



Article Imported SARS-CoV-2 Variants of Concern Drove Spread of Infections across Kenya during the Second Year of the Pandemic

Carolyne Nasimiyu ^{1,2,†}, Damaris Matoke-Muhia ^{3,†}, Gilbert K. Rono ^{4,†}, Eric Osoro ^{1,2}, Daniel O. Ouso ⁴, J. Milkah Mwangi ³, Nicholas Mwikwabe ³, Kelvin Thiong'o ³, Jeanette Dawa ¹, Isaac Ngere ¹, John Gachohi ^{1,5}, Samuel Kariuki ³, Evans Amukoye ³, Marianne Mureithi ⁶, Philip Ngere ⁷, Patrick Amoth ⁷, Ian Were ⁷, Lyndah Makayotto ⁷, Vishvanath Nene ⁴, Edward O. Abworo ⁴, M. Kariuki Njenga ^{1,2,*,‡}, Stephanie N. Seifert ^{2,‡} and Samuel O. Oyola ^{4,‡}

- ¹ Washington State Global Health Program-Kenya, Washington State University, Nairobi 00200, Kenya; carolyne.nasimiyu@wsu.edu (C.N.); eric.osoro@wsu.edu (E.O.); jeanette.dawa@wsu.edu (J.D.); isaac.ngere@wsu.edu (I.N.); john.gachohi@wsu.edu (J.G.)
- ² Paul G. Allen School for Global Health, Washington State University, Pullman, WA 99164, USA; stephanie.seifert@wsu.edu
- ³ Kenya Medical Research Institute, Nairobi 00200, Kenya; dmatoke@kemri.org (D.M.-M.); mmuthoni@kemri.org (J.M.M.); nmwikwabe@kemri.org (N.M.); kthiongo@kemri.org (K.T.); skariuki@kemri.org (S.K.); eamukoye@kemri.org (E.A.)
- ⁴ International Livestock Research Institute, Nairobi 00200, Kenya; g.kibet@cgiar.org (G.K.R.); d.ouso@cgiar.org (D.O.O.); v.nene@cgiar.org (V.N.); e.abworo@cgiar.org (E.O.A.); s.oyola@cgiar.org (S.O.O.)
- ⁵ School of Public Health, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000, Nairobi 00200, Kenya
 - Department of Medical Microbiology, University of Nairobi, Nairobi 00200, Kenya; marianne@uonbi.ac.ke Kenya Ministry of Health, Nairobi 00200, Kenya; philip.ngere@wsu.edu (P.N.);
- patrickamoth@gmail.com (P.A.); wereian12@gmail.com (I.W.); makayotto@gmail.com (L.M.)
- Correspondence: Mkariuki.njenga@wsu.edu

6

- + These authors contributed equally to this work.
- t These authors contributed equally to this work.

Abstract: Using classical and genomic epidemiology, we tracked the COVID-19 pandemic in Kenya over 23 months to determine the impact of SARS-CoV-2 variants on its progression. SARS-CoV-2 surveillance and testing data were obtained from the Kenya Ministry of Health, collected daily from 306 health facilities. COVID-19-associated fatality data were also obtained from these health facilities and communities. Whole SARS-CoV-2 genome sequencing were carried out on 1241 specimens. Over the pandemic duration (March 2020–January 2022), Kenya experienced five waves characterized by attack rates (AR) of between 65.4 and 137.6 per 100,000 persons, and intra-wave case fatality ratios (CFR) averaging 3.5%, two-fold higher than the national average COVID-19 associated CFR. The first two waves that occurred before emergence of global variants of concerns (VoC) had lower AR (65.4 and 118.2 per 100,000). Waves 3, 4, and 5 that occurred during the second year were each dominated by multiple introductions each, of *Alpha* (74.9% genomes), *Delta* (98.7%), and *Omicron* (87.8%) VoCs, respectively. During this phase, government-imposed restrictions failed to alleviate pandemic progression, resulting in higher attack rates spread across the country. In conclusion, the emergence of *Alpha, Delta*, and *Omicron* variants was a turning point that resulted in widespread and higher SARS-CoV-2 infections across the country.

Keywords: COVID-19 pandemic; variants of concern; attack rates

1. Introduction

In most countries globally, the COVID-19 pandemic progressed in a series of waves characterized by rapid increase in infection rates followed by a few months of decline before the next wave [1]. Factors associated with emergence of new waves included declined application of mitigation measures, climatic changes, and emergence of new virus



Citation: Nasimiyu, C.; Matoke-Muhia, D.; Rono, G.K.; Osoro, E.; Ouso, D.O.; Mwangi, J.M.; Mwikwabe, N.; Thiong'o, K.; Dawa, J.; Ngere, I.; et al. Imported SARS-CoV-2 Variants of Concern Drove Spread of Infections across Kenya during the Second Year of the Pandemic. *COVID* **2022**, *2*, 586–598. https://doi.org/10.3390/ covid2050044

Academic Editor: Joan Puig-Barberà

Received: 24 March 2022 Accepted: 3 May 2022 Published: 5 May 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). variants [2,3]. The global genomic surveillance of SARS-CoV-2 played a pivotal role in identifying emerging variants and associated mutations that impacted virus transmissibility, disease severity, vaccine efficacy, and clinical case management [3,4]. So far, key variants of public health importance, designated by World Health Organization (WHO) as variants of concern (VoC), had mutations that enhance transmissibility, reduced virus neutralization by antibodies generated following infection or vaccination, interfered with diagnostic testing, and often caused more severe disease [5]. These variants appeared to gain competitive advantage on existing strains to exert immediate global dominance, and most were associated with increased hospitalization or higher mortality, and re-infection of vaccinated or previously infected persons [6].

The paucity of SARS-CoV-2 genomic surveillance data in Africa has limited our understanding of role of virus variants in progression of COVID-19 pandemic in the continent. During the early phase of the pandemic, epidemiologic data from the region suggested lower morbidity and mortality in the region, attributed to factors such as youthful population, favorable weather, and prior exposure to cross-reactive viruses [7]. However, later studies showed infections rates comparable to global trends, but significantly lower levels of severe disease and mortality [8]. The emergence of VoCs with global impact in the later phase of the pandemic was associated with increased disease severity, rapid transmission, and re-infection of vaccinated or previously infected persons, continuing to strain the global public health infrastructure and economies despite availability of effective vaccines [9]. Among the VoCs that had a global impact were B.1.1.7 (Alpha) first identified in United Kingdom in September 2020, B.1.351 (Beta) first reported in South Africa in December 2020, B.1.525 (*Eta*) first identified in the UK and Nigeria in December of 2020, B.1.617.1 (Delta) first identified in India in October 2020, P.1 (or B.1.1.28.1, Gamma) first reported in Brazil in January 2021, and B.1.1.529 (Omicron) first reported in South Africa in November 2021 [4,10–12] and retroactively detected in samples in the US and other countries around the same time [13]. Two other VOCs, B.1.427 and B1.429 (Epsilon), were detected in California, United states in February 2021, but they did not have significant global spread [14].

Progression of COVID-19 pandemic in Kenya may be classified into three phases. The first phase (March 2020–February 2021) started with virus introduction into the country and ended with emergence of VoCs. The second phase (March 2021–October 2021) was characterized by introduction of various VoCs and vaccination while most COVID-19 restriction remained in place. The third phase (November 2021-Present) started when the government lifted most restrictions but also ensured vaccines were widely available. Here, we tracked the pandemic in country over 23 months using classical and genomic surveillance approaches in order to assess the impact of the emerging virus variants on progression of the pandemic. Following confirmation of the first COVID-19 case on 13 March 2020, and through subsequent waves, the government of Kenya implemented various mitigation measures to control its spread, including closure of international borders, banning social gatherings, and lockdown of hotspots located primarily in urban and periurban regions of the country [15]. Despite these measures, the SARS-CoV-2 prevalence in capital city of Nairobi was reported as 35% in the first 8 months of the pandemic (in November 2020) [8], and studies predicted that 75% of the Nairobi's population would be infected by June 2021 [16]. On 30 January 2022, Kenya had reported five waves of COVID-19 pandemic, with a total of 331,324 confirmed cases and 5488 deaths (case fatality ratio = 1.7%) [17]. By then, only 17.3% of the adult population had been vaccinated, in large part due to limited availability of vaccines, and a level of vaccine hesitancy [18–20].

2. Materials and Methods

2.1. COVID-19 Surveillance Data

We abstracted data from the Kenya Ministry of Health (KMOH) COVID-19 daily situation reports [17]. The data included date of report, number of confirmed cases and deaths at national and county level, age group, and sex of cases and deaths, and number of tests conducted. The KMOH situation reports were based on the COVID-19 surveillance system that collected samples from patients presenting at health facilities in 306 sub counties across the entire country and meeting the suspect case definition for COVID-19. The surveillance system also collected samples from healthcare workers with symptoms of a respiratory illness and/or meeting the COVID-19 suspect case definition, people coming in contact with confirmed COVID-19 cases, and self-initiated testing at 50 biomedical laboratories for a variety of reasons such as heightened suspicion index and international travel.

2.2. SARS-CoV-2 Testing and Reporting

From each surveilled individual, nasopharyngeal and oropharyngeal swabs were collected, immediately preserved into virus transport medium (VTM), and transported in cool boxes to any of about 200 designated COVID-19 testing laboratories within major hospitals and biomedical research laboratories across the country. In most laboratories, three aliquots of the sample were prepared, and one immediately tested for presence of SARS-CoV-2 virus using RT-PCR. The other two aliquots were transferred to the Sample Management and Receiving Facilities (SMRF) at the Kenya Medical Research Institute (KEMRI) for long-term storage in -80 °C. Testing laboratories reported results daily to the National Public Health Laboratories at KMOH through an integrated laboratory information management system.

2.3. SARS-CoV-2 Testing Inequity

Nationally, the cumulative testing rate was 0.7 tests per 1000 persons per week, against a target of 1 per 1000 persons per week as of 30 January 2022 [17]. The testing rate was higher in the major cities of Nairobi, Mombasa, and other urban counties when compared to rural counties. For example, between August and December 2021, the testing rate in Nairobi was 4.7 tests per 1000 persons per week, whereas in 9 rural counties, the rate was ~0.7 test per 1000 persons per week [18].

2.4. Collection of Fatality Data

COVID-19 related fatalities occurring within health facilities were reported daily through a standard KMOH death reporting tool developed specifically for the pandemic. Fatalities occurring within the communities were reported directly to 306 Sub-County Disease Surveillance Coordinators (SCDSCs) nationally by the patient's relatives, community health volunteers, or local government administrators in accordance Kenya Civil Registration Act. All the SCDSCs in the country also collated and reported COVID-19 related mortality data daily to Disease Surveillance and Response Unit at the KMOH national headquarters in Nairobi.

2.5. Epidemiology Data Analysis

The reported COVID-19 cases and deaths were analyzed by week of occurrence and county of origin and presented as counts, percentages, ranges, median and in epidemic curves. We defined a wave by epi-week based on three criteria: (i) increase in number of reported cases for three consecutive weeks; (ii) the start of the wave was the first week of at least three consecutive increases where the increase from the previous week was at least 35%; and (iii) the end of the wave was defined as the week when the reported cases were equal to or lower than those reported cases divided by the human population at national and county level. Case fatality ratio (CFR) was defined as the ratio of deaths to reported cases. We estimated the 95% confidence interval of the proportion of cases and deaths on the binomial distribution defined by the observed proportions.

2.6. SARS-CoV-2 Genomic Surveillance

Starting from May 2020, we selected up to 200 real-time PCR-positive specimens with $C_T \leq 32.0$ per month from the KEMRI SMRF for whole genome sequencing of SARS-CoV-2

at either the Regional Genomic Center of International Livestock Research Institute (ILRI) or Center for Biotechnology Research and Development of KEMRI.

2.7. Whole Genome Sequencing and Variant Identification

The SARS-CoV-2 whole genome sequencing was carried out as described previously [21]. Briefly, viral RNA was extracted from sample either manually or using TANBead[®] Maelstrom 9600 (Taiwan Advanced Nanotech Inc, Taoyuan, Taiwan) automated nucleic acid extractor according to the manufacturer's directions. The NEBNext-Artic SARS-CoV-2 library preparation workflows for both Illumina and Oxford Nanopore Technologies (ONT) were used [22]. For Illumina, the protocol NEBNext[®] ARTIC SARS-CoV-2 Library Prep Kit (Illumina[®]) (Version 2.0_3/21) was used following manufacturer's instructions. Sequencing was done on the Illumina MiSeq or NextSeq 550 platforms. Size distribution was estimated using agarose gel electrophoresis. Base calling, demultiplexing, and adapter trimming was performed using Guppy v5.0.11 and fastq outputs used for downstream analyses.

Variant calling and lineage/clade assignment were carried out using the singularity container of the nf-core/viralrecon v2.2: an analysis pipeline for assembly and intrahost/low-frequency variant calling for viral samples [23]. Further downstream, consensus sequences were used by Pangolin USHER for lineage assignments based on parsimony and Nextclade [24] for clade specification.

2.8. Phylogenetic Analyses

Apart from our sequences (n = 1241), we downloaded an additional 894 genomes for phylogenomic comparison. To compare with global sequences, consensus sequences were aligned using NextAlign, embedded in NextClade, and resulting multiple sequence alignment (MSA) fed into IQ-TREE [25] for inferring maximum likelihood to determine the most likely phylogram. Tree visualization and annotation were done using the FigTree software [26]. For time-resolved phylogenetic trees, we used Mafft aligner v1.10.0 to generate MSA and ClonalFrameML to estimate the phylogeny with corrected branch lengths [27].

Lineage designation was implemented in pangolin v 3.0.1.17 [28]. Multiple sequence alignment was performed on all SARS-CoV-2 sequences whereas separate alignments were performed for *Delta* variants using NextAlign [29]. For both alignments, the maximum likelihood phylogenetic tree was inferred using IQ-TREE v 2.1.3 [25] with ModelFinder [30] and 1000 UltraFast bootstrap replicate approximation [31]. The time-resolved phylogenetic tree for all Kenya sequences inferred in TreeTime using Wuhan-Hu-1 variant as the outlier [32]. The new Kenyan SARS-CoV genomes sequenced were submitted to either global initiative on sharing avian influenza data (GISAID, https://www.gisaid.org/accessed on 10 January 2022) or National Center for Biotechnology Information (NCBI, https://www.ncbi.nlm.nih.gov/ accessed on 18 February 2022 and accession numbers provided in Supplement Tables S1 and S2, respectively.

3. Results

3.1. Pandemic Waves and Regional Spread of Infections

Between March 2020 and January 2022, Kenya experienced five waves of COVID-19 (Figure 1). Wave-1 and wave-2 occurred during the first phase of the pandemic before global emergence of VoCs, wave-3 and wave-4 during second phase when VoCs emerged and vaccination started, and wave-5 during the current phase of the pandemic after Kenya had lifted most restrictions. Wave-2 was the longest at 10 weeks, while wave-1, wave-3, and wave-4 lasted for 8 weeks each, and wave-5 for 7 weeks. The shortest inter-wave period of 4 weeks was observed between waves 1 and 2, while those between waves 2 and 3, waves 3 and 4, and wave-4 were higher when compared to the cases reported between the other waves.



Figure 1. Number of reported COVID-19 cases and deaths by epidemiological week, 2020–2022, Kenya. The five waves are highlighted in different colours. The numbers of fatalities are denoted by the red line graph with a secondary axis to the right.

The national attack rate (AR) during the waves ranged from 65.4 to 137.6 cases per 100,000 persons with the highest AR reported in wave-5 and the lowest in wave-1. During wave 1, the median AR per county was 14.6 (Inter-quartile range = 29.9) cases per 100,000 persons across the countries 47 counties, with only 4 counties surrounding Nairobi city in southcentral Kenya, and Mombasa city along the Indian Ocean coastal region reporting AR >100 cases per 100,000 persons (Figure 2).



Figure 2. SARS-CoV-2 attack rate by county and wave in Kenya.

In contrast, during wave-3 and wave-4, the median AR rate was 70.3 (IQR = 98.5) cases per 100,000 persons, with 17 (36.2%) of the counties reporting AR >100 cases per 100,000 persons. Overall, Nairobi city accounted for 43% of all the cases reported during the five waves (range 36.9–60.7%), and the highest intra-wave AR ranging between 460.9 and 627.2 per 100,000 persons.

3.2. Case Fatality Ratio

The number of COVID-associated deaths reported was higher during the waves when compared to the number reported between the waves (Figure 1). Whereas the average CFR over the 23-month pandemic period was 1.7%, the intra-wave CFR was 3.5%. Interestingly,

while the intra-wave CFR was between 3.9% and 6.6% during waves 1–4, it dropped to 0.3% in wave 5. People aged below 20 years, who constitute >50% of the population, contributed 10.0% of cases, but only 2.9% of deaths. In contrast, people aged \geq 60 years old (4.2% of the population) contributed 13.7% of the cases and 56.5% of deaths (Table 1).

		All Cases	All Deaths		Female Cases	Male Cases	Male Deaths	Female Deaths
Age Group	n	% (95% CI)	n	% (95% CI)				
0–9	12,064	3.8 (3.7–3.8)	89	1.6 (1.3–2)	43.7 (42.8–44.6)	56.3 (55.4–57.2)	65.2 (54.3–74.8)	34.8 (25.2–45.7)
10–19	19,832	6.2 (6.1–6.3)	72	1.3 (1–1.6)	47.6 (46.9–48.3)	52.4 (51.7–53.1)	58.3 (46.1–69.6)	41.7 (30.4–53.9)
20–29	60,860	19 (18.9–19.1)	162	2.9 (2.5–3.4)	47.3 (46.9–47.7)	52.7 (52.3–53.1)	51.9 (43.9–59.7)	48.1 (40.3–56.1)
30–39	83,067	25.9 (25.8–26.1)	428	7.7 (7–8.4)	43.1 (42.8–43.5)	56.9 (56.5–57.2)	51.9 (47–56.7)	48.1 (43.3–53)
40-49	59,099	18.5 (18.3–18.6)	683	12.2 (11.4–13.1)	40.1 (39.7-40.5)	59.9 (59.5–60.3)	63.5 (59.8–67.1)	36.5 (32.9-40.2)
50-59	41,394	12.9 (12.8–13)	996	17.8 (16.9–18.9)	41.5 (41.1–42)	58.5 (58–58.9)	68.4 (65.4–71.2)	31.6 (28.8–34.6)
≥ 60	43,998	13.7 (13.6–13.9)	3152	56.5 (55.2–57.8)	44.2 (43.8–44.7)	55.8 (55.3–56.2)	64.6 (62.9–66.3)	35.4 (33.7–37.1)
Total	320,314	-	5582	-	43.6 (43.4–43.8)	56.4 (56.2–56.6)	63.7 (62.5–65)	36.3 (35–37.5)

Table 1. Categorization of COVID-19 cases and deaths by age groups and sex in Kenya.

Although only 26.6% of the cases occurred in persons >49 years, this age group contributed 74.3% of the deaths. Reported deaths among males were almost double that of those reported among females (Table 1).

3.3. Dominant SARS-CoV-2 Lineages during Waves

The 1241 SARS-CoV-2 genomes sequenced between May 2020 and January 2022 were assigned to 24 distinct Pango lineages with the most common lineages being B.1.617.2 (Delta, 38.4%), B.1(non-VOC, 24.6%), B.1.1.7 (Alpha, 16.5%), and B.1.1.529 (Omicron, 7.5%).

During the first phase of pandemic, the B.1 global parental lineage, which circulated from the beginning of the pandemic in the country, dominated accounting for 94% of all genomes in wave-1, and 71% in wave-2 (Figure 3).



Figure 3. Kenyan COVID-19 Epi-curve as of January 30, 2022, showing the dominant SARS-CoV-2 variants during each of the 5 waves. The grey bars represent number of cases by epidemiological week, 2020–2022.

Diverse virus variants started emerging in wave-2 through to wave-3, both VoCs such as B.1.351 (Beta) and B.1.1.7 (Alpha) and non-VoCs such as B.1.3x, B.1.5x, B.1.525 (Eta), A,

and A.23x. However, midway through wave-3, Alpha emerged as the dominant variant, accounting for 74.9% of all genomes sequenced (Figures 3 and 4).

The B.1.617.2 (Delta) and its sub-variant AY.x were first detected in March 2021 and swept away other variants to become the dominant variant (99.3% of the genomes sequenced) during wave-4 (Figures 3 and 4).

The B.1.1.529 (Omicron) lineage was first detected in Kenya on 20 November 2021, and by mid-December, its sub-variant BA.1 became dominant, accounting for 87.8% of all genomes sequenced (Figures 3 and 4). Of the major VoCs, only Beta, Alpha, Delta, and Omicron were detected in the Kenya samples sequenced. Genetic evolution analysis showed intra-lineage diversity of various variants (Figure 5).



Figure 4. A time calibrated phylogenetic tree of 1241 SARS CoV-2 genomes sequenced from Kenyan patients between May 2020 and December 2022. Pango lineage designations are indicated by the circles on the branch tips, including VoCs and variants of interest as designated by World Health Organiza-tion. Using the 2019 Wuhan-Hu-1 genome (GenBank accession number MN908947.3) as the root of the tree.



Figure 5. Circular phylogenetic tree depicting evolutionary relationship of Kenyan SARS-CoV-2 sequences (n = 1241) against global genomes (n = 894) clustered by pangolin lineage annotation as shown in different background colours.

Of the VoCs, Delta variant showed greater genetic diversity, including multiple globally circulating AY.X lineages, consistent with multiple introductions as depicted by the three divergent clusters (Figure 4, Figure 5 and Figure S1). This analysis indicates that the Alpha variant and the Omicron have a closer common ancestor compared to the Delta variant, which appears to have diverged from a more distant ancestor (Figure 5).

4. Discussion

We used both classical and genomic epidemiologic approaches to track the COVID-19 pandemic in Kenya over 23 months (March 2020–January 2022) and assess the impact of emerging virus variants on pandemic progression and severity in the country. In the first phase of the pandemic, the country experienced two waves, characterized by national AR of between 65.4 and 118.2 per 100,000 persons (Nairobi 404-474 cases per 100,000 persons), and CFR of 3.9–4.2%. The B.1 lineages of the virus dominated, except toward the end of that period (January 2021) when Alpha, the first VoC in the country, was detected. During this phase, most cases were reported within and around the two main ports of entry into Kenya, the capital city of Nairobi in the southcentral region that received most of the international travellers, and Mombasa, along the Indian ocean, where most cargo deliveries to the east Africa region are received (Figure 2). Therefore, incoming travellers seems to have been the primary drivers of infections in this early phase of the pandemic. The government responded to this phase by implementing various mitigation measures, including the closure of borders, in-person schooling closures, and bans on social gatherings. Most of these measures remained in place through to October 2021 (18 months into the pandemic), but they became less effective in preventing widespread infections in the country in the subsequent phases of the pandemic when global VoCs started to emerge.

The second phase (March–October 2021) was characterized by the emergence of imported VoCs starting with Alpha and shortly after Delta variants, which were associated with two major waves (wave-3 and wave-4). The Delta variant dominated through 5 of the 8 months in this period, and the two waves were associated with the high AR (national 115.6–125.7 per 100,000 persons, Nairobi 457.5–614.2 per 100,000 persons) and CFR (up to 6.6%). This period saw spread of infections across all 47 counties in the country. In addition to the early mitigation measures, lockdowns were introduced for over 2 months in defined hotspot of the country characterized by high AR. Interestingly, this phase was also marked by introduction of COVID-19 vaccines, albeit slowly, because of low vaccine availability in low-income countries globally. During this 8 month-period, only 19% of the 27 million eligible Kenyans had received at least one dose of the vaccine [18]. Since October 2021, Kenya has been in the third phase of pandemic, characterized by lifting of most restrictions to re-open the economy and increase the availability of vaccines. During this phase, the *Omicron* variant emerged, resulting in wave-5 associated with the highest AR (national 137.6 per 100,000 persons, Nairobi 627.3 per 100,000 persons) but lowest CFR (CFR = 0.3%). The government did not re-introduce restrictions, and vaccines became more widely available. By the end of January 2022, 42% of eligible Kenyans had received at least one dose of the vaccine, but only 0.4% had received the recommended 3rd booster doses [17].

Studies show that the globally wave-associated progression of the COVID-19 pandemic was driven by various factors, including the large naïve populations, varied immune responses [33], rapid waning of immunity [34-36], and emergence of virus variants capable of escaping immunity [37–40]. In Kenya, the inter-wave duration over the 2-year pandemic period was between 4 and 11 weeks, with wave-1 and wave-2 having the shortest (4 weeks) duration. This was likely because of the low level of population immunity to SARS-CoV-2 during the first phase of the pandemic. These early waves were also smaller in magnitude because of the effectiveness of mitigation measures during this phase when community level SARS-CoV-2 transmission in the country was low, as observed in other countries [41,42]. The subsequent waves (wave-3 to wave-5) had longer inter-wave duration (8–11 weeks), perhaps pointing to the time required to allow population immunity to wane, particularly around the ports of entry, and the introduction of VOCs capable of evading population immunity to cause reinfections [37–39]. These waves were of higher magnitude associated with widespread transmissions even in rural areas of the country that had been characterized by minimal transmission during phase 1 of the pandemic. By January 2022, despite low vaccine coverage, studies pointed to widespread SARS-CoV-2 transmission in the country, but low morbidity and mortality, giving the Kenya government confidence to resist the re-introduction of restrictions [8,16].

Of the >2800 SARS-CoV-2 genomes reported from Kenya in the current and other recent studies [42,43], there has been no VoC emerging from the country, with only B.1.525 (*Eta*), which was detected in February 2021 in Nairobi, classified as a variant of interest. Studies point to increased transmissibility and capacity to evade the immune response as the key factors associated with the dominance of the VoCs [37,44]. There is raging public debate associating vaccine inequity with the emergence of these variants; however, the evidence so far remains inconclusive. For instance, the emergence of Delta from India and Omicron from South Africa, countries that had low vaccination coverage at the time, appears to support this hypothesis. However, the fact that we have not seen many VoCs emerging from Kenya and other African countries (apart from South Africa), most of them with <20% vaccine coverage by the end of 2021, does not support the argument. Studies suggest that new VoCs can competitively gain advantage over existing variants through various mechanisms, including having higher infectivity, longer duration of infection, or being less virulent to cause asymptomatic disease that is harder to detect [6,45,46]. Breakthrough infections of vaccinated individuals have been widespread with *Omicron*; however, a complete vaccination regimen that includes the third booster dose improves virus neutralization against the *Omicron* variant and may result in reduced transmission [47].

Our genomic analyses suggest multiple introductions of imported SARS-CoV-2 variants from both regional and international sources. Though later waves were dominated by a single imported VoC (*Alpha, Delta, or Omicron*), we detected subtypes of these major variants associated with the US, Europe, India, Nigeria, DRC, and Uganda, supporting multiple introductions. There are nearly 8 million SARS-CoV-2 genomes available in GISAID and more than 50% of these sequences originate from just two regions, North America and Europe. Only about 1% of SARS-CoV-2 genomes are from Africa. Of these African genomes, nearly 40% originate from South Africa (GISAID, accessed 2 February 2022). This sampling bias reduces the likelihood that most African countries would have detected emerging variants with consequential mutations in a timely manner. However, we expect that if a VoC with sustained global impact emerged in the region, it could have been detected through a clinical disease profile.

A limitation of the study is that the reported COVID-19 cases and deaths and samples used for genomic surveillance were based on the KMOH surveillance, which likely underestimated the extent of the pandemic at any one time. Nonetheless, surveillance plays a critical role in monitoring trends and control of global pandemics.

5. Conclusions

The emergence of *Alpha*, *Delta*, and *Omicron* VoCs was a turning point that resulted in widespread and higher SARS-CoV-2 infections across the country, with varying fatality rates. Enhanced genomic and molecular surveillance for SARS-CoV-2 in developing countries can support early detection of VoCs and guide public health control measures such application of mitigation measures.

Supplementary Materials: The following supporting information can be downloaded at: https: //www.mdpi.com/article/10.3390/covid2050044/s1, Table S1: Accession Numbers for SARS-CoV genomes submitted to GSAID; Table S2: Accession Numbers for SARS-CoV genomes submitted to NCBI; Figure S1: Maximum likelihood tree showing global con-text of SARS-CoV-2 Delta variants circulating in Nairobi, Kenya. Region of origin for each SARS-CoV-2 variant is indicated by the colour of the circles at the branch tips.

Author Contributions: C.N. collected data, analysed the epidemiological data, drafted, and revised the paper. D.M.-M. collected data, drafted, and revised the paper. G.K.R. collected, cleaned, and analysed genomic data. C.N., D.M.-M. and G.K.R. contributed equally. E.O. developed the study design, wrote the data analysis plan, analysed epidemiological data, drafted, and revised the paper. D.O.O., J.M.M., N.M. and K.T. designed data collection tools and collected epidemiological data. J.D., I.N. and J.G. drafted and revised the paper. S.K., E.A. and M.M. reviewed and revised the manuscript while P.N. collected data. P.A., I.W. and L.M. revised the paper. V.N. and E.O.A. collected data and revised the paper. M.K.N. conceptualized the study, developed the study design, wrote the data analysis plan, drafted, and revised the paper. He is the guarantor. S.N.S. and S.O.O. analysed the genomic data, drafted, and revised the paper. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by US National Institute of Allergy and Infectious Disease/National Institutes of Health (NIAID/NIH), grants number U01AI151799 and U01AI151799-02S1, through the Centre for Research in Emerging Infectious Diseases—East and Central Africa (CREID-ECA). Funding was also provided by Research Program on Livestock of the Consultative Group for International Agricultural Research, Rockefeller Foundation, German Federal Ministry of Economic Cooperation and Development (BMZ) through the project One Health Research, Education and Outreach Centre in Africa (OHRECA) (Grant number BMZ002), Africa-Centers for Disease Control and Prevention, Kenya Medical Research Institute Grant # KEMRI/COV/SPE/012. Carolyne Nasimiyu was supported by the Fogarty International Center and NIAID/NIH under grant number D43TW011519.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board of Kenya Medical Research Institute (KEMRI/SERU/CVR/006/4035), ILRI Institutional Research Ethics Committee (ILRI-IREC2020-52), and a reliance approval by Washington State University Institutional Review Board based on in-

country ethical reviews as provided for in Code of Federal Regulations (45 C.F.R part 46 and 21 C.F.R. part 56). The COVID-19 surveillance and testing data were collected from public database of the Kenya Ministry of Health (KMOH) with administrative approval from the ministry.

Informed Consent Statement: Patient consent was waived due to the nature of the activity, which is a response to a pandemic, consent was not obtained from the patients by the hospital staff.

Data Availability Statement: The new Kenyan SARS-CoV genomes sequenced were submitted to either global initiative on sharing avian influenza data (GISAID, https://www.gisaid.org/ accessed on 10 January 2022) or National Center for Biotechnology Information (NCBI, https://www.ncbi. nlm.nih.gov/ accessed on 18 February 2022).

Acknowledgments: We wish to thank Shebbar Osiany, Paul Dobi, Edward Nyaga, Collins. Muli, Regina Njeru, Reuben Mwangi for supporting genomic work, Missiani Ochwoto, Ruth Cheruto, James Kimotho, and Jeremiah Omar for supporting testing, and the Washington State University Global Health Kenya staff for administrative support. The findings and conclusions in this study, are those of the authors and do not necessarily represent the official position of the Kenya MOH, KEMRI, US NIH, or CGIAR/ILRI.

Conflicts of Interest: The authors declare no competing interests. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

- Salyer, S.J.; Maeda, J.; Sembuche, S.; Kebede, Y.; Tshangela, A.; Moussif, M.; Ihekweazu, C.; Mayet, N.; Abate, E.; Ouma, A.O.; et al. The first and second waves of the COVID-19 pandemic in Africa: A cross-sectional study. *Lancet* 2021, 397, 1265–1275. [CrossRef]
- Hale, T.; Angrist, N.; Hale, A.J.; Kira, B.; Majumdar, S.; Petherick, A.; Phillips, T.; Sridhar, D.; Thompson, R.N.; Webster, S.; et al. Government responses and COVID-19 deaths: Global evidence across multiple pandemic waves. *PLoS ONE* 2021, *16*, e0253116. [CrossRef]
- 3. Jassat, W.; Mudara, C.; Ozougwu, L.; Tempia, S.; Blumberg, L.; Davies, M.-A.; Pillay, Y.; Carter, T.; Morewane, R.; Wolmarans, M.; et al. Difference in mortality among individuals admitted to hospital with COVID-19 during the first and second waves in South Africa: A cohort study. *Lancet Glob. Health* **2021**, *9*, e1216–e1225. [CrossRef]
- Aleem, A.; Akbar Samad, A.B.; Slenker, A.K. *Emerging Variants of SARS-CoV-2 and Novel Therapeutics against Coronavirus (COVID-19)*; StatPearls Publishing: Treasure Island, FL, USA, 2022. Available online: http://www.ncbi.nlm.nih.gov/books/NBK570580/ (accessed on 27 January 2022).
- Konings, F.; Perkins, M.D.; Kuhn, J.H.; Pallen, M.J.; Alm, E.J.; Archer, B.N.; Barakat, A.; Bedford, T.; Bhiman, J.N.; Caly, L.; et al. SARS-CoV-2 Variants of Interest and Concern naming scheme conducive for global discourse. *Nat. Microbiol.* 2021, *6*, 821–823. [CrossRef] [PubMed]
- Cantón, R.; Ramos, P.D.L.; García-Botella, A.; García-Lledó, A.; Gómez-Pavón, J.; Del Castillo, J.G.; Hernández-Sampelayo, T.; Martín-Delgado, M.C.; Martín Sánchez, F.J.; Martínez-Sellés, M.; et al. New variants of SARS-CoV-2. *Rev. Esp. Quimioter.* 2021, 34, 419–428. [CrossRef] [PubMed]
- Njenga, M.K.; Dawa, J.; Nanyingi, M.; Gachohi, J.; Ngere, I.; Letko, M.; Otieno, C.F.; Gunn, B.M.; Osoro, E. Why is There Low Morbidity and Mortality of COVID-19 in Africa? *Am. J. Trop. Med. Hyg.* 2020, 103, 564–569. [CrossRef]
- Ngere, I.; Dawa, J.; Hunsperger, E.; Otieno, N.; Masika, M.; Amoth, P.; Makayotto, L.; Nasimiyu, C.; Gunn, B.M.; Nyawanda, B.; et al. High seroprevalence of SARS-CoV-2 but low infection fatality ratio eight months after introduction in Nairobi, Kenya. *Int. J. Infect. Dis.* 2021, 112, 25–34. [CrossRef]
- McKibbin, W.; Fernando, R. The Global Macroeconomic Impacts of COVID-19: Seven Scenarios. Asian Econ. Pap. 2021, 20, 1–30. [CrossRef]
- 10. Tegally, H.; Wilkinson, E.; Giovanetti, M.; Iranzadeh, A.; Fonseca, V.; Giandhari, J.; Doolabh, D.; Pillay, S.; James San, E.; Msomi, N.; et al. Detection of a SARS-CoV-2 variant of concern in South Africa. *Nature* **2021**, *592*, 438–443. [CrossRef]
- 11. Novelli, G.; Colona, V.L.; Pandolfi, P.P. A focus on the spread of the delta variant of SARS-CoV-2 in India. *Indian J. Med. Res.* 2021, 153, 537–541. [CrossRef]
- da Silva, J.F.; Esteves, R.J.; Siza, C.; Soares, E.P.; Ramos, T.C.; Campelo, E.C.; da Costa, C.F.; de Alencar, L.C.; Cavalcante, R.P.; Florêncio, C.R.; et al. Cluster of SARS-CoV-2 Gamma Variant Infections, Parintins, Brazil, March 2021. *Emerg. Infect. Dis.* 2022, 28, 262–264. [CrossRef] [PubMed]
- Jansen, L. Investigation of a SARS-CoV-2 B.1.1.529 (Omicron) Variant Cluster—Nebraska, November–December 2021. MMWR Morb. Mortal. Wkly. Rep. 2021, 70, 1782–1784. Available online: https://www.cdc.gov/mmwr/volumes/70/wr/mm705152e3
 .htm (accessed on 4 February 2022). [CrossRef] [PubMed]

- Yang, S.; Hemarajata, P.; Hilt, E.E.; Price, T.K.; Garner, O.B.; Green, N.M. Investigation of SARS-CoV-2 Epsilon Variant and Hospitalization Status by Genomic Surveillance in a Single Large Health System during the 2020–2021 Winter Surge in Southern California. Am. J. Clin. Pathol. 2021, aqab203. [CrossRef] [PubMed]
- Wangari, E.N.; Gichuki, P.; Abuor, A.A.; Wambui, J.; Okeyo, S.O.; Oyatsi, H.T.N.; Odikara, S.; Kulohoma, B.W. Kenya's response to the COVID-19 pandemic: A balance between minimising morbidity and adverse economic impact. AAS Open Res. 2021, 4, 3. [CrossRef] [PubMed]
- Brand, S.P.C.; Ojal, J.; Aziza, R.; Were, V.; Okiro, E.A.; Kombe, I.K.; Mburu, C.; Ogero, M.; Agweyu, A.; Warimwe, G.M.; et al. COVID-19 transmission dynamics underlying epidemic waves in Kenya. *Science* 2021, 374, 989–994. Available online: https://www.science.org/doi/abs/10.1126/science.abk0414 (accessed on 25 December 2021). [CrossRef]
- 17. Ministry of Health—Republic of Kenya. Available online: https://www.health.go.ke/ (accessed on 9 June 2021).
- Orangi, S.; Pinchoff, J.; Mwanga, D.; Abuya, T.; Hamaluba, M.; Warimwe, G.; Austrian, K.; Barasa, E. Assessing the level and determinants of COVID-19 Vaccine Confidence in Kenya. *Vaccines* 2021, *9*, 936. Available online: https://www.medrxiv.org/ content/10.1101/2021.06.11.21258775v1 (accessed on 4 December 2020). [CrossRef]
- COVID-19 Vaccination: Campaign Targeting Public Transport Operators Launched—Ministry of Health. Available online: https://www.health.go.ke/covid-19-vaccination-campaign-targeting-public-transport-operators-launched/ (accessed on 9 January 2022).
- Kenya Increases Uptake and Equity for COVID-19 Vaccinations. Available online: https://www.who.int/news-room/featurestories/detail/kenya-increases-uptake-and-equity-for-covid-19-vaccinations (accessed on 7 January 2022).
- Gohl, D.M.; Garbe, J.; Grady, P.; Daniel, J.; Watson, R.H.B.; Auch, B.; Nelson, A.; Yohe, S.; Beckman, K.B. A rapid, cost-effective tailed amplicon method for sequencing SARS-CoV-2. *BMC Genom.* 2020, 21, 863. [CrossRef]
- 22. Grubaugh, N.D.; Gangavarapu, K.; Quick, J.; Matteson, N.L.; De Jesus, J.G.; Main, B.J.; Tan, A.L.; Paul, L.M.; Brackney, D.E.; Grewal, S.; et al. An amplicon-based sequencing framework for accurately measuring intrahost virus diversity using PrimalSeq and iVar. *Genome Biol.* **2019**, *20*, 8. [CrossRef]
- Releases nf-Core/Viralrecon. GitHub. Available online: https://github.com/nf-core/viralrecon/releases (accessed on 28 January 2022).
- 24. Hadfield, J.; Megill, C.; Bell, S.M.; Huddleston, J.; Potter, B.; Callender, C.; Sagulenko, P.; Bedford, T.; Neher, R.A. Nextstrain: Real-time tracking of pathogen evolution. *Bioinformatics* **2018**, *34*, 4121–4123. [CrossRef]
- Nguyen, L.-T.; Schmidt, H.A.; von Haeseler, A.; Minh, B.Q. IQ-TREE: A Fast and Effective Stochastic Algorithm for Estimating Maximum-Likelihood Phylogenies. *Mol. Biol. Evol.* 2015, *32*, 268–274. [CrossRef]
- 26. FigTree. Available online: http://tree.bio.ed.ac.uk/software/figtree/ (accessed on 28 January 2022).
- Didelot, X.; Wilson, D.J. ClonalFrameML: Efficient Inference of Recombination in Whole Bacterial Genomes. *PLoS Comput. Biol.* 2015, 11, e1004041. [CrossRef] [PubMed]
- O'Toole, Á.; Scher, E.; Underwood, A.; Jackson, B.; Hill, V.; McCrone, J.T.; Colquhoun, R.; Ruis, C.; Abu-Dahab, K.; Taylor, B.; et al. Assignment of epidemiological lineages in an emerging pandemic using the pangolin tool. *Virus Evol.* 2021, 7, veab064. [CrossRef] [PubMed]
- 29. Aksamentov, I.; Roemer, C.; Hodcroft, E.; Neher, R. Nextclade: Clade assignment, mutation calling and quality control for viral genomes. *JOSS* **2021**, *6*, 3773. [CrossRef]
- Kalyaanamoorthy, S.; Minh, B.Q.; Wong, T.K.F.; Haeseler, A.; von Jermiin, L.S. ModelFinder: Fast model selection for accurate phylogenetic estimates. *Nat. Methods* 2017, 14, 587–589. [CrossRef]
- Hoang, D.T.; Chernomor, O.; Haeseler, A.; von Minh, B.Q.; Vinh, L.S. UFBoot2: Improving the Ultrafast Bootstrap Approximation. *Mol. Biol. Evol.* 2018, 35, 518–522. [CrossRef]
- 32. Sagulenko, P.; Puller, V.; Neher, R.A. TreeTime: Maximum-likelihood phylodynamic analysis. *Virus Evol.* **2018**, *4*, vex042. [CrossRef]
- Chia, W.N.; Zhu, F.; Ong, S.W.X.; Young, B.E.; Fong, S.W.; Bert, N.L.; Tan, C.W.; Tiu, C.; Zhang, J.; Tan, S.Y.; et al. Dynamics of SARS-CoV-2 neutralising antibody responses and duration of immunity: A longitudinal study. *Lancet Microbe*. 2021, 2, e240–e249. [CrossRef]
- Harvey, W.T.; Carabelli, A.M.; Jackson, B.; Gupta, R.K.; Thomson, E.C.; Harrison, E.M.; Ludden, C.; Reeve, R.; Rambaut, A.; Robertson, D.R.; et al. SARS-CoV-2 variants, spike mutations and immune escape. *Nat. Rev. Microbiol.* 2021, 19, 409–424. [CrossRef]
- 35. Xu, X.; Nie, S.; Wang, Y.; Long, Q.; Zhu, H.; Zhang, X.; Sun, J.; Zeng, Q.; Zhao, J.; Liu, L.; et al. Dynamics of neutralizing antibody responses to SARS-CoV-2 in patients with COVID-19: An observational study. *Signal Transduct. Target Ther.* **2021**, *6*, 197. [CrossRef]
- 36. Anand, S.P.; Prévost, J.; Nayrac, M.; Beaudoin-Bussières, G.; Benlarbi, M.; Gasser, R.; Brassard, N.; Laumaea, A.; Gong, S.Y.; Bourassa, C.; et al. Longitudinal analysis of humoral immunity against SARS-CoV-2 Spike in convalescent individuals up to 8 months post-symptom onset. *Cell Rep. Med.* 2021, 2, 100290. [CrossRef]
- Li, B.; Deng, A.; Li, K.; Hu, Y.; Li, Z.; Shi, Y.; Xiong, Q.; Liu, Z.; Guo, Q.; Zou, L.; et al. Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 Delta variant. *Nat. Commun.* 2022, 13, 460. [CrossRef] [PubMed]

- Hirabara, S.M.; Serdan, T.D.A.; Gorjao, R.; Masi, L.N.; Pithon-Curi, T.C.; Covas, D.T.; Curi, R.; Durigon, E.L. SARS-CoV-2 Variants: Differences and Potential of Immune Evasion. *Front. Cell. Infect. Microbiol.* 2022, 11, 781429. Available online: https://www.frontiersin.org/article/10.3389/fcimb.2021.781429 (accessed on 23 April 2022). [CrossRef] [PubMed]
- Thomson, E.C.; Rosen, L.E.; Shepherd, J.G.; Spreafico, R.; da Silva Filipe, A.; Wojcechowskyj, J.A.; Davis, C.; Piccoli, L.; Pascall, D.J.; Dillen, J.; et al. Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity. *Cell* 2021, 184, 1171–1187.e20. [CrossRef] [PubMed]
- López, M.; Peinado, A.; Ortiz, A. Characterizing two outbreak waves of COVID-19 in Spain using phenomenological epidemic modelling. *PLoS ONE* 2021, 16, e0253004. [CrossRef]
- Salfi, F.; D'Atri, A.; Tempesta, D.; Ferrara, M. Sleeping under the waves: A longitudinal study across the contagion peaks of the COVID-19 pandemic in Italy. J. Sleep Res. 2021, 30, e13313. [CrossRef]
- 42. Kimita, G.; Nyataya, J.; Omuseni, E.; Sigei, F.; Lemtudo, A.; Muthanje, E.; Andika, B.; Liyai, R.; Githii, R.; Masakhwe, C.; et al. A genomics dissection of Kenya's COVID-19 waves: Temporal lineage replacements and dominance of imported variants of concer. *Res. Sq.* **2021**. Available online: https://europepmc.org/article/PPR/PPR408814 (accessed on 28 January 2022).
- Githinji, G.; Laurent, Z.R.; de Mohammed, K.S.; Omuoyo, D.O.; Macharia, P.M.; Morobe, J.M.; Otieno, E.; Kinyanjui, S.M.; Agweyu, A.; Maitha, E.; et al. Tracking the introduction and spread of SARS-CoV-2 in coastal Kenya. *Nat. Commun.* 2021, 12, 4809. [CrossRef]
- Grabowski, F.; Kochańczyk, M.; Lipniacki, T. Omicron strain spreads with the doubling time of 3.2–3.6 days in South Africa province of Gauteng that achieved herd immunity to Delta variant. *medRxiv* 2021. Available online: https://www.medrxiv.org/ content/10.1101/2021.12.08.21267494v1 (accessed on 28 January 2022).
- 45. Xia, F.; Yang, X.; Cheke, R.A.; Xiao, Y. Quantifying competitive advantages of mutant strains in a population involving importation and mass vaccination rollout. *Infect. Dis. Model.* **2021**, *6*, 988–996. [CrossRef]
- Russell, A.; O'Connor, C.; Lasek-Nesselquist, E.; Plitnick, J.; Kelly, J.P.; Lamson, D.M.; George, K.S. Spatiotemporal analyses illuminate the competitive advantage of a SARS-CoV-2 variant of concern over a variant of interest. *medRxiv* 2021. Available online: https://www.medrxiv.org/content/10.1101/2021.09.14.21262977v1 (accessed on 14 September 2021).
- Garcia-Beltran, W.F.; Lam, E.C.; St Denis, K.; Nitido, A.D.; Garcia, Z.H.; Hauser, B.M.; Feldman, J.; Pavlovic, M.N.; Gregory, D.J.; Poznansky, M.C.; et al. Multiple SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity. *Cell* 2021, 184, 2372–2383.e9. [CrossRef] [PubMed]