Title: A new Omicron lineage with Spike Y451H mutation that dominated a new COVID-19 wave in Kilifi, Coastal Kenya: March-May 2023

Authors

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Running Title

New FY.4 Omicron lineage in Kilifi, Kenya

Key Words

FY.4, SARS-CoV-2, Omicron, Kilifi, Kenya

Abstract

We report a newly emerged SARS-CoV-2 Omicron lineage, named FY.4, with two unique mutations; spike:Y451H and ORF3a:P42L. FY.4 emergence coincided with increased SARS-CoV-2 cases in coastal Kenya between April and May 2023. We demonstrate the value of continued SARS-CoV-2 genomic surveillance in post-acute pandemic era in understanding new COVID-19 outbreaks.

Main Text

To date >340,000 test-confirmed COVID-19 cases and 5,688 COVID-19-related deaths have been reported in Kenya[1]. Sero-surveillance indicated high seropositivity in rural and urban populations despite low vaccine uptake (~28% of the adult population received at least one dose)[2]. By August 2022, 69-81% of rural (Kilifi and Siaya) and 89-95% of urban (Nairobi and Kisumu) Kenya adult population had anti-Spike IgG antibodies (unpublished data).

Genomic surveillance has been critical in informing origins of new waves, evolution, and spread patterns of SARS-CoV-2. By June 2023, seven distinct waves of SARS-COV-2 infections had been observed in Kenya[1][3]. The last three were dominated by Omicron sub-variants: BA.1-like, BA.5-like and BQ-like, respectively. These sub-variants were associated with an increase in SARS-CoV-2 cases due to possession of mutations conferring escape from pre-existing immunity and/or transmission advantage[4].

In coastal Kenya, the KEMRI-Wellcome Trust Research Programme (KWTRP) is conducting SARS-CoV-2 genomic surveillance across five health facilities (HFs) within the Kilifi Health and Demographic Surveillance System (KHDSS)[5]. Up to 75 respiratory samples are collected weekly from individuals across all ages presenting with acute respiratory illness to the participating HFs. SARS-CoV-2 RT-PCR testing and sequencing is performed on: (i) positive samples from the KHDSS HFs surveillance and (ii) positive SARS-CoV-2 samples from other collaborating HFs across Kenya.

Beginning late March, SARS-CoV-2 positivity rate in the KHDSS HFs increased from 1.2% in the week commencing 27th March, and peaked at 42.9%, in the week commencing 24th April (Figure, panel A). This then dropped in the first week of May to 23.5% and ranged between 5.0%-7.7% over the next three weeks. Between January – May, 120/1612 (7.4%) SARS-CoV-2 positives were identified from samples collected from the KHDSS surveillance. Ninety-six samples (80%) with cycle threshold (Ct) values <35 were sequenced either on Oxford Nanopore Technologies – GridION (n=35) or Illumina Miseq (n=61), recovering 76(79%) genomes with coverage ≥70%. Additionally, we received 39 positives from HFs outside the KHDSS, of which 32(82%) were sequenced yielding 25(78%) genomes, Supplementary Table 1.

The 76 genomes from KHDSS HFs were assigned into two lineages; BQ.1.1(n=1), and FY.4(n=75). The increase in the positivity rate starting late March coincided with detection of a new Omicron lineage FY.4 (Figure, panel B). In Kenya, the FY.4 lineage was first observed in Lamu County(n=6) on 10th March 2023, (Figure panel A). By 31st May, (GISAID accessed on 21st August), this new FY.4 lineage had been detected in four other counties; Mombasa(n=2), Narok(n=2), Nairobi(n=7) and Kiambu(n=31). In the KHDSS, FY.4 lineage was first identified from samples collected on 27th March and by April and May it became the dominant lineage, representing 98% of all the detected SARS-CoV-2 cases. Other than Kenya, the FY.4

lineage had been detected in 13 other countries; Austria, Belgium, Germany, Italy, India, Sweden, Canada, France, China, Australia, Spain, United Kingdom and United States of America (GISAID accessed on 21st August)[6].

In the KHDSS HFs, participants infected with FY.4 presented with cough (98%), fever (78%) and nasal discharge (74%) while 7% presented with difficulties in breathing (Table). Only 13 (16%) participants reported receiving at least one dose of a COVID-19 vaccine. A sero-surveillance study (February – June 2022) found that 67% of the unvaccinated KHDSS residents have anti-SARS-CoV-2 IgG antibodies indicating that a high proportion of this population may have been naturally infected[7].

Relative to other Omicron lineages, the FY.4 has two additional amino acid(aa) changes; spike(Y451H) and ORF3a(P42L). The exact impact of the Y451H change is unknown. Previous studies have shown that spike aa change in the receptor binding domain near the Y451H, such as L452R increases virus infectivity and fusogenicity by enhancing spike stability and cleavage[8]. Changes within the ORF3a $CD8^+$ T cell epitopes have been reported to cause complete loss of recognition in the ancestral lineages and Alpha VOC[9].

We applied a Bayesian hierarchical model[10] to estimate the growth rate of the FY.4-like lineage in Kenya. These estimates serve as warning system for lineages showing consistent increase in frequency for at least two consecutive weeks in Kenya and/or other countries. Growth rate estimates on Kenyan data was compared to data from Germany and USA, as these were the only countries with reported FY.4 cases in at least two consecutive weeks as of the last weeks of May (Figure, panel C). The model warned of a high concern in Kenya as from week of March 26 towards May, suggesting continued increase in cases attributed to FY.4 lineage.

In summary, SARS-CoV-2 genomic surveillance in coastal Kenya has detected the emergence of a new Omicron lineage with unique spike and ORF3a gene mutations. Detection

of FY.4 lineage coincided with increase in SARS-CoV-2 cases in Kilifi and has also been detected in other parts of the country. Growth estimates suggests potential for continued spread of FY.4. Further analysis on the phenotypic impacts of the observed mutations are ongoing.

Acknowledgement

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Data Availability

Genome sequences generates in this study are available on GISAID. Generated genomes are listed in the Supplemental_File.docx. The dataset and analysis scripts used are available in Harvard Dataverse at https://doi.org/10.7910/DVN/ZMGR5P.

Conflict of Interest

Authors declare no conflict of interest.

Ethical Statement

The whole genome sequencing study protocol was reviewed and approved by the Scientific and Ethics Review Committee (SERU) residing at the Kenya Medical Research Institute (KEMRI) headquarters in Nairobi (SERU # 4035).

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Table: Distribution of observed clinical symptoms among the FY.4 cases observed in Kilifi Health Demographic Surveillance System between January – May 2023

Symptoms	Omicron FY.4 (n=73)
Fever	
Yes	57 (78.1%)
No	16 (21.9%)
Cough	
Yes	72 (98.6%)
No	1 (1.4%)
Nasal discharge	
Yes	54 (74.0%)
No	19 (26.0%)
Difficulty in breathing	
Yes	5 (6.8%)
No	68 (93.2%)
Sore throat	
Yes	28 (38.4%)
No	45 (61.6%)
Body malaise	
Yes	25 (34.2%)
No	48 (65.8%)
Conscious level	
Alert	73 (100.0%)
COVID-19 Vaccination status	
Yes	12 (16.4%)
No	60 (82.2%)
No data	1 (1.4%)
COVID19 vaccine doses	
1	3 (4.1%)
2	7 (9.6%)
No data	63 (86.3%)

Figure legend

Figure: Panel A – Weekly number of collected samples (horizontal continuous line) and

positive SARS-CoV-2 cases (bars) in health facilities within the Kilifi Health Demographic Surveillance System (KHDSS) between January – May 2023. Vertical dotted lines represent time points when FY.4 lineage was first detected in Kenya (red) and in Kilifi (black). Panel B – Weekly distribution of SARS-CoV-2 lineages observed on samples processed at the KWTR from HFs within the KHDSS and HFs outside the KHDSS between January – May 2023. Lineages in red were identified on samples collected from HFs within the KHDSS while lineages in blue were identified on samples collected from HFs outside the KHDSS. Panel C – Growth rate estimates of the FY.4 variant in Kenya relative to USA and Germany.

Supplementary Table 1.
Summary showing the number of samples collected, positives, and sequenced at KEMRI Wellcome Trust Research Program (KWTRP) between January – May 2023. The KHDSS column represents samples collected from health facilities within the mapped Kilifi Health Demographic Surveillance System (KHDSS) area. The Non-KHDSS column represents already tested positive samples collected outside the KHDSS area and sequenced at KWTRP.

	KHDSS	**Non-KHDSSS**
Samples Collected	1612	x
SARS-CoV-2 Positives	120	39
Cycle Threshold Value (<35) & PCR Concetration (>18)	96	32
Sequences >70% Coverage	76	25
Variants by County	Kilifi (FY.4 – 75, BQ.1 – 1)	Kilifi (BA.1.1 – 2), Kwale (FY.4 - 2), Kiambu (FY.4 – 5), Mombasa (XBB.1.5-like – 1), Nairobi (BQ.1.1 – 1, CH.1.1-1, XBB.1.5-like – 4, XBB.1.9-like – 3, XBB.1.16-1, XBB.1.22.2-1, FY.4 - 4)

X – No samples were shared for testing. We only received already tested samples

Data Availability

GISAID Identifier: EPI_SET_230627zw
doi: 10.55876/gis8.230627zw

All genome sequences and associated metadata in this dataset are published in GISAID's EpiCoV database. To view the contributors of each individual sequence with details such as accession number, Virus name, Collection date, Originating Lab and Submitting Lab and the list of Authors, visit 10.55876/gis8.230627zw

Data Snapshot

EPI_SET_230627zw is composed of 101 individual genome sequences.
The collection dates range from 2023-03-27 to 2023-05-31;
Data were collected in 1 countries and territories;
All sequences in this dataset are compared relative to hCoV-19/Wuhan/WIV04/2019 (WIV04), the official reference sequence employed by GISAID (EPI_ISL_402124). Learn more at https://gisaid.org/WIV04.

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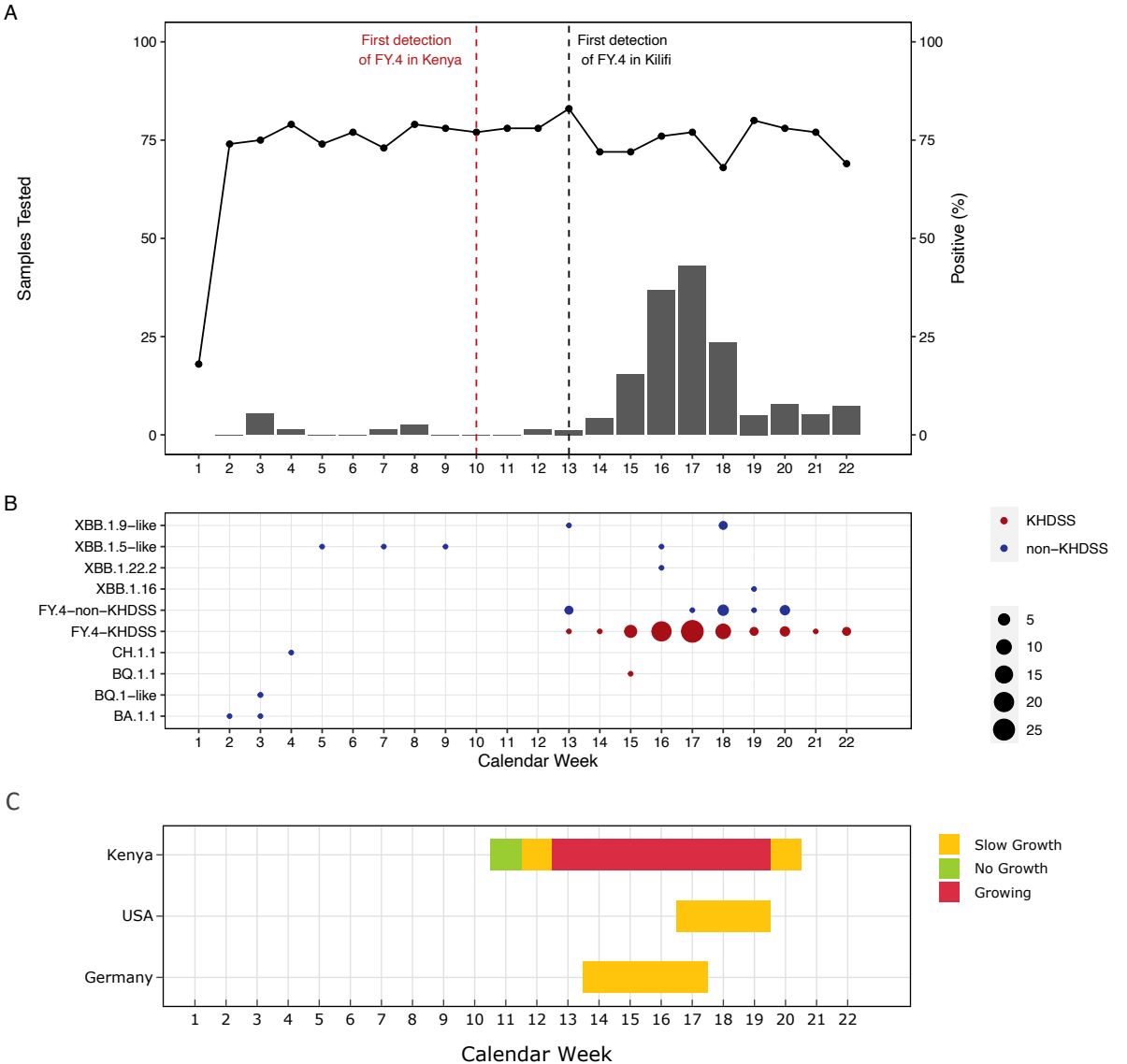
A
First detection of FY.4 in Kenya
First detection of FY.4 in Kilifi
Samples Tested
Positive (%)
100
75
50
25
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
B
XBB.1.9–like
XBB.1.5–like
XBB.1.22.2
XBB.1.16
FY.4–non–KHDSS
FY.4–KHDSS
CH.1.1
BQ.1.1
BQ.1–like
BA.1.1
Calendar Week
KHDSS
non–KHDSS
5
10
15
20
25
C
Kenya
USA
Germany
Calendar Week
Slow Growth
No Growth
Growing