



ANALYSIS OF SARS-COV-2 GENOMES SAMPLES FROM PERU

ANÁLISIS DE GENOMAS DE SARS-COV-2 EN MUESTRAS DE PERÚ

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ABSTRACT

Introduction: Genomic analysis of samples from documented COVID-19 cases can be used successfully to help track sources of Sars-Cov-2 infection, which can be quarantined to prevent the recurrent spread of the disease around the world. **Objectives:** To describe the SARS-CoV-2 sequences isolated from Peruvian patients. **Methods:** All genomes published up to March 2021, uploaded in the GISAID and Nextstrain repository, were selected. All data is on the web in a public way; In addition, the information was filtered by continent, country, region, clade, lineage, and sex from March 2020 to February 2021. **Results:** It was evidenced that the region with the most isolated genomes was Lima, the most frequent clade is GR, the viral lineage B.1.1 is the most frequent and persistent in time and most of the genomes were isolated from people of the female sex. **Conclusions:** The clade GR is common to all South American countries and the European and Asian continents, followed by clades G and GH with greater frequency; on the other hand, the most persistent viral lineage in Peru is B.1.1, this being not common with other countries.

Key words: Coronavirus Infections; Genome; Viral; Whole Genome Sequencing; Mutation; Peru (source: MeSH NLM).

RESUMEN

Introducción: El análisis genómico de muestras de casos documentados de COVID-19 puede usarse con éxito para ayudar a rastrear fuentes de infección por Sars-Cov-2, que pueden ponerse en cuarentena para prevenir la propagación recurrente de la enfermedad en todo el mundo. **Ojetivos:** Describir las secuencias de SARS-CoV-2 aisladas de pacientes peruanos. **Métodos:** Se seleccionaron todos los genomas publicados hasta marzo del 2021, subidos en el repositorio de GISAID y Nextstrain. Todos los datos están en la web de manera pública; además se filtró la información por continente, país, región, clado, linaje y sexo desde marzo de 2020 hasta febrero de 2021. **Resultados:** Se evidenció que la región con la mayoría de los genomas aislados fue Lima, el clado más frecuente es el GR, el linaje viral B.1.1 es el más frecuente y persistente en tiempo y la mayor parte de genomas fueron aislados de personas del sexo femenino. **Conclusión:** El clado GR es común para todos los países sudamericanos y los continentes europeos y asiáticos, seguido de los clados G y GH con mayor frecuencia; por otro lado, el linaje viral más persistente en Perú es el B.1.1, siendo este dato no común con otros países.

Palabras clave: Infecciones por Coronavirus; Genoma Viral; Secuenciación Completa del Genoma; Mutación; Perú (fuente: DeCS BIREME).

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INTRODUCTION

At the beginning of 2020, the COVID-19 pandemic raised multiple concerns. It caused a great impact in multiple areas of clinical research⁽¹⁾, specifically in the disciplines of molecular biology and virology specialized in molecular and genomic epidemiology⁽²⁾. The appearance of new genomic tools has been very relevant to understand the different aspects of the SARS-CoV-2 virus⁽³⁾. The initial complete genomic analysis of the sequence of this virus has revealed its taxonomic status as a member of the Betacoronavirus family, with an evident divergence from SARS-CoV and MERS-CoV^(4,5).

The genomic analysis includes three components: DNA sequencing, assembling the sequence to create a representation of the original chromosome, and annotating and analyzing the representation⁽⁶⁾. In a phylogenetic analysis of whole genomes of the human severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), variants are found that are distinguished by amino acid changes. The samples are obtained from documented cases of COVID-19 disease, indicating that phylogenetic networks can also be used successfully to help track sources of COVID-19 infection, which can be quarantined to prevent the recurrent spread of the disease. . worldwide⁽⁷⁾.

Phylogenetic analyzes can be used to elucidate the SARS-CoV-2 reinfected patient in which two genetically different viruses are found from which samples are taken⁽⁸⁾. This is due to recently reported cross-genome mutations at various times and places⁽⁹⁾. Large-scale genomic analysis of the SARS-CoV-2 genome reveals the clonal geographic distribution of mutations hotspot and abundant genetic variation⁽¹⁰⁾. Information on virus variation has considerable medical and biological impact on the prevention, diagnosis, and therapy of infectious diseases⁽⁹⁾. The objective of this manuscript is to

describe the SARS-CoV-2 sequences isolated from Peruvian patients.

METHODS

The following study is descriptive and observational, all genomes published up to January 2021 were selected, public data posted in the GISAID repository (The Global Initiative on Sharing All Influenza Data) and viewed through the Nextstrain website were used. All data is on the web in a public way, uploaded by the same institutions.

The information was filtered by: region, GISAID clade, lineage, and the information was downloaded in TSV format and a phylogenetic tree was created using the iTOL web tool. The images shown were viewed on the Nextstrain website using the rectangular display form of the phylogenetic tree and ordered by date.

The information was filtered by continent, country, region, clade, lineage and gender from March 2020 to February 2021. The statistical software InfoStat was used to prepare the frequency tables and the Chi-square test.

RESULTS

750 sequencing samples were obtained (there is no information on the type of sequencing) of SARS-CoV-2 samples from Peru, of which 392 belonged to male patients (52.3%) and 358 to female patients (47.7%). In addition, a phylogenetic tree was made with the iTOL v5 Interactive Tree Of Life application (Figure 1). The visualizations of the isolated genomes correspond to the samples of patients from Peru obtained from March 2020 to March 2021; in addition, the data were filtered by clade (Figure 2), by region (Figure 3), by viral lineage (Figure 4) and by gender (Figure 5). The frequencies can be found in table 1.



Table 1. Frequency of lineages and clades by gender isolated from patients in Peru from March 2020 to March 2021.

Lineage	Female	Male	Total	%	p
A	2	0	2	0.27	0.278
A.1	2	0	2	0.27	
A.2	5	1	6	0.8	
A.5	3	1	4	0.53	
B	1	1	2	0.27	
B.1	24	28	52	6.93	
B.1.1	87	93	180	24	
B.1.1.1	41	49	90	12	
B.1.1.10	0	2	2	0.27	
B.1.1.110	5	7	12	1.6	
B.1.1.158	2	3	5	0.67	
B.1.1.16	0	1	1	0.13	
B.1.1.166	1	0	1	0.13	
B.1.1.207	1	0	1	0.13	
B.1.1.220	1	3	4	0.53	
B.1.1.221	5	4	9	1.2	
B.1.1.25	1	0	1	0.13	
B.1.1.274	0	1	1	0.13	
B.1.1.28	1	0	1	0.13	
B.1.1.348	14	13	27	3.6	
B.1.1.370	0	1	1	0.13	
B.1.1.372	0	1	1	0.13	
B.1.1.381	6	6	12	1.6	
B.1.1.485	4	6	10	1.33	
B.1.1.500	1	1	2	0.27	
B.1.1.7	3	0	3	0.4	
B.1.111	1	2	3	0.4	
B.1.13	1	0	1	0.13	
B.1.177	3	1	4	0.53	
B.1.177.45	2	0	2	0.27	
B.1.2	4	1	5	0.67	
B.1.205	15	12	27	3.6	
B.1.234	0	2	2	0.27	

B.1.547	0	1	1	0.13	
B.1.596	0	1	1	0.13	
B.1.610	0	4	4	0.53	
B.1.8	0	1	1	0.13	
B.3	1	0	1	0.13	
C.11	13	23	36	4.8	
C.13	7	14	21	2.8	
C.14	58	52	110	14.67	
C.22	1	1	2	0.27	
C.23	0	1	1	0.13	
C.25	1	6	7	0.93	
C.32	12	9	21	2.8	
C.33	5	4	9	1.2	
C.37	4	3	7	0.93	
C.4	20	29	49	6.53	
N.4	0	2	2	0.27	
P.1	0	1	1	0.13	
Total	358	392	750	100	
Clade	Female	Male	Total	%	p
G	34	37	71	9.47	0.0264
GH	10	14	24	3.2	
GR	292	335	627	83.6	
GRY	3	0	3	0.4	
GV	5	1	6	0.8	
L	1	0	1	0.13	
O	1	2	3	0.4	
S	12	2	14	1.87	
V	0	1	1	0.13	
Total	358	392	750	100	



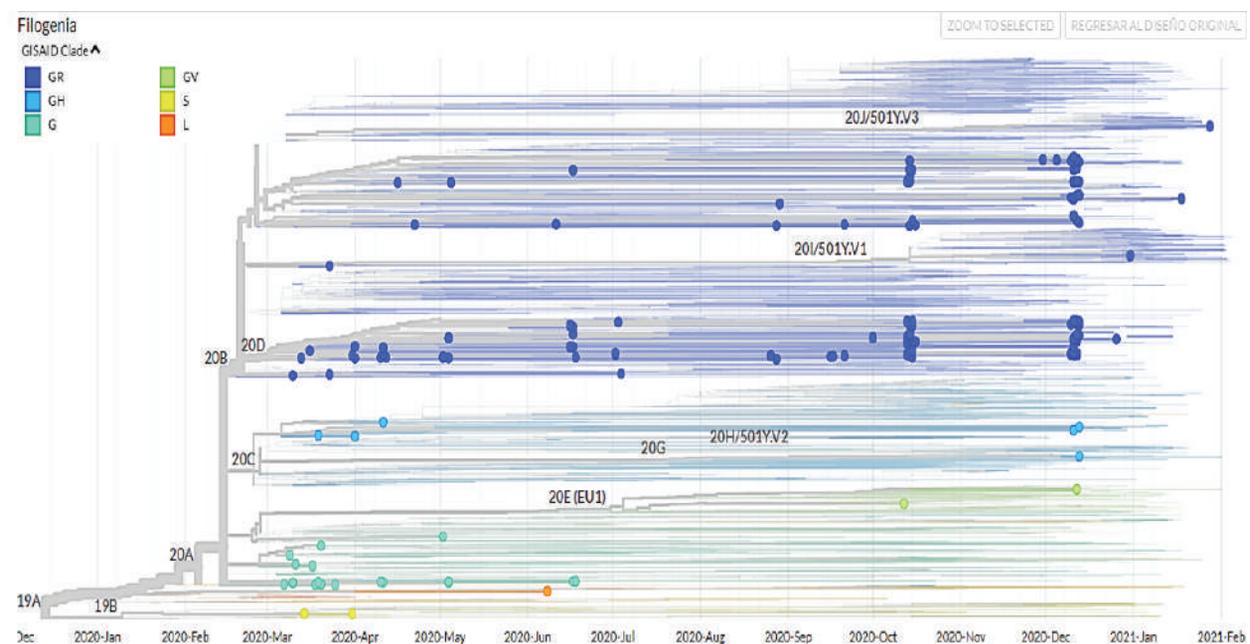
Table 2. Frequency of lineages and clades by region isolated from patients in Peru from March 2020 to February 2021.

Lineage	AMA	ANC	APU	ARE	AYA	CAJ	CAL	CUS	HCV	HUA	ICA	JUN	LAL	LAM	LIM	LOR	MOQ	PAS	PIU	SMN	TAC	UCA	Total	p	
A	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	0	0	0	0	0	0	0	3	<0.0001
A.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	3	
A.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	0	0	0	0	0	0	0	0	8	
A.5	0	0	0	0	0	0	2	0	0	0	2	0	0	0	5	0	0	0	0	0	0	0	0	9	
B	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	2	
B.1	0	2	0	8	0	0	5	1	2	0	1	14	0	2	38	1	0	0	0	0	0	0	0	74	
B.1.1	11	4	1	21	1	0	17	1	1	6	9	1	1	3	160	33	2	1	8	4	1	1	1	287	
B.1.1.1	3	5	0	0	0	0	5	0	0	2	5	1	0	3	85	4	0	0	0	0	0	0	0	113	
B.1.1.10	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	
B.1.1.110	0	0	0	0	0	0	2	0	0	0	0	3	0	0	7	0	0	0	0	0	0	0	0	12	
B.1.1.158	0	1	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	5	
B.1.1.16	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	
B.1.1.166	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	
B.1.1.207	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	
B.1.1.220	0	0	0	1	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	5	
B.1.1.221	0	1	0	0	0	0	2	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0	0	9	
B.1.1.25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	
B.1.1.274	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	
B.1.1.28	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	2	
B.1.1.319	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	0	0	0	0	0	0	0	0	4	
B.1.1.348	0	3	0	2	0	0	3	0	0	3	0	0	0	0	43	4	2	0	0	0	0	0	0	60	
B.1.1.370	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	
B.1.1.372	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2	
B.1.1.381	0	0	0	0	0	0	2	0	0	1	0	0	0	0	10	0	0	0	0	0	0	0	0	13	
B.1.1.398	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	
B.1.1.434	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	
B.1.1.485	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0	0	10	
B.1.1.500	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	
B.1.1.54	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	
B.1.1.7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	3	
B.1.1.11	0	0	0	2	0	0	1	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	7	
B.1.1.3	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	
B.1.1.77	0	1	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	4	

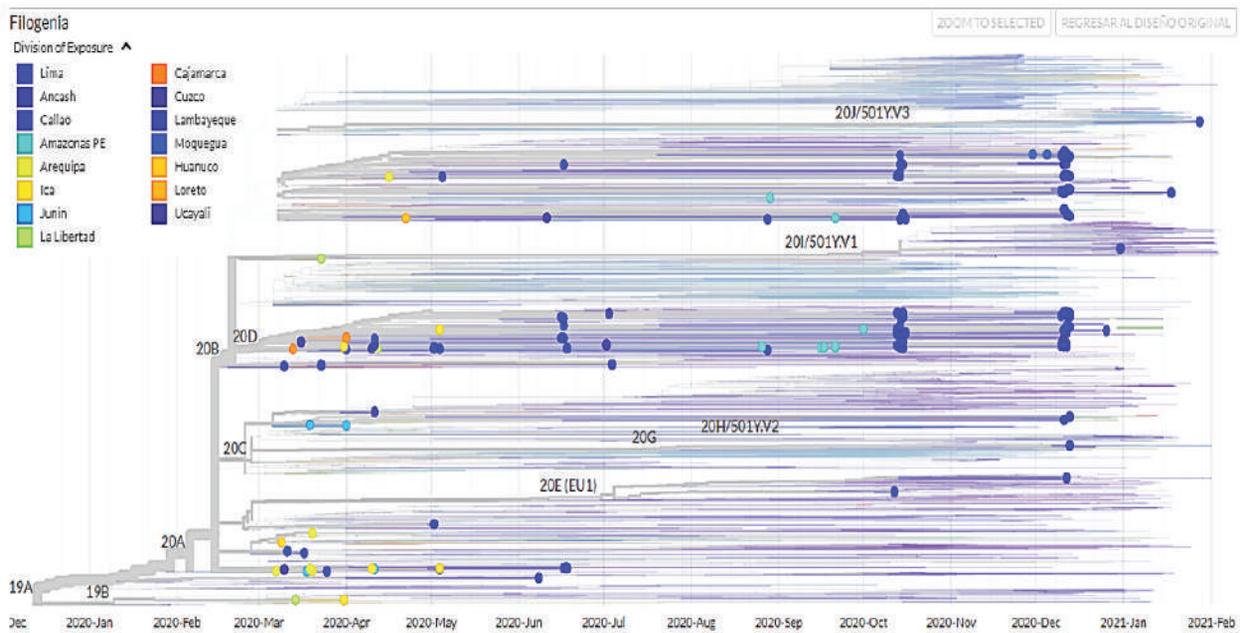
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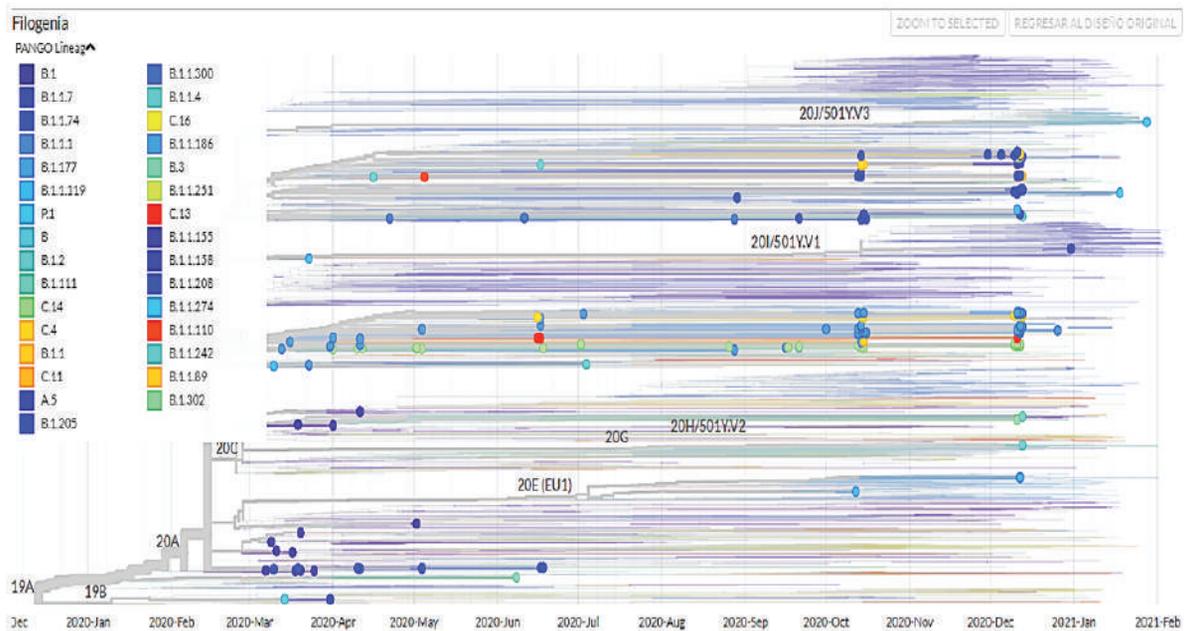
Graphic 1. Phylogenetic tree of genomes isolated from patients from Peru.



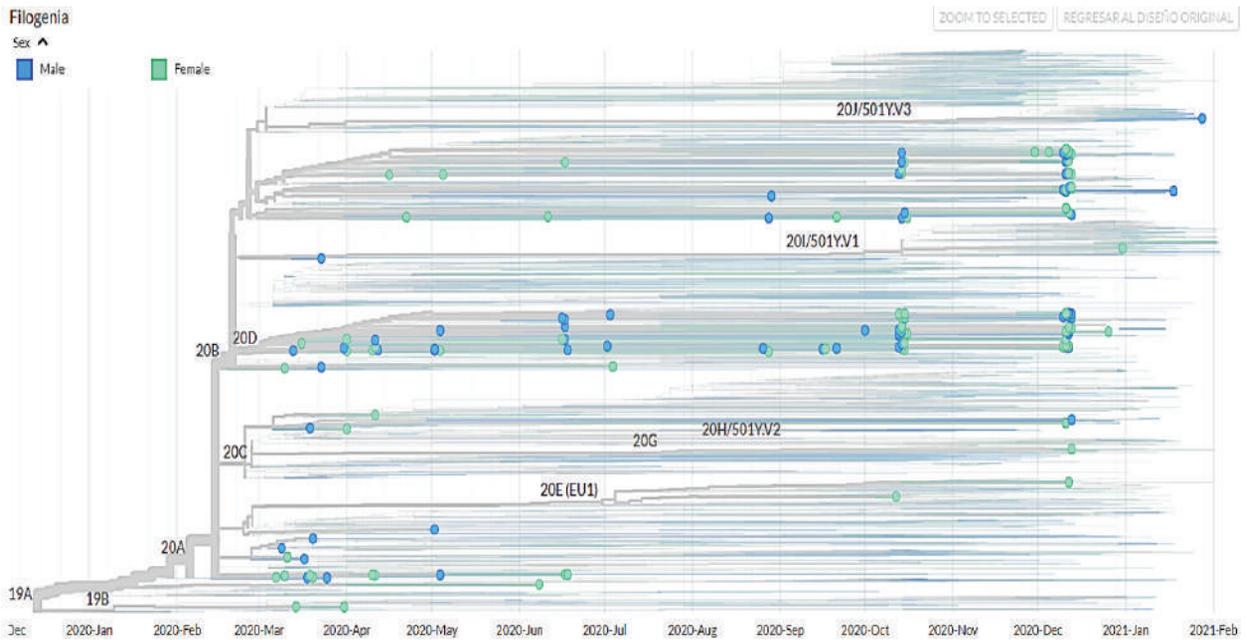
Graphic 2. Isolated genomes of COVID-19 patients in Peru by clade.



Graphic 3. Isolated genomes of COVID-19 patients in Peru by region



Graphic 4. Isolated genomes of COVID-19 patients in Peru by viral lineage.



Graphic 5. Genomes isolated from COVID-19 patients in Peru by gender.

DISCUSSION

The analysis of the different genomes has been very useful to track the SARS-CoV-2 virus in different regions, not only in Peru but also in Latin America and the world. Regarding clades, Peru has identified the GR clade as in all South American countries with the exception of Paraguay, which has not identified SARS-CoV-2 genomes to date; on the other hand, clade G is common among all countries except Venezuela and clade GH in all except Bolivia and Uruguay, these being the most common, followed by clades S, L and GV. Other clades identified in this continent but not in Peru were clades O and V⁽¹¹⁾.

In Uruguay, genetic analysis shows that clades S and G (G, GH, GR) dominate, representing more than 90% of the virus strains in our study; the fatal outcome of SARS-CoV-2 infection is significantly related to hypertension, renal failure and ICU admission (FDR <0.01), but there are no mutations in structural or non-structural proteins such as the D614G peak protein⁽¹²⁾. As in Peru, North American countries such as Canada have tracked the GR clade more frequently, followed by the G and GH clades and the S and L clades less regularly. The latter were identified at the same frequency in the United States. However, in this country the clade GH has been identified with more frequency followed by the clades GR and G; In Mexico, the same does not happen, since the most frequent clades are GR and G followed by GH, being the same in the case of clades S and L being very minor, in addition to the fact that in this part

of the American continent clades were found O and V⁽¹¹⁾. In Europe and Asia, as in Peru, the clades GR, G, and GH have been registered more, and below are the clades S, L, and GV, taking into account that in these continents, a greater number of analyzes of genomes of the virus have been carried out SARS-CoV-2⁽¹¹⁾.

Regarding the viral lineages, differences were found with the genomes isolated in Argentina since the lineage found with the highest frequency and persistence was B.1 followed by B.1.1.33 and B.1.499; the same happens in Bolivia. Although only 14 genomes have been identified, the B.1 lineage persisted through time; in Brazil and Uruguay, the lineages B.1.1.33 and B.1.1.28 were present for approximately the entire time spanned by the pandemic in that country. While in Chile, Colombia and Ecuador, the most frequent and persistent lineages are B.1 and B.1.1.74. In North America, Europe and Asia, the majority lineage is B.1 but in the middle and end of 2020, there was an increase in lineages B.1.2, B.1.1.7 and B.1.177⁽¹³⁾, data that differ with the present study.

In addition to the analysis of genomes found on web platforms, studies published in journals should be considered, as is the case of the research carried out in Ecuador where the most dominant lineage in all sequences from that country was B.1.1.74, followed by B.1 and B.1.1.1⁽¹⁴⁾, which does not coincide with our results. On the other hand, the P.1 lineage was identified in cities of the Brazilian Amazon such as

Manaus⁽¹⁵⁾, which is related to its transmission in the Loreto region where it was the most frequent lineage after B.1.1. Regarding a study carried out in Venezuela, the lineages B.1.1 and B.1.111 were the most persistent in different provinces⁽¹⁶⁾, which is not related to the present investigation, like the lineages identified with the highest incidence in South Africa as are C.1, B.1.1.56 and B.1.1.54⁽¹⁷⁾.

In the case of lineages by regions, Lima has presented the highest number of identified lineages and clades. Therefore, it is suggested that it presents the highest number of infections in that city followed by Callao, Loreto, Áncash, and Arequipa, making the transmissibility of the virus in those cities is very high.

It should be noted that the B.1.1.7 lineage has been very important in terms of the hospitalization of patients in a serious way or in their death, as indicated by a study from the United Kingdom, where more than 60% of patients sampled presented these characteristics⁽¹⁸⁾, as in the United States where the rapid transmission of this lineage caused an increase in deaths⁽¹⁹⁾, which would be related to the present study, since the decreased manifestation of this lineage in Peru did not it is expressed in a disproportionate increase in hospitalizations and deaths, as occurred in the European country. Finally, in a study carried out in India, it has been shown that

the clades GR, GH, and G are the most predominant with more than 70%⁽²⁰⁾, coinciding with our results.

This retrospective study has limitations such as the small sample size, there is no control over the quality of the data that is uploaded, and the bias in data collection.

For these reasons, it is important to carry out a genomic epidemiological surveillance since it could give us a glimpse of the new changes in the variants of SARS-CoV-2 and the use of this information to take containment measures, such as new forms of diagnosis, monitoring, clinic, etc. It is important to track how it spreads and whether the mutations are clinically important in infected patients. This is achieved in a joint work of the state with the researchers.

CONCLUSION

The clade GR is common to all South American countries, European and Asian continents, followed by clades G and GH most frequently; on the other hand, the most persistent viral lineage in Peru is B.1.1, this being not common with other countries. In addition, most of the lineages were identified in the Lima, Callao, Loreto, Ancash, and Arequipa regions.

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