Communication

Omicron sublineages current status in Ecuador

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Abstract: The Omicron variant of SARS-CoV-2 is the latest pandemic lineage causing COVID-19. Despite having a vaccination rate ≥ 85% Ecuador recorded a high incidence of Omicron from December 2021 to March 2022. Since Omicron emerged it is evolving into multiple sublineages with distinct prevalence in different regions. In this work, we use all Omicron sequences from Ecuador available at GISAID until March 2022 and the software Nextclade and Pangolin to identify which lineages circulate in this country. We detected 12 different sublineages (BA.1, BA.1.1, BA.1.1.1, BA.1.1.14, BA.1.1.2, BA.1.14, BA.1.15, BA.1.16, BA.1.17, BA.1.6, BA.2, BA.2.3), which has been reported in Africa, America, Europe, and Asia suggesting multiple introduction events. Sublineages BA.1.1 and BA.1 were the most prevalent. Genomic surveillance must continue to evaluate the dynamic of current sublineages, early introduction of new ones and vaccine efficacy against evolving SARS-CoV-2.

Keywords: COVID-19**;** Omicron; Sublineages; Ecuador

1. Introduction

The novel coronavirus identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the infectious agent causing the pandemic of COVID-19 [1], by April 2022 have led to 483.556.595 positive cases and 6.132.461 deaths worldwide [2]. The mutation rate of this virus is still in debate, but in two years it has evolved into different

variants, some of which have higher transmission rates [3]. The initial SARS-CoV-2 variants have an R0 factor between 2.5- 3.0; however, latest variants such as Delta and Omicron have R0 value of 7, and 10, respectively [4]. Moreover, each emerging variant could diverge into sublineages that needs to be surveilled locally in order to evaluate any change in their transmission dynamics.

Omicron, unlike previous variants, harbor a wide variety of mutations within its genome [5]. Fifteen mutations have been reported only in the Receptor Binding Domain (RBD) region, which enable Omicron to be more transmissible, by allowing the virus to bind more easily to the human Angiotensin-Converting Enzyme 2 (ACE2) protein as compared with the original strain [6]. Other relevant mutations include R203K and G204R, linked to viral replication [4]. According to WHO by April 2022 [7] five major sublineages has been detected globally: BA.1, BA.2, BA.3, BA.4, BA.5 with different frequencies in different regions.

Ecuador is among the countries with a vaccine coverage ≥ 85%; however, following the introduction of the Omicron Variant (lineage BA.1.1 in December 2021) [8] the Ministry of Public Health reported the highest frequency of positive cases since the beginning of the pandemic, accumulating more than 300.000 cases from January to March 2022 [9]. During those months, Omicron became the dominant variant and as elsewhere rapidly replaced Delta which predominated previously (Figure 1). By the end of March, the lineage B.2 was also detected.

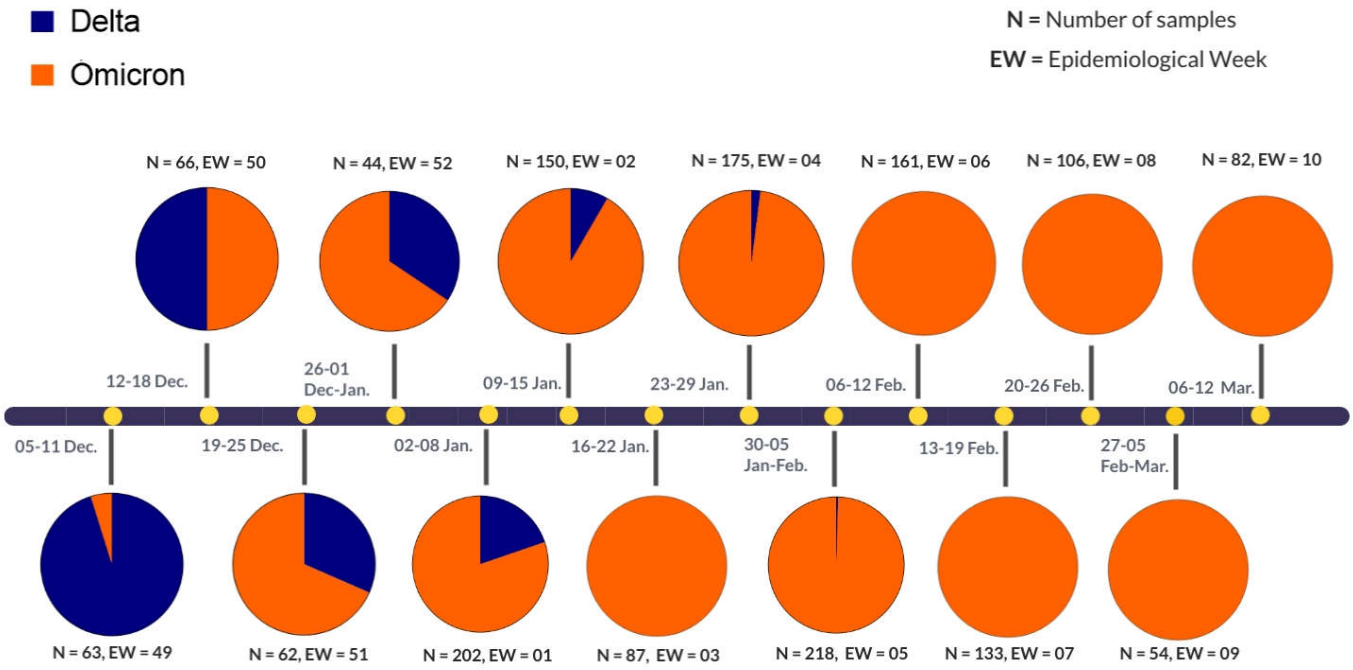

Figure 1. Variants of Concern in Ecuador since Omicron's first detection.

At least four institutions from public and private sector are involved in the genomic surveillance of the virus locally and submit sequences to the public repository GISAID (https://www.gisaid.org/) within two weeks frequency [10]. It allow us to understand the epidemiological trends and incidence of the COVID-19 disease and the effects of the detection and spread of new variants [11]. Giving the emergence of sublineages of Omicron variants, this work aims to identify which sublineages are circulating and prevailing in Ecuador. Our analyses focused on the presence and trend of each Omicron sublineage reported since epidemiological week 49 in 2021, when we detected the first case in Ecuador [8].

2. Materials and Methods

2.1. Sequence production and Data collection

The institutions involved in SARS-CoV-2 sequencing in Ecuador use different platforms including MinION (Oxford Nanopore), MiSeq and MiniSeq (Illumina). We downloaded 1245 Omicron sequences submitted to GISAID from Ecuador until March 2022; 703 obtained by the Instituto Nacional de Investigación en Salud Publica (INSPI) using MinION (ONT) and MiSeq (Illumina), 456 obtained by "Universidad San Francisco de Quito-USFQ" using MinION and 86 sequences obtained by the "Universidad de Especialidades Espiritu Santo-using MiniSeq (Illumina).

2.2. Lineage assignment and Phylogenetics

Sequences were classified by epidemiological week then submitted to Nextclade (https://clades.nextstrain.org/) [12] and Pangolin COVID-19 (https://pangolin.cog-uk.io/) [13] for clade and lineage assignment. Lineages nomenclature are assigned according to the PANGO (Phylogenetic Assignment of Named Global Outbreak Lineages) software updated on March 2022. It relies on establishing a numerical value to descendants that meet certain conditions that belong to lineages A or B, with a maximum of three sublevels, whereby new lineages will be assigned with a letter [13]. The criteria used for lineage assignment involved minimum lineage size, genome quality, genetic specificity, and epidemiological significance, which vary over time and depend on the degree of adaptation [14]. Consequently, each lineage is assigned a unique alphanumeric code that includes partial information regarding the phylogenetic history of that lineage based on a common ancestor [13].

A staked bar chart of lineages by epidemiological week was done using R [15] and GraphPad software [16]. A phylogenetic tree was built in Nextclade using the nearest neighbor method and visualized by Nextrain Auspice [12].

3. Results

We detected 12 sublineages of the Omicron variant circulating in Ecuador, with different worldwide origins (Table 1). The different sublineages present from 40 to 54 mutations comprising the following detail [13]:

BA.1 has 52 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V; ORF1b: P314L, I1566V; S: A67V, del69/70, T95I, G142D, del143/145,N211I, del212/212, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F; E: T9I; M: D3G, Q19E, A63T; ORF8: S84L; N: P13L, del31/33, R203K, G204R);

BA.1.1 has 51 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V; ORF1b: P314L, I1566V, S:A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, R346K, S371L, S373P, S375F, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954HN969K, L981F; E: T9I; M: D3G, Q19E, A63T; ORF8: S84L; N: P13L, del31/33, R203K, G204R);

BA.1.1.1 has 50 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V; ORF1b: P314L, I1566V; S: A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, R346K, S371L, S373P, S375F, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F; E: T9I; M: D3G, Q19E, A63T; ORF8: S84L; N: P13L, del31/33, R203K, G204R);

BA.1.1.14 has 49 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V ORF1b: P314L, I1566V S: A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, R346K, S371L, S373P, S375F, S477N, T478K, E484A,

Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, D796Y, N856K, Q954H, N969K, L981F E: T9I M: D3G, Q19E, A63T ORF8: S84L N: P13L, del31/33, R203K, G204R);

BA.1.1.2 has 54 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, T3432S, del3674/3676, I3758V ORF1b: P314L, I1566V S: A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, R346K, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F E: T9I M: D3G, Q19E, A63T ORF8: S84L N: P13L, del31/33, R203K, G204R);

BA.1.14 has 40 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V ORF1b: P314L, I1566V S: A67V. del69/70, T95I,G142D, del143/145, G339D, S371L, S373P, S375F, G446S, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F E: T9I, M: D3G, Q19E, A63T ORF8: S84L N: P13L del31/33, R203K, G204R);

BA.1.15 has 51 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V; ORF1b: P314L, I1566V S: A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, S371L, S373P, S375F, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F ORF3a: L106F E: T9I M: D3G, Q19E, A63T ORF8: S84L N: P13L, del31/33, R203K, G204R, D343G);

BA.1.16 has 48 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V ORF1b: P314L, I1566V S: A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, S371L, S373P, S375F, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, D796Y, N856K, Q954H, N969K, L981F E: T9I M: D3G, Q19E, A63T ORF8: S84L N: P13L, del31/33, R203K, G204R);

BA.1.17 has 50 mutations (ORF1a: K856R, V1887I, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V ORF1b: P314L, I1566V S: A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, S371L, S373P, S375F, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F E: T9I M: D3G, Q19E, A63T ORF8: S84L N: P13L, del31/33, R203K, G204R);

BA.1.6 has 50 mutations (ORF1a: K856R, S2083I, del2084/2084, A2710T, T3255I, P3395H, del3674/3676, I3758V ORF1b: P314L, S1391L, I1566V S: A67V, del69/70, T95I, G142D, del143/145, N211I, del212/212, G339D, S371L, S373P, S375F, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F E: T9I M: D3G, Q19E, A63T ORF8: S84L N: P13L, del31/33, R203K, G204R);

BA.2 has 53 mutations (ORF1a:S135R, T842I, G1307S, L3027F, T3090I, L3201F, T3255I, P3395H, del3675/3677 ORF1b: P314L, R1315C, I1566V, T2163I S: T19I, L24S, del25/27, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440KS477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K ORF3a:T223I E: T9I M: Q19E, A63T ORF6: D61L ORF8: S84L N: P13L, del31/33, R203K, G204R, S413R)

BA.2.3 has 53 mutations **(**ORF1a: S135R, T842I, G1307S, L3027F, T3090I, L3201F, T3255I, P3395H, del3675/3677 ORF1b: P314L, R1315C, I1566V, T2163I S: T19I, L24S, del25/27, G142D, V213G, G339D, S371F, S373P, S375F, T376A, D405N, R408S, K417N, N440KS477N, T478K, E484A, Q493R, Q498R, N501Y, Y505H, D614G, H655Y, N679K, P681H, N764K, D796Y, Q954H, N969K ORF3a: T223I E: T9I M: Q19E, A63T ORF6: D61L ORF8: S84L N: P13L, del31/33, R203K, G204R, S413R)

Table 1. List of Omicron sublineages circulating in Ecuador. For each Omicron sublineage, the place or places of origin and the number of mutations that characterize them are recorded.

Sublineage	Clade names	Origin	Genes								
			ORF1a	ORF1b	S	ORF3a	E	M	ORF6	ORF8	N
BA.1	21K (Omicron)	South Africa	8	2	33	0	1	3	0	1	4
BA.1.1	21K (Omicron)	South Africa	8	2	32	0	1	3	0	1	4
BA.1.1.1	21K (Omicron)	Europe	8	2	31	0	1	3	0	1	4
BA.1.1.14	21K (Omicron)	Europe	8	2	30	0	1	3	0	1	4
BA.1.1.2	21K (Omicron)	Japan	9	2	34	0	1	3	0	1	4
BA.1.14	21K (Omicron)	Brazil	8	2	21	0	1	3	0	1	4
BA.1.15	21K (Omicron)	USA	8	2	30	1	1	3	0	1	5
BA.1.16	21K (Omicron)	UK	8	2	29	0	1	3	0	1	4
BA.1.17	21K (Omicron)	Europe	9	2	30	0	1	3	0	1	4
BA.1.6	21K (Omicron)	Canada and Sint Maarten	8	3	30	0	1	3	0	1	4
BA.2	21L (Omicron)	India and South Africa	9	4	29	1	1	2	1	1	5
BA.2.3	21L (Omicron)	Philippines	9	4	29	1	1	2	1	1	5

Among all the sequences analyzed, 62.33% correspond to the BA.1.1 sublineage, 24.82% to BA.1, 6.18% to BA.1.14, 4.33% to BA.1.15, 1.12% to BA.1.17, the remaining sublineages BA.1.6, BA.1.16, BA.2, BA.2.3, BA.1.1.1; BA.1.1.2, BA.1.1.14, were found with a frequency ≤ 1% (Figure 1a). The phylogenetic tree built in Nextclade is showed in Figure 2b.

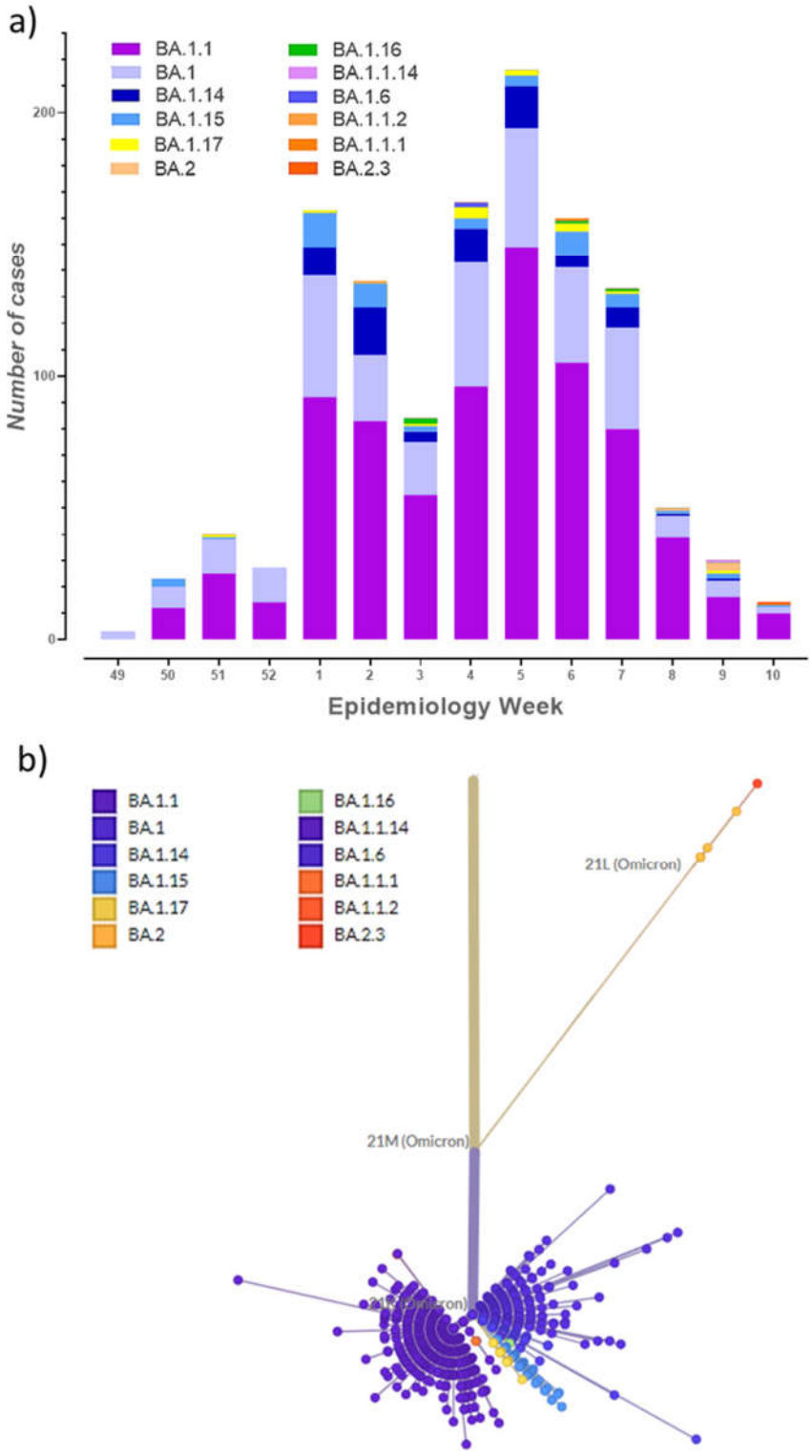

Figure 2. Omicron sublineages in Ecuador. a) Sublineages by epidemiological week, b) Phylogenetic tree of all lineages.

4. Discussion

Until March 2022, we detected 12 sublineages of Omicron in Ecuador, which has been detected in other countries comprising Africa, America, Europe, and Asia, suggesting they correspond to multiple introductions events. The BA.1 and BA.1.1 sublineages are currently dominating; BA.1.14 and BA.1.15 have registered a considerable increase in cases during the latest epidemiological weeks.

Following Omicron first identification, an increasing number of sublineages is being reported globally. Of all the worldwide Omicron sequences available in GISAD, at least 36 sublineages (all into the major BA.1-BA.5 as reported by WHO) have been identified until April 2022 [17-18]. In Latin America, a study by the laboratory of Microbiology of the University of Feevale in Brazil has reported the circulation of 7 sublineages in that country, with BA.1, BA.1.1 and BA.2 being the predominant [19]. In Chile the Ministry of Health reported the circulation of 10 sublineages, with BA.1.1 and BA.2 displacing BA.1 [20]. In Europe, Denmark, has reported the prevalence of BA.1, BA.1.1 and BA.2 sublineages [21]. In northern Italy the predominant sublineages are BA.1.15, BA.1.1, and BA.1.17 [17]. A study conducted in Hong Kong using 542 Omicron genomes, showed the BA.2.2, BA.1 and BA.1.1 sublineages predominate [22]. The data from all these countries are consistent with those observed in Ecuador, where BA.1.1 is the current predominant sublineage.

Despite a low positivity rate detected in the last weeks, Public Health Authorities needs to keep the genomic surveillance to evaluate any change in the predominance of Omicron sublineages detected already in the country or to early detect the introduction or other lineages reported globally, as well as to evaluate vaccine efficacy against the evolving lineages of SARS-CoV-2.

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