Poster: 6046

malaria consortium
disease control, better health

Molecular surveillance of sulfadoxine-pyrimethamine and amodiaquine resistance markers in northeastern Uganda

Read more
brnw.ch/21wCIyH

Richard Kajubi,[1] Anthony Nuwa,[1] Craig Bonnington,[2] Kevin Baker,[2] Musa Odongo,[1] Tonny Kyagulanyi,[1] Victor Asua,[5] Chris Ebong,[3] David Salandini,[1] Jimmy Opigo,[3] Maureen Nakirunda,[1] James Tibenderana[2]

[1] Malaria Consortium, Uganda
[2] Malaria Consortium, United Kingdom
[3] Ministry of Health, Uganda
[4] Makerere University, Uganda
[5] Infectious Diseases Research Collaboration, Uganda

Seasonal malaria chemoprevention has not notably altered sulfadoxine-pyrimethamine resistance after two consecutive annual rounds in northeastern Uganda.

Introduction

Seasonal malaria chemoprevention (SMC) effectively prevents malaria episodes and deaths in children during the high transmission season.[1] However, adoption of SMC is challenged by parasite resistance to sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) in East and southern Africa[2,3]. In Uganda's Karamoja region, we evaluated SPAQ resistance marker changes in children 3–59 months during the 2021 (85,000 children) and 2022 (270,000 children) SMC rounds as part of a protective effectiveness study.

Methods

- Cross-sectional surveys were conducted in intervention areas and comparison areas (where standard malaria care was provided). These surveys took place before SMC implementation in April 2021 and after two rounds of SMC in November 2022.
- Blood spots from symptomatic children 3–59 months underwent chelex-based DNA analysis.
- We examined molecular markers associated with resistance to SP (PfDHFR 164L, PfDHPS 581G, PfDHFR 51I, 59R, 108N, PfDHPS 437G and 540E) and AQ (PfCRT, PfMDR1 including copy number).
- The proportion of samples in each group was compared between baseline and endline using chi-squared tests.

Results

- Five mutations (PfDHFR 51I, 59R, 108N, PfDHPS 437G and 540E) associated with SP resistance were prevalent (>88 percent) in both intervention and comparison areas. However, no change was seen over time.
- PfDHFR 164L and PfDHPS 581G mutations remained below five percent prevalence. Notably, PfDHFR 164L exhibited a slight but significant increase, rising from less than one percent to 2.3 percent (p=<0.05) in the intervention area, while other mutations remained stable (Table 1).
- Significant variations in the prevalence of AQ resistance markers (PfCRT 76T, PfMDR1 1246Y, 86Y and 184F) were observed over time. Specifically, at the endline, lower proportions of mutations were observed for PfCRT 76T, PfMDR1 1246Y, and 86Y mutations. However, there was an increase in prevalence for the 184F mutation.

Conclusion

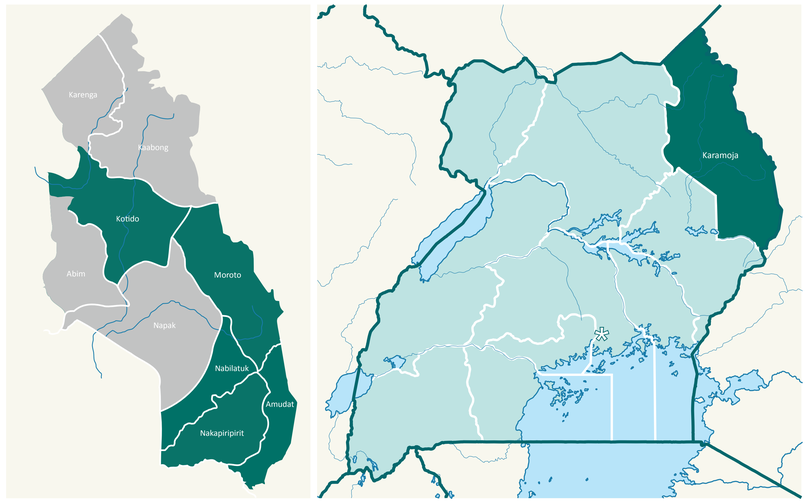
The prevalence of PfDHFR and PfDHPS mutations, associated with moderate SP resistance, was high. Notably, a subtle increase in PfDHFR 164L mutation prevalence occurred in the intervention group from baseline to endline, suggesting possible selection for higher SP resistance. However, actual PfDHFR 164L mutations remained low throughout the study. Key AQ resistance mutations were rare but 184F mutation prevalence, with an unclear AQ resistance role, increased. As SMC expands in Karamoja, ongoing SP and AQ resistance marker surveillance is needed.

Results

Table 1: Prevalence of *Plasmodium falciparum* genetic polymorphisms associated with antimalarial drug resistance

Area	Genetic loci	Baseline (%)	Endline (%)	p value
SP resistance-associated polymorphisms				
Comparison	PfDHFR N51I	130 (100)	129 (97.73)	0.25
	PfDHFR C59R	130 (96.30)	123 (97.62)	0.08
	PfDHFR I164L	5 (3.65)	4 (2.99)	0.99
	PfDHFR S108N	135 (100)	130 (99.24)	0.99
	PfDHPS A437G	115 (100)	126 (96.92)	0.05
	PfDHPS K540E	113 (99.12)	119 (90.84)	0.01
Intervention	PfDHFR N51I	278 (100)	347 (100)	0.99
	PfDHFR C59R	197 (98.5)	336 (97.96)	0.99
	PfDHFR I164L	2 (0.71)	8 (2.33)	0.02
	PfDHFR S108N	290 (100)	343 (99.71)	0.99
	PfDHPS A437G	261 (97.39)	345 (98.29)	0.99
	PfDHPS K540E	180 (88.67)	333 (94.33)	0.99
	PfDHPS A581G	4 (1.52)	3 (0.86)	0.72
AQ resistance-associated polymorphisms				
Comparison	PfCRT K76T	7 (5.65)	9 (8.41)	0.50
	PfMDR1 D1246Y	7 (5.65)	1 (0.71)	0.11
	PfMDR1 N86Y	6 (4.84)	1 (0.79)	0.17
	PfMDR1 Y184F	4 (3.23)	119 (85.61)	<0.001
Intervention	PfCRT K76T	42 (15.44)	22 (6.01)	<0.001
	PfMDR1 D1246Y	38 (13.97)	13 (3.76)	<0.001
	PfMDR1 N86Y	34 (12.5)	6 (1.65)	<0.001
	PfMDR1 Y184F	35 (12.87)	304 (76)	<0.001

Figure 1: Resistance markers study districts, Karamoja, Uganda



Acknowledgements

The SMC programme is funded through philanthropic donations received as a result of being awarded Top Charity status by GiveWell, a non-profit organisation dedicated to finding outstanding giving opportunities. The authors thank the National Malaria Control Division, Ministry of Health, Uganda, Kotido, Moroto and Nabilatuk district local governments, Malaria Consortium UK, Malaria Consortium Uganda and the study respondents. The authors also thank the Bill & Melinda Gates Foundation which funded this study.

References

1. World Health Organization. World Malaria Report 2022. World Health Organization, 2022.
2. Tumwebaze P et al. Changing antimalarial drug resistance patterns identified by surveillance at three sites in Uganda. Journal of Infectious Diseases, 2017.
3. Plowe CV. Malaria chemoprevention and drug resistance: A review of the literature and policy implications. Malaria Journal, 2022.