# Rising K13 validated artemisinin resistance mutations in Western Kenya

## Key Points

- Kelch 13 (K13) molecular surveillance was conducted in 8 Western Kenya counties
- The following Pfk13 mutations were detected: the A675V mutation was the most prevalent (5%), followed by the C469Y mutation at 1% and the R561H mutation was less common, 0.5%.
- Compared with previous data from samples collected in the same region in 2022 [1], an increase was observed in the A675V mutation from 1% in 2022 to ~5% in 2023.
- The A675V was present in all 8 counties: Homa Bay (11), Kakamega (9), Siaya (9), Busia (7), Bungoma (6), Migori (4), Kisumu (1) and Vihiga (1).

## Background

Effective antimalarial drugs are essential for controlling and managing malaria cases. However, antimalarial drug resistance is a major threat to malaria control, resulting in increased malaria cases and deaths [2,3]. Since 2015, there have been reports of genetic mutations associated with artemisinin resistance in the East African region, including Rwanda [4], Uganda [5], Ethiopia [6] and Tanzania [7]. These mutations in the Plasmodium falciparum kelch 13 gene (k13) are linked to delayed parasite clearance to artemisinin and include R561H, C469Y, A675V, and R622I. Consequently, k13 molecular surveillance was conducted in 2023 from primarily asymptomatic infections. The data presented here calls for urgency to respond to the threat of a rising frequency of k13 WHO validated artemisinin resistance mutations. It strengthens the call for maintenance and scaling up of molecular surveillance k13 mutations in the Western Kenya region to ensure early detection. These data provide guidance for a prioritisation approach of intensive therapeutic efficacy studies to inform the efficacy of the first- and second-line malaria treatment strategies.

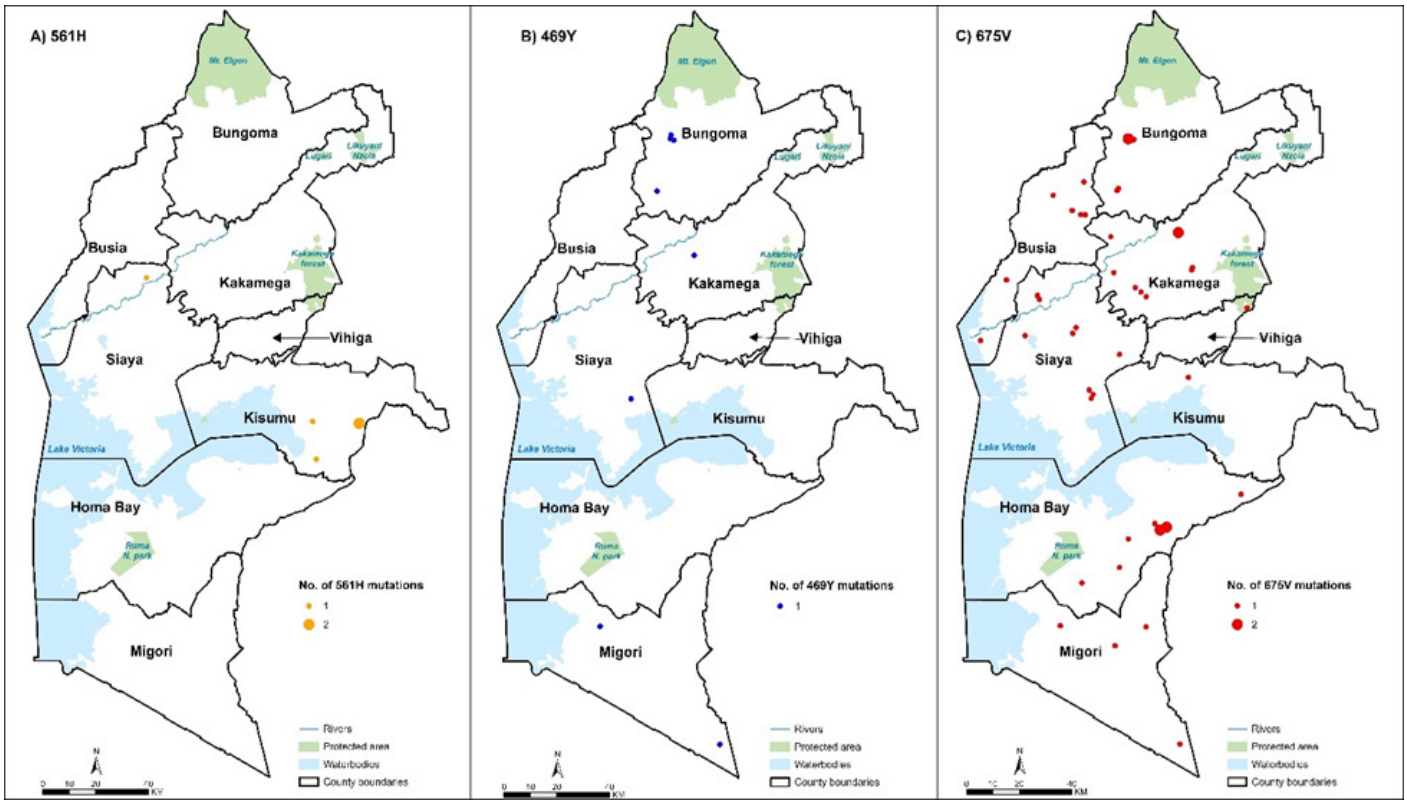
## Findings

- Surveillance among school children from March to April 2023, with asymptomatic malaria was focused on **8 counties in Western Kenya**, lake endemic region: Kisumu, Bungoma, Busia, Homa Bay, Migori, Kakamega, Siaya and Vihiga. 82 Schools were randomly selected, and 100 children aged 5-14 years were chosen from each school's register. The k13 gene was successfully sequenced from 727 samples.
- Overall, three validated k13 mutations associated with artemisinin resistance were identified, **C469Y, R561H**, and **A675V** (Table 1). Siaya was the only county with all 3 validated mutations.
- The R561H mutation was found in 5 samples (0.5%), C469Y in 8 samples (1.1%), and the A675V mutation was the most abundant in 48 samples (5%).
- Both **R561H** and another mutation R561C were identified in both Kisumu and Siaya counties (Figure 1A), while Bungoma and Busia counties only showed R561C.
- The **C469Y** mutation was present in 4 counties, with Bungoma having the largest number (3) of mutant samples (Figure 1B). **The overall proportion of this mutation decreased from 4% in 2022 to 1% in 2023.** However, a county level analysis revealed an increase in Bungoma 7.7% and a reduction in Migori 1% and Siaya 3% from 5.9%, 2.1% and 6.9% in 2022, respectively. It was only observed in Kakamega at 1.3% in 2023.
- **All 8 counties contained the A675V mutation** (Figure 1C). Homa Bay topped the list with 11 mutant samples, followed by Siaya (10) and thereafter Busia (7). Overall, **there is an increase in the prevalence of the A675V mutations in 2023 at 5% compared to previous data from the same area in 2022 of 1%.**

**Table 1: Full list of K13 mutations observed between 2022 and 2023 in Western Kenya**

| | 2022 | | 2023 | |
|---|---|---|---|---|
| Codon | Number of samples | Mutation (%) | Number of samples | Mutation (%) |
| P441A* | **523** | 1.1 | **612** | - |
| G453C | **523** | 1.3 | **612** | - |
| **C469Y** | **523** | 4 | **727** | 1.1 |
| R471C | **523** | - | **727** | 1.1 |
| N489K | **523** | 2.3 | **727** | 3.3 |
| N499S | **523** | 1 | **727** | - |
| D501Y | **523** | - | **727** | 0.8 |
| A504V | **523** | 1.1 | **727** | - |
| V517I | **523** | 1.7 | **727** | - |
| S522C* | **523** | 3.4 | **727** | 1.8 |
| N537S | **523** | 0.4 | **727** | - |
| P553S | **523** | 1.2 | **727** | - |
| **P553L** | **523** | 1.2 | **727** | - |
| Y558C | **523** | 2.7 | **727** | - |
| R561H | **110** | - | **965** | 0.5 |
| R561C | **110** | - | | 0.9 |
| A569T | **523** | 2.1 | **727** | 1.2 |
| A578S | **523** | 15.3 | **727** | 8 |
| P667A | **110** | 7.3 | **965** | 0.1 |
| P667S | | - | | 3.9 |
| **A675V** | **110** | 0.9 | **965** | 5 |
| S679T | **110** | 2.7 | **965** | - |
| E691D | **110** | 89.1 | **965** | - |

## Figure 1: Spatial distribution of k13 validated resistance mutations by village in Western Kenya




*The 8 counties have been demarcated and labelled, and each dot represents the village of the child harbouring the parasite with the mutation. The size of the dot varies depending on the number of mutations identified in that village. (A) Illustrates the distribution of the R561H mutation (yellow dot) (B) the C469Y mutation (blue dot); and (C) the A675V mutation (red dot).*

## Conclusion and Recommendations

There is a sustained presence of C469Y, R561H and A675V (as shared in the previous policy brief) and **an increasing prevalence of the A675V mutation.** This mutation is predominant in Uganda and its rising prevalence in Western Kenya calls for urgent action. Molecular surveillance needs to be maintained and scaled up across the lake endemic and neighbouring counties. Of greater importance a **Therapeutic Efficacy Studies (TES) is critically required** to evaluate the ongoing effectiveness of current antimalarial treatments. Continued combined efforts with the Ministry of Health, DNMP, and county health management teams is required to guide national treatment policies and sustain effective malaria control strategies in Kenya. **Urgent action is now required to swiftly initiate targeted interventions to prevent the spread of the k13 mutations.**

## References: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