POLICY BRIEF
NOVEMBER 2024

Identification of Artemisinin Resistant Mutations in 13 counties in Kenya

Key Points

- Three research groups in Kenya (Two KEMRI partners: KEMRI Wellcome and WRAIR-A and Mount Kenya University) separately conducted molecular surveillance on human malaria parasites, *Plasmodium falciparum* to identify key mutations in the kelch 13 (k13) genetic marker conferring resistance to artemisinin.
- The following k13 mutations were identified in areas of varying malaria transmission: **R561H**- Kericho; **C469Y-** Busia (3 studies), Kisumu (2 studies), Bungoma, Migori, West Pokot, Turkana, Vihiga; **P553L**- Busia, Siaya, Kakamega, Kisumu, Migori; **A675V**- Baringo, Busia, Kericho, Kisii, Kisumu, West Pokot.
- WHO validated artemisinin resistance mutations are present in Kenya. This calls for therapeutic efficacy studies to determine whether these mutations will impact first- (artemether-lumefantrine) and second- (dihydroartemisin-piperaquine)-line treatment efficacy.
- Molecular surveillance should be maintained and scaled up to determine the extent of resistance as well as whether there is an increase in the frequency of these mutations.

Background

Having effective antimalarial drugs is 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 [1,2]. Since 2015, there have been reports of genetic mutations associated with artemisinin resistance in the East African region, including Rwanda [3], Uganda [4], Ethiopia [5] and Tanzania [6]. These mutations in the *Plasmodium falciparum* kelch 13 gene (*k13*) are linked to delayed parasite clearance to artemisinin and include R561H, C469Y, P553L, A675V, and R622I. Together, these data highlight the need for the surveillance of *k13* mutations in Kenya to ensure early detection. Furthermore, monitoring these mutations is crucial for implementing more intensive therapeutic efficacy studies and recommending effective malaria treatment strategies. Consequently, research groups in Kenya have been conducting *k13* molecular surveillance between 2018 and 2024 from symptomatic and asymptomatic malaria infections.

Summary of the three studies

- **KEMRI /Wellcome** (PI: Prof. Oyier): This study conducted surveillance in 100 school children each, aged 5-14 years with asymptomatic malaria in 10 randomly selected schools in 15 counties between March to November 2022. The 15 counties had varying malaria endemicity: Kisumu, Bungoma, Busia, Homa Bay, Migori, Kakamega, Siaya, Vihiga (lake-endemic), Kilifi, Kwale (coastal-endemic), Kisii, West Pokot (highland-epidemic), Tana River, Turkana (semi-arid, seasonal transmission), and Kirinyaga (low-risk) [7].
- **Mount Kenya University** (PI: Dr. Gitaka): The study was a directly observed treatment of AL involving 226 participants ranging from 1- >30 with uncomplicated malaria at Alupe Level 4 Hospital, Busia County, Western Kenya, between October to December 2022. Sixty-three individuals exhibited parasitemia reduction rate equal to or less than 90% on day 1 after AL treatment. The C469Y mutation was identified in 4.8% of samples (n=3) from the group with reduced parasite clearance on day 1 [8].
- **KEMRI/Walter Reed Army Institute of Research - Africa** (PI: Dr. Hoseah Akala): This study collected 626 blood samples between 01 January 2018 and June 2024 from patients in 8 health facilities located in 7 counties spanning four malaria transmission zones: Lake endemic malaria zone (Busia, Kisumu), highland epidemic malaria zone (Kisii and Kericho), a Low risk zone (Nakuru and Laikipia) and a Semi-arid seasonal malaria (Baringo) [9]

Findings

Table 1: Frequency of WHO validated artemisinin resistance mutations per County

County	Mutation	Number of samples	Frequency (%)
Baringo	A675V	13/92	14.1
Bungoma	C469Y	2/54*	3.7*
Busia	A675V	6/245	2.5
	C469Y	2/245, 3/63#, 4/181*	0.8, 4.7#, 2.2*
	P553L	1/181*	0.6*
Kakamega	P553L	1/55*	1.8*
Kericho	R561H	1/53	1.9
	A675V	1/53	1.9
Kisii	P553L	1/110	0.9
	A675V	1/110	0.9
Kisumu	C469Y	1/421, 3/92*	0.2, 3.3*
	P553L	1/92*	1.1*
	A675V	1/92*	1.1*
Migori	C469Y	2/137	1.5*
	P553L	1/137	0.7*
Nakuru	A675V	1/4	25[a]
Siaya	C469Y	9/201*	4.5*
	P553L	2/201*	1.0*
Turkana	C469Y	1/42*	2.4*
Vihiga	C469Y	1/51*	2.0*
West Pokot	C469Y	1/20*	5*[a]
	P553L	1/20*	5*[a]
	A675V	1/20*	5*[a]

*[a] Represents an elevated frequency due to the small number of samples tested. # Gitaka lab data, *Oyier lab data and no label Akala lab data*

Conclusion and Recommendations

Three validated artemisinin resistance k13 mutations, C469Y and A675V previously identified in Uganda, R561H previously identified in Rwanda and Tanzania and P553L a mutation described in Southeast Asia were all detected in four of the five malaria transmission zones of Kenya. With the identification of artemisinin resistance mutations, alongside evidence of rapid increase in frequency based on surveillance studies, there is an urgent need for intensified surveillance of antimalarial resistance; and follow up Therapeutic Efficacy Studies in these regions are urgently required. Enhanced monitoring to include regions classically categorized as less endemic for malaria will allow for the accurate estimation of the burden of artemisinin resistant parasite strains, updating of malaria risk map, therefore enabling swift and targeted interventions to improve case management and prevent their spread.

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