutate more rapidly, which should allow to track the spread of the virus (Grubaugh et al., 2019). However, with confirmed cases exceeding

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46.5 million, it has become difficult to track individual transmission chains due to the small size of sequences, notwithstanding more than 147 thousand whole-genome sequences, which have been deposited in GISAID, an open access global science initiative, as of October 23, 2020 (GISAID, 2020). Another striking feature of coronaviruses, when compared with other RNA viruses, is the likelihood to mutate slowly due to their ability to proofread; a fact accounted for 3' to 5' exoribonuclease (Minskaia et al., 2006). It has been reported that the estimated mutation rate of SARS-CoV-2 is 0.71–1.40 × 10–3 (Hill and Rambaut, 2020).

The first confirmed cases of COVID-19 was reported in Oman on 24 February of two Omani nationals who returned from a visit to Iran. Initially, a steady increase in the number of imported confirmed cases was observed in the following weeks, with the first suspected case of local transmission reported on March 23, 2020 in Mutrah, a city within Muscat, the capital of Oman (Al Wahaibi et al., 2020). To date, the number of infected cases has increased to more than 115,000 and approximately 1200 deaths (Ministry of Health, Oman, 2020) were recorded. The cases continue to increase up to ±400 infections daily.

The aim to perform retrospective research using both whole viral genome sequencing and molecular and epidemiological data to understand the clusters of SARS-CoV-2 infection in Oman was to add context to the global data and international genomic consortiums, and to give insight into the efficiency of the contact tracing system in the country.

## Material and methods

### *Outbreak investigation and early transmission of SARS-CoV-2 in Oman*

Data of laboratory-confirmed COVID-19 surveillance of Oman were included in this study from February 24 to May 23, 2020. Samples were selected based on epidemiological characteristics that represent various cluster types (company versus family), geographical location, and nationality. The epidemiological investigation was conducted by public health teams throughout the country, who fed data into a national electronic database. All confirmed cases underwent epidemiological investigations and included the information of each patient's demography (age, gender, residency, and nationality), epidemiology (source of infection if known, date of onset, primary case [infector] or secondary case [infected], and designation [cluster or sporadic]). The data were then analyzed to find out the relationship between the patients using the Epicontact R library; further the description of the methods is found in a recent article by Al Wahaibi et al. (2020).

### *Specimen collection and inclusion criteria*

Respiratory specimens collected from confirmed cases per the Ministry of Health national case definition were used in this study. Samples were selected from main clusters since the start of local transmission for a period of two months, from March 23 to May 5, 2020.

### *RNA extraction, library preparation, and sequencing*

A new method for SARS-CoV-2 sequencing by Thermo Fisher Scientific was followed (Supplementary information 1). Briefly, the RNA extraction of samples was carried out through MagMax™ Viral Pathogen Extraction Kit (Thermo Fisher Scientific, Waltham, MA, USA) or Viral RNA Isolation Kit with Liferiver EX3600 (Liferiver Biotech, Hangzhou Bay, China), following manufacturer protocol. For the detection of the SARS-CoV-2 virus by real-time polymerase chain reaction (RT-PCR) system, Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic Kit, CE-IVD, FDA-EUA (Sansure Biotech, Changsha, China) was used in accordance with the manufacturer's instructions. The assay targets two genomic regions of the SARS-CoV-2 (N and ORF1ab). All samples included in the study had a cycle threshold (Ct) value of the gene target of less than 30. SuperScript VILO cDNA Synthesis Kit (Thermo Fisher, USA) was used to reverse transcribe the SARS-CoV RNA with the qPCR program (42 °C for 30 min, 85 °C for 5 min, and hold on 10 °C). To ensure enough cDNA content for NGS workflow, we requantified it on Qubit 3.0 fluorometer (Thermo Fisher Scientific, Waltham, MA, USA). The cDNA (60 ng/ul) was used to prepare libraries with Ion Xpress barcodes (Thermo Fisher Scientific, Waltham, MA, USA) through Ion AmpliSeq Library Kit Plus and predefined Ion AmpliSeq SARS-CoV-2 Research Panel (Thermo Fisher Scientific, Waltham, MA, USA). The panel provides 99% coverage to viral genomes with fewer copy numbers and consists of two primer pools comprising 237 amplicons of SARS-CoV-2 genomes. The panel comprises five additional primer pairs that target human expression control. Workflow according to manufacturer guidelines was used to prepare libraries and quantify, was template-enriched, and sequenced on Ion 530 Chip Ion Torrent S5 (Thermo Fisher Scientific, Waltham, MA, USA).

### *Genome assembly, annotation, and analysis*

The Torrent Suite Software (version 12) (Thermo Fisher Scientific, Waltham, MA, USA) with SARS-CoV-2 plugins (COVID19AnnotateSnpEff, IRMAreport, and AssemblerTrinity) were installed and preoptimized with the reference sequence (ion_ampliseq_sars-cov2) and target regions (Ion_Ampliseq_SARS-CoV-2.2020323. Designed.bed) to trim, filter, quality check, assemble, and annotate the samples. Additional built-in plugins such as coverage analysis and variant caller were also used to understand the SNPs and mutations. Specifically, iterative refinement meta-assembler plugins were used to identify low-frequency variants for highly variable RNA viruses as revealed by the manufacturer's guidelines. To further validate, the obtained sequenced data were remapped with Wuhan-Hu-1 (GenBank accession number NC_045512.2).

### *Phylogenomic analysis*

The sequence alignment and phylogenetic trees were generated by following the Rob Lanfear's method (Roblanf and Richard, 2020) for a global phylogeny of SARS-CoV-2. All the sequences were downloaded from GISAID websites and created a global sequence alignment. First, every sequence was aligned to the Wuhan reference genome (NC_045512.2) with the help of the script, global_profile_alignment.sh, then joining the individually aligned sequences into a global alignment at the end. To construct a phylogenetic tree, the maximum likelihood (ML) method was used using the FastTree software (MicrobesOnline, Berkeley, CA, USA) with the best setting determined by GISAID. We further optimized that tree with a series of minimum evolution SPR moves and ML NNI moves in FastTree. The Letunic and Borks' tool (2007) was used to visualize the trees. In the second phylogenetic analysis, 349 complete SARS-CoV-2 genome sequences (including 203 sequences from Oman) were downloaded from GISAID. These sequences were aligned to the Wuhan reference genome (NC_045512.2) using the above script. The above phylogenetic inference method was used to infer the tree as described above.

## Results

### *Epidemiology of SARS-CoV-2 infection in Oman*

In this study, 21 clusters were identified with a total of 456 laboratory-confirmed cases of which 94 representative cases of

different clusters with high viral load were selected for whole-genome sequencing. Figure 1 describes selected clusters with their month of transmission, genotype, geographical location, and type of cluster. Significant correspondence between the epidemiological and genetic data was observed. Five were major intrafamilial clusters, three from the workplace, and two clusters were a mixture of both. The results also showed that the initial SARS-CoV-2 infection cases were detected in March in the capital city of Muscat within a major trade and tourist destination (Mutrah) and were classified epidemiologically as cluster B (Figure 1). This cluster expanded during the months of April and May and spread to North Sharqiyah and Dhahira as a result of community transmission and trade. Cases selected from this cluster belonged to B.1.1.27 (GR) genotype, and most of the clusters were distributed across different geographical locations because the origin of the cluster emerged from major cluster B extended to other locations. In addition, cluster P occurred in a company, and labor camps belonged to clade B.1.127 (GR) genotype and spread the epidemic into four geographical locations (Muscat, Dakhiliyah, Al Batinah South, and Dhofar governorate). Family clusters have also contributed to the spread of the epidemic to the entire country, as seen in cluster V, C, and I. As shown in Table 1, around 50% of the cases were males, Omani nationals, and from Muscat governorate. The majority (78.7%) were from the working age group, (15–50

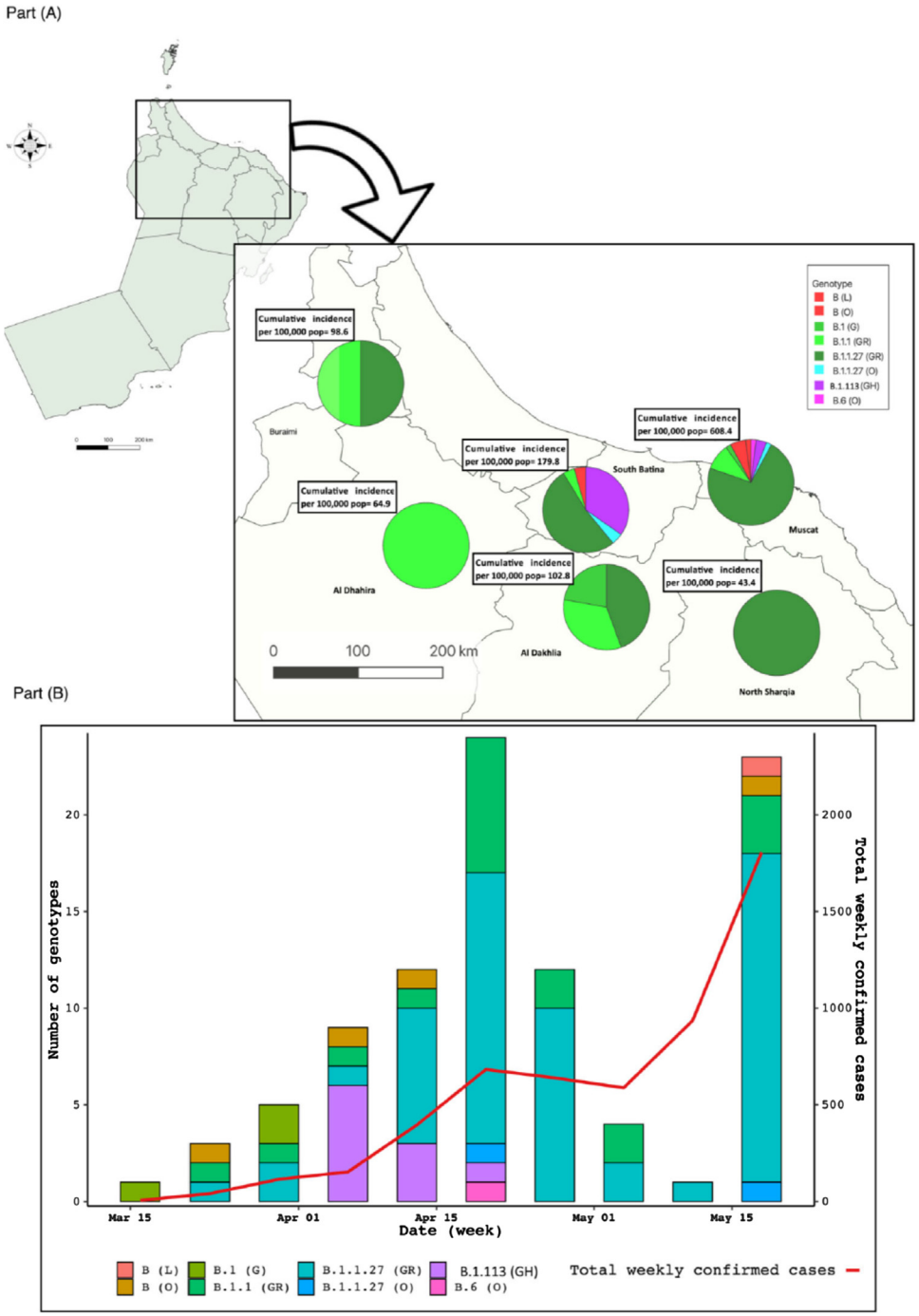


**Figure 1.** Location of the governorates of the genotyped sample with the corresponding cumulative incidence of lab-confirmed COVID-19 per 100,000 population (part A), and the weekly distribution of the genotyped sample with the total weekly confirmed cases (part B) in Oman from March 15 to May 23, 2020.

**Table 1**
Descriptive statistics of the genotyped samples infected with SARS-CoV-2.

| Parameters | Sample distribution (%) Overall (N = 94) |
|---|---|
| Age group | |
| 0–14 Years | 9 (9.6%) |
| 15–50 Years | 74 (78.7%) |
| >50 Years | 11 (11.7%) |
| Gender | |
| MALE | 54 (57.4%) |
| Nationality | |
| Omani | 52 (55.3%) |
| Governorate | |
| Muscat | 51 (54.3%) |
| Al Batinah South | 23 (24.5%) |
| Dakhiliyah | 9 (9.6%) |
| Dhahirah | 8 (8.5%) |
| Buraimi | 2 (2.1%) |
| North Sharqiyah | 1 (1.1%) |
| Genotype | |
| B (L) | 1 (1.1%) |
| B (O) | 4 (4.3%) |
| B.1 (G) | 3 (3.2%) |
| B.1.1 (GR) | 18 (19.1%) |
| B.1.1.27 (GR) | 55 (58.5%) |
| B.1.1.27 (O) | 2 (2.1%) |
| B.1.113 (GH) | 10 (10.6%) |
| B.6 (O) | 1 (1.1%) |

years). The results showed that the most frequent genotype was B.1.1.27 (GR), 58.5%, followed by B.1.1 (GR), 19.1%.

*Whole-genome sequencing of SARS-CoV-2 samples*

An amplicon-sequencing approach developed by Ion Torrent for COVID-19 was adopted for the project that yielded a total of 13 Gb of sequence data and over 56 million reads from 94 SARS-CoV-2 samples (Supplementary Table S1). The genome coverage was 99.8%, and the average genome size of SARS-CoV-2 was 29,834 bp (Supplementary Table S2). SARS-CoV-2 genome sequences generated in this study have been deposited to GISAID.[1] A list of all sequences with their accession numbers is provided in Supplementary Table S3.

*SARS-CoV-2 genomes from Oman*

The results of whole-genome sequencing of SARS-CoV-2 revealed the presence of common mutations when compared with the Wuhan reference sequence (hCoV-19/Wuhan/WIV04/2019). In this study, around 66 variants were identified with variable frequencies and across different gene regions. The most prevalent mutation was P323L (94.7%) found in the non-structural protein 12 followed by the D614G (92.6%) in the Spike glycoprotein (Supplementary Figure S1). Another mutation (G71S) in the nonstructural protein 5 region was present at a frequency of 70% in the study sample (Supplementary Figure S1). Some of the identified mutations were defining a specific clade such as G204R and D614G in the Spike protein that constitutes the B.1.1.27 and the B.1.1 (GR). Interestingly, the common G71S mutation was not seen in the family cluster I, which belonged to B.1.1 (GR).

Two unique missense mutations were detected in this study; I280V in the NSP15 and R502C in the NSP13, which existed at low frequencies of 6 (5.3%) and 2 (2.1%), respectively (Supplementary Figure S1). The mutation I280V belonged to lineage B.1.113 (GH), it was detected in cluster V in Al Batinah South and Muscat. The second mutation was detected in two cases that belonged to B.1.1 (GR) lineage within the E cluster of the Al Batinah South region (EPI_ISL_491143 and EPI_ISL_491144) as shown in Figure 2.

*Phylogenomic analysis*

We performed a detailed phylogenomic analysis through ML of the 94 sequenced samples. The whole viral genomes were aligned through a multiple alignment analysis and compared with the Wuhan reference genome (Genbank: MN908947). The phylogenetic analysis was also supplemented with epidemiological datasets of epi week of infection onset and distribution of the identified clusters across different geographical locations in Oman (Figure 3). Generally, there was a good correlation between the epidemiologically defined clusters and their phylogenomic relationship as shown with cluster B, V, I, G, R, X, and W. The phylogenetic tree in Figure 3 showed that cluster B started early, under a month following the first laboratory-confirmed cases identified in Oman. The outbreak continued for around six weeks. Sequences from this cluster belonged to B.1.1.27 (GR) and all were closely related to each other except for one case lineage B (O) but was found to be epidemiologically linked to the index case and was within the same geographical location. It is also observed from Figure 4 that during weeks 16 and 17, multiple outbreaks were detected that affected different geographical locations; clusters: B, C, H, I, J, O, V, and W. The clusters were found to belong mostly to B.1.1 lineage except for one cluster (V) that was B.1.36 (GH). Some clusters were localized in specific governorates that shared a monophyletic clade within the phylogenetic tree such as cluster I, which belonged to Dhahira and cluster V that was found in Al Batinah South having >90% bootstrap support.

To compare the distribution of SARS-CoV-2 sequences from Oman with other countries in the region and globally, we obtained a subset of sequences from neighboring countries and cases with travel history within the same period of this study. In the second phylogenetic tree (Figure 4), we analyzed 349 complete SARS-CoV-2 genomes sequences (including 203 sequences from Oman) that were downloaded from GISAIDS on September 1, 2020. The results revealed that most sequences from Oman are closely related to each other and shared the B.1.1 (GR) clade with related genomes within the tree (Figure 4). Those sequences were closely related to sequences from the United Arab Emirates, the Kingdom of Saudi Arabia, Kuwait, Bahrain, Bangladesh, Southeast Asia, and Europe. Another clade, the B.1.36 (GH), was closely related to sequences obtained from KSA, Bahrain, Bangladesh, Iran, Tunisia, and UK. Additionally, it was observed from the tree that Oman had sequences from most of the identified clades or Pangolin lineages. (Figure 4).

## Discussion

To add context to the global data and international genomic consortiums, understand the spread of the virus, and support the epidemiological surveillance for pandemic management, in Oman a sequencing initiative for SARS-CoV-2 was established. Herein, we describe the sequencing of genomes of 94 samples of SARS-CoV-2 selected based on epidemiological and laboratory characteristics, collected from initial cases from the early outbreak clusters between March 22 and May 23, 2020. The consistency between the epidemiological and genetic information highlights the effectiveness of epidemiological surveillance and outbreak investigations. The epidemiological data illustrate the extensive interaction between different types of clusters (company and family) and the vast spread of the infection between other governorates in Oman. This could be explained by the origin of the epidemic that started from the main trade and tourist area in Muscat. Furthermore, the spread of infections between governorates was

[1] https://www.gisaid.org

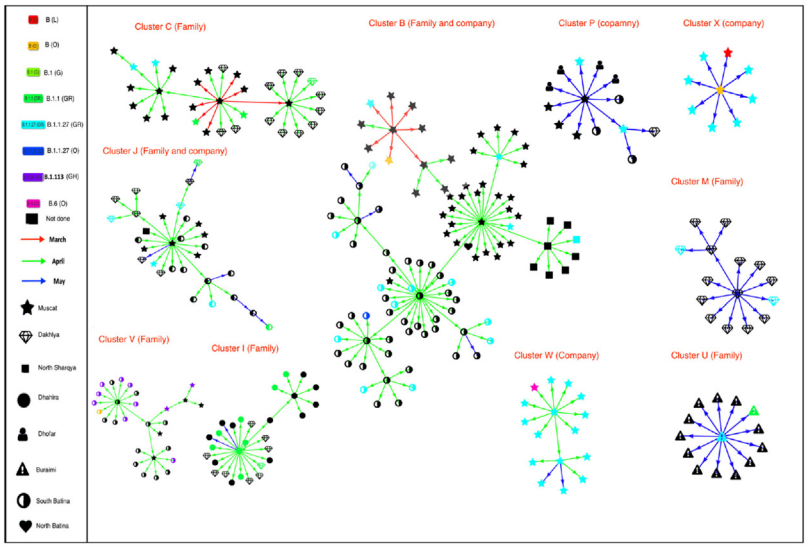


**Figure 2.** Selected clusters with their month of transmission, genotype, geographical location, and type of cluster.

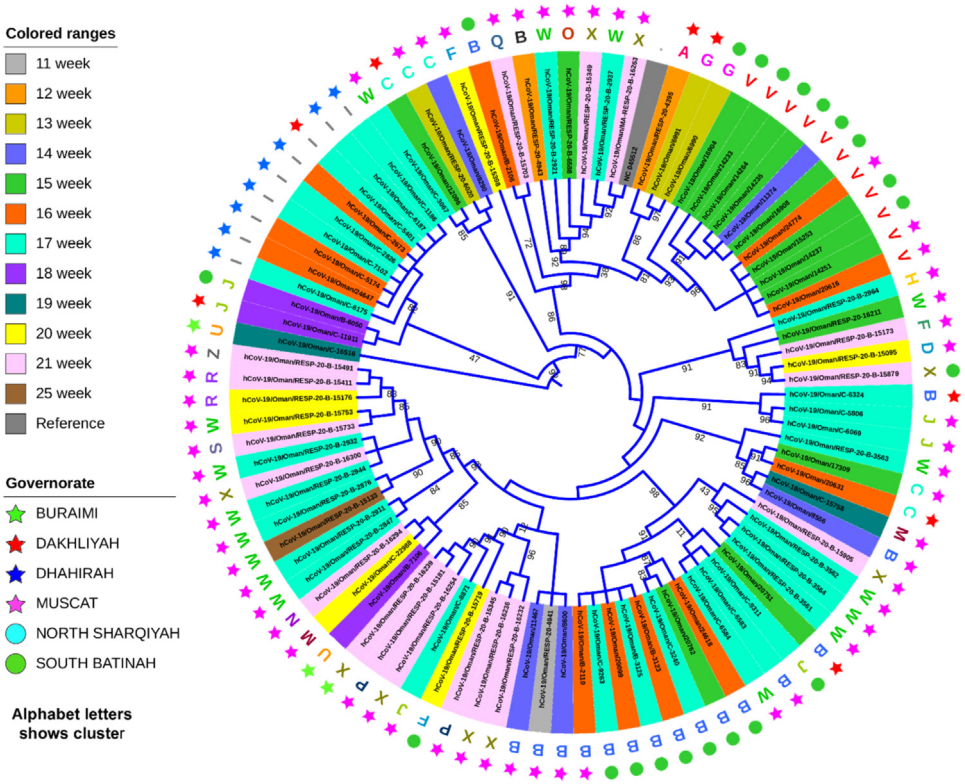


**Figure 3.** Phylogenetic trees were constructed for 94 SARS-CoV-2 complete genomes collected from Oman. The tree was constructed using the ML method. The numbers above the branches are the bootstrap values for ML. Colored ranges represent epi weeks (from weeks 11 to 25). Stars and other ligands represent governorates of Oman, while alphabetic letters denote different clusters in Oman.

propagated by the gatherings among extended Omani families as well as in crowded labor camps, thereby resulting in infection among nonnationals.

In this study, common and unique variants were identified from the genomic analysis of SARS-CoV-2. The D614G mutation in the Spike protein has been reported in 116 countries mostly of B1 lineages (GR, G, and GH clades). In Oman, it has been detected since March 2020 among patients with travel history to Europe (UK, Turkey, Spain, and Netherlands), India, Tanzania, and Qatar (Al-Mahruqi et al., unpublished data). The D614G was found to be the second-highest mutation with a frequency of 92.6% (87/94) in our study. Sallam et al. (2020) showed that the D614G mutation appeared to be taking over COVID-19 infections in the Middle East and North Africa (MENA) region as a significant increase in the proportion was noticed from 63.0% in February 2020 to 98.5% in June 2020 ($p < 0.001$). Two large phylogenetic clusters were identified through the ML analysis, which showed the evidence of intercountry mixing of sequences dating back to February 8, 2020

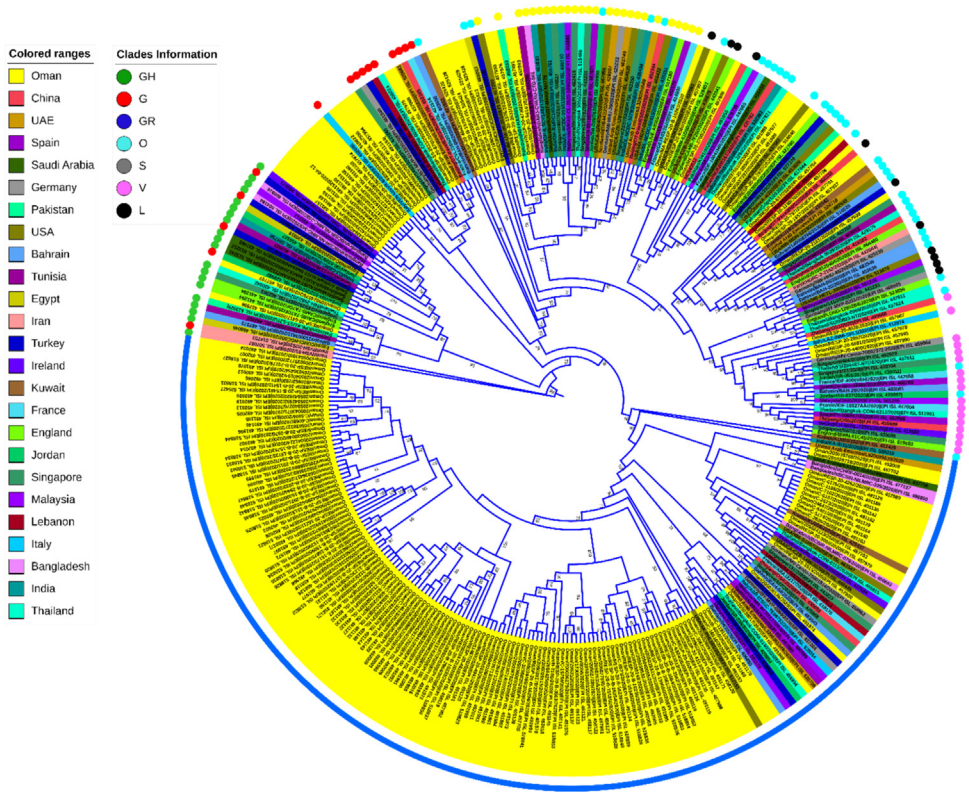


**Figure 4.** Phylogenetic trees constructed for 349 complete SARS-CoV-2 genome sequences (including 203 sequences from Oman) were downloaded from GISAID from March to May 2020. The tree was constructed using the ML method. The numbers above the branches are the bootstrap values for ML. Colored ranges represent different countries. Different color circles show different clades according to GISAID phylogeny.

and March 15, 2020. Another commonly observed mutation in this study, P323L, was described as the most common in other countries; furthermore, the increasing ratio of P323L indicates that this type of mutation may favor and enhance the transmission capacity of SARS-CoV-2 (Wang et al., 2020). Both D614G and P323L were prevalent and coexisted in this study with almost the same frequency. It was suggested that these coevolving mutations and how they could impact viral fitness, breadth, and complexity of clinical symptoms may be associated with new mutations and adaptations (Kannan et al., 2020). According to GISAID, this G71S common mutation was first reported in February 2020 in Germany (hCoV-19/Germany/BW-ChVir-1577/2020) and belongs to the B.1 lineage (G and GR clades) (https://www.gisaid.org/, 6-11-2020). This mutation was reported in 26 countries, Oman had the second-highest prevalence rate of 125/203 (61%) of the globally reported cases (COVID-19 Genomics UK Consortium).

The unique mutation NSP15-I280V detected in this study is in the endoRNAse of the NSP15 genomic region of SARS-CoV-2. The I280V mutation has been reported in only three countries, Oman was the first to report this mutation from a strain (hCoV-19/Oman/11374/2020) collected on April 7, 2020 among the V cluster that was observed in Al Batinah South Governorate. The mutation was later reported in UK in a strain collected in April 2020, B.1. lineage (G), hCoV-19/England/CAMB-1AE373/2020 (CVR Bioinformatics, Glasgow, UK). Unfortunately, the origin of this mutation is not known as no travel history could be linked to the index case of this cluster. This unique mutation is worth further investigation for its biological effect on the pathogenesis of the virus. It is of grave importance to know the level of impact novel variants have on disease severity (Hodcroft et al., 2020).

Phylogenetic analysis of all SARS-CoV-2 Oman sequences deposited in GISAID and compared with a subset of sequences obtained from other countries revealed the presence of several lineages in the country initially. This lined up with the multiple introductions due to travel and before the travel restrictions on March 29. Similar findings were observed in UAE (Tayoun et al., 2020; Alandijany et al., 2020). Early cases detected in Oman in February 2020 with a travel history from Iran belonging to B.4 (O) (Al-Mahruqi et al., unpublished data) were also closely related to cases from UAE, Lebanon, Bahrain, Pakistan, and Kuwait. However, this clade was absent in the selected clusters of this study. Similar findings were observed from sequences in other clades, except for the dominant clade B.1.1 and B.1.1.27 lineage (GR clade) that caused major outbreaks in the country. The B1.1 lineage (GR) comprising both Spike D614G and nucleocapsid RG203KR mutations, was the major clade found in Oman, which is inconsistent with the current globally predominant clade in Europe, Asia, South America, and Africa.

In general, and according to data deposited to GISAID, countries tend to resemble the clades of their continents, with a few exceptions. In China, the L clade (original) still dominates but other clades were obviously introduced after the reopening of the country (Mercatelli and Giorgi, 2020).

Currently and globally, the predominant clade worldwide is G and its offspring GH and GR (74% of world sequenced genomes), which vary remarkably within continents, and this variation is well pronounced in Europe.

Interestingly, GH is most prevalent in USA while GR is dominant in Europe and the most common worldwide. Regionally, in KSA, GH has the highest prevalence, which is possibly due to related travel history with USA. Not unexpectedly, UAE has a blend of all clades, but GR is dominant. In contrast to KSA, GR is dominating in Oman, which could be explained by related travel history with UK where GR is prevalent (Mercatelli and Giorgi, 2020).

According to GISAID, scarce published data are available on genetic characteristics of SARS-CoV-2 in the GCC region. Reviewing

these sequences from KSA (419), UAE (148), Bahrain (27), Qatar (16), Iran (18), and Kuwait (8) during the same period of our study revealed that GR clade was predominant in Oman and UAE, while GH clade was dominant in KSA. However, the mutation G71S is only present in Oman. The genome sequencing of SARS-CoV-2 has proceeded worldwide at an extraordinary rate with numerous published reports following the first published genome from Wuhan. This fact, however, does not prove true in the MENA region where the literature in this area is scarce. It is noteworthy mentioning that there are a few reports from UAE (49 isolates), Egypt (2 isolates), and Iran (7 isolates). However, in addition to the small number of samples used, these studies are based on the phylogenetic analysis only and no association with epidemiological surveillance was performed (Tabibzadeh et al., 2020; Tayoun et al., 2020; Kandeil et al., 2020).

From a timeline perspective, the current pandemic started with an original strain (L) then mutated in early 2020 to clade S and to a lesser extent, clade O. About two weeks later, clade V appeared that mutated in NSP6 and ORF3a. Then clade G appeared at the end of January 2020 and the first appearance of its subclades, GR and GH (mutated in Spike D614G, ORF3a, and Q57H), emerged about three weeks later (February 20, 2020). Since then, clade G and its derivatives have become the most dominant.

While infectiousness and transmissibility are closely related, they are not necessarily synonymous to one another, and therefore, detailed studies are needed to decide whether or not the D614G mutation has contributed to an increase in the number of infections and not simply higher viral loads during infection (Volz et al., 2021 and COVID-19 Genomics UK Consortium, 2020a). Interestingly the entire region is sharing the same common mutations within the same clades (COVID-19 Genomics UK Consortium, 2020b). As the pandemic is ongoing, so is the likely rise to further mutations and possible exhibition of phenotypic changes; our ability to assess and trace these variations will aid in apt and timely response measures.

To the best of our knowledge, this is the first large-scale molecular epidemiology study of COVID-19 in the MENA region where the whole-genome sequencing of 94 samples of SARS-CoV-2 was coupled with epidemiological surveillance of the early transmission of COVID-19 in Oman. This has allowed us to link the surveillance information with the genetic analysis of the virus and enabled genotype tracking and identifying the mutations present in circulating strains. In addition, these results provide baseline information to which future genomes can be compared to study evolution.

The main limitation of our study is that it is retrospective and limited our ability in selecting certain epidemiological features for the genotyped samples such as travel-related and severe admissions. However, with the excess sample selected, we managed to involve sufficient samples to cover adequate epidemiological variations in our genotyped sample. This work needs to continue to get accumulated sequencing data and genomic analysis across the spectrum of the cases in the country for understanding diversity, future mutation, and fine-tuning primers used for the diagnosis based on local strains. The study confirms through genetic analysis the good quality of surveillance systems that prove to be robust during the early pandemic.

## Conclusion

Oman's robust surveillance system was very efficient in guiding outbreak investigation processes in the country, and illustrates the future importance of molecular epidemiology in guiding the national response to outbreaks and pandemics. Our work adds context to the global data and international genomic consortiums.

## Authors' contributions

Samira Al-Mahruqi, Amina Al-Jardani, Hanan Al-Kindi, Samiha Al-Kharusi, Intisar Al-Shukri and Aisha Al-Busaidi conducted the lab work and wrote the draft of the manuscript. Adil Al Wahaibi conducted the epidemiological work and the sampling methodology for the clusters and wrote the draft manuscript. Sajjad Asaf, Ahmed N. Al-Rawahi, Ahmed Al-Rawahi, Abdul Latif Khan, Majid Al-Salmani conducted the WGS, the bioinformatics work, and the writing of the draft of the manuscript. Ahmed Al-Harassi and Seif Al-Abri supervised the study and participated in all stages of the manuscript.

## Conflict of interest

The authors declare that they have no conflict of interest.

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## Ethical approval

The study was approved by the Directorate General for Disease Surveillance and Control, and there was no need for patients' consent as the study was anonymous and used the data produced for public health purposes.

| Sr# | Authors | No of strains | Country | Originating Laboratory | Accession ID |
|---|---|---|---|---|---|
| 1 | Fatma Bayrakdar et al | 7 | Turkey | Ministry of Health Turkey | EPI_ISL_428718, EPI_ISL_417413, EPI_ISL_428719, EPI_ISL_429862, EPI_ISL_429871, EPI_ISL_428723, EPI_ISL_429864 |
| 2 | Mehmet Turgut et al. | 1 | Turkey | T.C. Sağlık Bakanlığı Adıyaman İl Sağlık Müdürlüğü Adıyaman Eğitim Ve Araştırma Hastanesi | EPI_ISL_455719 |
| 3 | Ilker Karacan et al | 1 | Turkey | enomic Laboratory (GLAB) (Conjoint lab of Health Directorate of Istanbul and Istanbul Technical University) | EPI_ISL_428368 |
| 4 | Michael Carr et al | 3 | Ireland | UCD National Virus Reference Laboratory | EPI_ISL_418582, EPI_ISL_437684, EPI_ISL_500573 |
| 5 | Rodriguez,C et al. | 3 | France | Hôpital Henri-Mondor Ap-Hp | EPI_ISL_447665, EPI_ISL_447658, EPI_ISL_447654 |
| 6 | Mélanie Albert et al | 2 | France | Sentinelles network | EPI_ISL_421514, EPI_ISL_414600 |
| 7 | Antonin Bal et al | 1 | France | Institut des Agents Infectieux (IAI), Hospices Civils de Lyon | EPI_ISL_419178 |
| 8 | Rasel Ahmed, Md et al | 1 | Bangladesh | Bangladesh Institute of Tropical & Infectious Diseases, COVID-19 Testing Laboratory | EPI_ISL_450339 |
| 9 | | 3 | Bangladesh | National Institute of Laboratory Medicine and Referral Center | EPI_ISL_504184, EPI_ISL_498816, EPI_ISL_466693 |

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| 10 | Md. Murshed Hasan Sarkar et al | 1 | Bangladesh | National Institute of Laboratory Medicine and Referral Center | EPI_ISL_498800 |
| 11 | Senjuti Saha et al | 1 | Bangladesh | Child Health Research Foundation | EPI_ISL_477127 |
| 12 | Siyuan Yang et al | 4 | Beijing | Laboratory of Infectious Diseases Center of Beijing Ditan Hospital | EPI_ISL_452344, EPI_ISL_452333, EPI_ISL_452345, EPI_ISL_455693 |
| 13 | Lin Qi et al | 1 | Fujian | Fujian Center for Disease Control and Prevention | EPI_ISL_431783 |
| 14 | Shengyue Wang et al | 1 | Shanghai | Shanghai Public Health Clinical Center, Shanghai Medical College, Fudan University | EPI_ISL_416382 |
| 15 | Gao,Q et al | 2 | Zhejiang | Department of Microbiology | EPI_ISL_455689, EPI_ISL_455688 |
| 16 | Rita Feghali et al | 2 | Lebanon | Rafik Hariri University Hospital | EPI_ISL_450512, EPI_ISL_450511 |
| 17 | Abi Habib,W et al | 1 | Lebanon | Lebanese American University | EPI_ISL_498551 |
| 18 | Issa Abu-Dayyeh et al | 6 | Jordan | Biolab Diagnostic Laboratories | EPI_ISL_429998, EPI_ISL_430011, EPI_ISL_429997, EPI_ISL_450187, EPI_ISL_429994, EPI_ISL_429992 |
| 19 | Mohd Noor Mat Isa et al | 2 | Malaysia | National Public Health Laboratory | EPI_ISL_416885, EPI_ISL_528739 |
| 20 | Yoong Min CHONG et al | 3 | Malaysia | Department of Medical Microbiology, University Malaya Medical Centre | EPI_ISL_501226, EPI_ISL_501206, EPI_ISL_501176 |
| 21 | Hajar Fauzan Ahmad et al | 1 | Malaysia | Microbiology Unit, Department of Pathology & Laboratory Medicine, IIUM Medical Centre | EPI_ISL_455313 |
| 22 | Suppiah J et al | 1 | Malaysia | Institute for Medical Research, Infectious Disease Research Centre, National Institutes of Health, Ministry of Health Malaysia | EPI_ISL_490089 |
| 23 | Mak TM et al | 12 | Singapore | National Public Health Laboratory, National Centre for Infectious Diseases | EPI_ISL_462415, EPI_ISL_443231, EPI_ISL_462350, EPI_ISL_428827, EPI_ISL_527370, EPI_ISL_462280, EPI_ISL_443233, EPI_ISL_435698, EPI_ISL_443240, EPI_ISL_462363, EPI_ISL_443223, EPI_ISL_475968 |
| 24 | Danielle E Anderson et al | 1 | Singapore | National Centre for Infectious Diseases | EPI_ISL_420104 |
| 25 | Chen YYC et al | 1 | Singapore | Department of Laboratory Medicine Tan Tock Seng Hospital | EPI_ISL_492979 |
| 26 | Pilailuk,Okada et al | 3 | Thailand | Ramathibodi Hospital | EPI_ISL_515468, EPI_ISL_447921, EPI_ISL_430842 |
| 27 | Elizabeth Batty et al | 5 | Thailand | Ramathibodi Hospital | EPI_ISL_429175, EPI_ISL_447011, EPI_ISL_512861, EPI_ISL_458024, EPI_ISL_455915, EPI_ISL_455934 |
| 28 | Rodpan,A et al | 2 | Thailand | Faculty of Medicine | EPI_ISL_437611, EPI_ISL_437624 |
| 29 | Samira Al-Maruqi et al | 30 | Oman | Oman-NIC | EPI_ISL_457701, EPI_ISL_457704, EPI_ISL_457706, EPI_ISL_457937, EPI_ISL_457938, EPI_ISL_457939, EPI_ISL_457974, EPI_ISL_457975, EPI_ISL_457976, EPI_ISL_457977, EPI_ISL_457978, EPI_ISL_457979, EPI_ISL_457980, EPI_ISL_491116, EPI_ISL_457987, EPI_ISL_457985, EPI_ISL_457986, EPI_ISL_457988, EPI_ISL_457989, EPI_ISL_457990, EPI_ISL_457991, EPI_ISL_457992, EPI_ISL_457993, EPI_ISL_457994, EPI_ISL_457995, EPI_ISL_457996, EPI_ISL_457997, EPI_ISL_457998, EPI_ISL_492065 |
| 30 | Fahad Zadjali et al | 68 | Oman | Oman-NIC | EPI_ISL_457702, EPI_ISL_457703, EPI_ISL_457705, EPI_ISL_457707, EPI_ISL_457981, EPI_ISL_457982, EPI_ISL_457983, EPI_ISL_457984, EPI_ISL_458116, EPI_ISL_458117, EPI_ISL_458118, EPI_ISL_458119, EPI_ISL_458120, EPI_ISL_458121, EPI_ISL_458122, EPI_ISL_458123, EPI_ISL_458124, EPI_ISL_458125, EPI_ISL_458126, EPI_ISL_458127, EPI_ISL_458128, EPI_ISL_458137, EPI_ISL_491968, EPI_ISL_491969, EPI_ISL_491970, EPI_ISL_491971, EPI_ISL_491972, EPI_ISL_491973, EPI_ISL_491974, EPI_ISL_491975, EPI_ISL_491976, EPI_ISL_491977, EPI_ISL_491978, EPI_ISL_491979, EPI_ISL_491980, EPI_ISL_491981, EPI_ISL_491982, EPI_ISL_491983, EPI_ISL_491984, EPI_ISL_491985, EPI_ISL_491986, EPI_ISL_491987, EPI_ISL_491988, EPI_ISL_491989, EPI_ISL_491990, EPI_ISL_491991, EPI_ISL_491992, EPI_ISL_491993, EPI_ISL_491994, EPI_ISL_491995, EPI_ISL_491996, EPI_ISL_491997, EPI_ISL_491998, EPI_ISL_491999, EPI_ISL_492000, EPI_ISL_492001, EPI_ISL_492002, EPI_ISL_492003, EPI_ISL_492004, EPI_ISL_492005, EPI_ISL_492006, EPI_ISL_492007, EPI_ISL_492008, EPI_ISL_492009, EPI_ISL_492010, EPI_ISL_492011, EPI_ISL_492012, EPI_ISL_492013, EPI_ISL_492014, EPI_ISL_492015, EPI_ISL_492016, EPI_ISL_492017, EPI_ISL_492018, EPI_ISL_492019, EPI_ISL_492020, |

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| 37 | Shahabzadeh,Z | 3 | Iran | Yaftabad Hospital, Covid Lab Center | EPI_ISL_507007, EPI_ISL_514753, EPI_ISL_442044 |
| 38 | Fahd Al-Mulla et al | 4 | Kuwait | Dasman Diabetes Institute | EPI_ISL_416543, EPI_ISL_421652, EPI_ISL_422426, EPI_ISL_422427 |
| 39 | Javed,A et al | 1 | Pakistan | Department of Healthcare Biotechnology, National University of Sciences and Technology (NUST) | EPI_ISL_417444 |
| 40 | Shakeel,M et al | 1 | Pakistan | Jamil-ur-Rahman Center for Genome Research, Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi | EPI_ISL_451958 |
| 41 | Massab Umair et al | 1 | Pakistan | Department of Virology, Public Health Laboratories Division, National Institute of Health | EPI_ISL_468163 |
| 42 | Khan,M.T et al | 1 | Pakistan | Microbiology & Bioinformatics and Biostatistics, Kohat University of Science and Technology (Pakistan) & Shanghai Jiao Tong University (China) | EPI_ISL_513925 |
| 43 | Sunil Raghav et al | 2 | India | Institute of Life Sciences, Bhubaneswar | EPI_ISL_463033, EPI_ISL_455761 |
| 44 | Pramod Kumar et al | 3 | India | National Centre for Disease control (NCDC) | EPI_ISL_436434, EPI_ISL_435111, EPI_ISL_435110 |
| 45 | Saurabh Kumar et al | 1 | India | Translational Health Science and Technology Institute -ESIC medical college and hospital, Faridabad | EPI_ISL_528383 |
| 46 | Dinesh Kumar et al | 1 | India | GMERS Medical College and Hospital, Dharpur, Patan | EPI_ISL_524758 |
| 47 | Arindam Maitra et al | 1 | India | Indian Institute of Science | EPI_ISL_508310 |
| 48 | Amit Kumar Subudhi et al | 2 | Saudia Arabia | Pathogen Genomics Lab King Abdullah University of Science and Technology(KAUST) | EPI_ISL_513248, EPI_ISL_513241 |
| 49 | Sharif Hala et al | 2 | Saudia Arabia | Pathogen Genomics Lab King Abdullah University of Science and Technology(KAUST) | EPI_ISL_437463, EPI_ISL_437756 |
| 50 | Majed Alghoribi et al | 1 | Saudia Arabia | Clinical Microbiology Lab | EPI_ISL_416432 |
| 51 | Sara Mfarrej et al | 1 | Saudia Arabia | Pathogen Genomics Lab King Abdullah University of Science and Technology(KAUST) | EPI_ISL_512978 |
| 52 | Afrah Alsomali et al | 1 | Saudia Arabia | Pathogen Genomics Lab King Abdullah University of Science and Technology(KAUST) | EPI_ISL_513257 |
| 53 | Ahmad Abou Tayoun et al | 6 | UAE | Mohammed Bin Rashid University of Medicine and Health Sciences | EPI_ISL_520695, EPI_ISL_463740, EPI_ISL_520718, EPI_ISL_520681, EPI_ISL_520708, EPI_ISL_520738 |
| 54 | Ortwin Adams et al | 2 | Germany | Center of Medical Microbiology, Virology, and Hospital Hygiene, University of Duesseldorf | EPI_ISL_425123, EPI_ISL_425130 |
| 55 | Max Muenchhoff et al | 3 | Germany | Max von Pettenkofer Institute, Virology, National Reference Center for Retroviruses, LMU München | EPI_ISL_466905, EPI_ISL_451940, EPI_ISL_437284 |
| 56 | Peter Bauer and Krishna Kumar Kandaswamy | 2 | Germany | Centogene AG | EPI_ISL_459964, EPI_ISL_459962 |
| 57 | Lorusso A et al | 1 | Italy | Ospedale "Ss. Annunziata" | EPI_ISL_529014 |
| 58 | Antonio Mori et al | 1 | Italy | IRCCS Sacro Cuore Don Calabria Hospital, Department of Infectious, Tropical Diseases & Microbiology | EPI_ISL_492985 |
| 59 | Paola Stefanelli et al | 1 | Italy | Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy | EPI_ISL_412974 |
| 60 | Guillermo Martín Gutiérrez et al | 1 | Spain | Servicio de Microbiología y Parasitología clínica. UCEIMP. Hospital Universitario Virgen del Rocío/IBIS/CSIC/US. | EPI_ISL_452570 |
| 61 | Salud Rodríguez-Pallares, et al | 2 | Spain | Hospital Universitario Puerta del Mar de Cádiz - INIBICA | EPI_ISL_467071, EPI_ISL_467080 |
| 62 | Gustavo Cilla et al | 1 | Spain | Servicio de Microbiología. Hospital Universitario Donostia. OSI Donostialdea. Área de Enfermedades Infecciosas, Grupo | EPI_ISL_452688 |
| 63 | Antonio Rezusta López et al | 1 | Spain | Servicio de Microbiología, Hospital Miguel Servet, Zaragoza | EPI_ISL_468780 |
| 64 | McHugh M | 1 | Schotland | Virology Department, Royal Infirmary of Edinburgh, NHS Lothian / School of Biological Sciences, University of Edinburgh / Institute of Genetics and Molecular Medicine, University of Edinburgh | EPI_ISL_426007 |
| 65 | Sam Haldenby et al | 1 | England | Liverpool Clinical Laboratories | EPI_ISL_517180 |
| 66 | Luke W Meredith et al | 3 | England | Department of Pathology, University of Cambridge | EPI_ISL_441294, EPI_ISL_442841, EPI_ISL_441294 |
| 67 | Claire McMurray et al | 2 | England | University of Birmingham | EPI_ISL_529403, EPI_ISL_529603 |
| 68 | | 1 | England | | EPI_ISL_421780 |

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| Sr# | Authors | No of strains | Country | Originating Laboratory | Accession ID |
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| 69 | PHE Covid Sequencing Team | 1 | England | Respiratory Virus Unit, Microbiology Services Colindale, Public Health England | EPI_ISL_464480 |
| 70 | Ling Li, et al | 1 | England | North West London Pathology, Imperial College Healthcare NHS Trust | EPI_ISL_524656 |
| 71 | Tracy Basler et al | 1 | USA | San Diego County Public Health Laboratory | EPI_ISL_467956 |
| 72 | Gage Moreno et al | 1 | USA | University of Wisconsin-Madison AIDS Vaccine Research Laboratories | EPI_ISL_417200 |
| 73 | CZB Cliahub Consortium | 1 | USA | Humboldt County Public Health Laboratory | EPI_ISL_454639 |
| 74 | Lemieux,J.E et al | 1 | USA | Massachusetts General Hospital | EPI_ISL_460422 |
| 75 | Michael Quigley et al | 1 | USA | Scripps Medical Laboratory | EPI_ISL_437582 |
| 76 | Anna Uehara et al | 1 | USA | Pathogen Discovery, Respiratory Viruses Branch, Division of Viral Diseases, Centers for Dieases Control and Prevention | EPI_ISL_413609 |
| 77 | Matt Plumb et al | 1 | USA | Minnesota Department of Health, Public Health Laboratory | EPI_ISL_482949 |
| 78 | Matluk,N et al | 1 | USA | Maine HETL | EPI_ISL_513470 |
| 79 | CZB Cliahub Consortium | 3 | USA | County of Santa Clara Public Health | EPI_ISL_437061, EPI_ISL_436679, EPI_ISL_468445 |
| 80 | Chu et al | 1 | USA | Washington State Department of Health | EPI_ISL_463547 |
| 81 | Chen J et al | 1 | USA | Alaska State Virology Laboratory | EPI_ISL_512151 |
| 82 | Fares,W. and Triki,H. | 3 | Tunisia | Clinical virology | EPI_ISL_463002, EPI_ISL_463003, EPI_ISL_463005 |
| 83 | Handrick,S et al | 1 | Tunisia | Bundeswehr Institute of Microbiology | EPI_ISL_458286 |
| 84 | Mohamed Ahmed Ali et al | 1 | Egypt | Center of Scientific Excellence for Influenza Viruses,National Research Centre (NRC), Egypt. | EPI_ISL_430819 |
| 85 | Zekri, Abdel Rahman et al | 2 | Egypt | Egyptian National Cancer Institute (ENCI) | EPI_ISL_468045, EPI_ISL_468062 |

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2020.12.049.

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