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Reversal of Malaria Control Gains and Factors associated with Parasitemia among Ugandan Children, 2019 – 2025

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Abstract

Background

Uganda recently launched an ambitious National Malaria Elimination Strategic Plan 2026–2030 that aims to achieve zero malaria deaths, reduce incidence by 75% and attain pre-elimination in at least 19 districts by 2030 and across the country by 2035. However, the 2025 Malaria Indicator Survey (MIS) revealed an increase in parasite prevalence among children < 5 to 13% up from 9% reported in 2019 underscoring the fragility of malaria control gains. This study investigated the demographic, socioeconomic, geographic, and intervention-related factors associated with malaria parasitemia reported in MIS 2025.

Method

Secondary data analysis was conducted using nationally representative datasets of the 2019 and 2025 MIS. The study population comprised of asymptomatic children under five years tested for malaria by blood smear microscopy. The primary outcome variable was malaria parasite positivity by blood smear microscopy while predictor variables were; age, residence (urban vs rural), use of Insecticide treated Mosquito Nets (ITN), indoor residual spraying (IRS) of household in the past 12 months, caretakers' education level, household wealth quintile and geographical region. Statistical analysis was done to assess differences in weighted point prevalence of parasitemia between 2019 and 2025 using the Z-test. Multivariable survey-weighted logistic regression models were conducted to assess and identify demographic, geographical, socioeconomic, and intervention-related predictors of malaria parasitemia. The ArchGIS software was used to map the clusters and households where the children were tested.

Results

National malaria parasite prevalence among children under five significantly increased from 9.1% (95% CI: 7.3% to 10.9%) in 2019 to 12.5% (95% CI: 10.9% – 14.1%) in 2025 (p = 0.005). Urban residence was protective against malaria parasitemia compared to rural settlements [(aOR 0.64; 95% CI: 0.47–0.88), p = 0.07]. Conversely, odds of parasitemia increased progressively with age, peaking at 48–59 months [(aOR 3.34; 95% CI: 1.81–6.16), p = 0.001]. Severe socioeconomic disparities persisted; children from the wealthiest quintile were less likely to have parasitemia than the poorest [(aOR 0.21; 95% CI: 0.11–0.39), p = 0.001]. IRS [(aOR 0.67; 95% CI: 0.44–1.01), p = 0.06] and ITN [(aOR 0.93; 95% CI: 0.76–1.15), p = 0.509] usage did not demonstrate statistically significant protective effect against asymptomatic malaria parasitemia though IRS was borderline non-significant. Sub-nationally, children living in Lango sub-region had increased odds of malaria parasitemia [(aOR 2.45; 95% CI: 1.05–5.67), p = 0.03] while those in Kigezi, Ankole and Kampala had less odd of having malaria parasites [(aOR 0.04; 95% CI: 0.00-0.30), p = 0.002], [(aOR 0.12; 95% CI: 0.04–0.39), p = 0.001] and [(aOR 0.11; 95% CI: 0.01–0.90), p = 0.03] respectively when compared to Bukedi sub-region.

Conclusion

The significant resurgence of malaria parasitemia between 2019 and 2025 MIS point prevalence across several survey sub-regions reveals a critical epidemiological regression in Uganda's malaria control milestones. The findings highlight a breakdown in primary defenses, as traditional vector controls ITNs and IRS failed to provide clear statistically significant protection against asymptomatic malaria parasitemia. Furthermore, malaria burden remains heavily influenced by structural inequalities and socioeconomic vulnerabilities disproportionately affecting rural households, the economically impoverished and poorest wealth quintiles, and older children (48–59 months). Geographically, malaria parasitemia was highly heterogenous, characterized by increasing malaria parasitemia in the Lango sub-region contrasted with near-elimination levels in Kigezi, Ankole, and Kampala suggesting the need for sub-regional specific malaria interventions based on local context. These findings also support the need for establishment innovative malaria control approaches that integrate malaria prevention into poverty-reduction programs to addresses both malaria transmission and underlying socioeconomic disparities and vulnerabilities particularly in rural settings where the lowest wealth quintile and the highest burden of malaria parasitemia were reported

Background

Malaria remains one of the most critical public health threats and economic burdens in Uganda, accounting for a substantial proportion of outpatient visits, health facility admissions, and under-five mortality [1, 2]. Over the past decade, Uganda achieved notable milestones in malaria control including intense scaling of interventions that drove the national parasite prevalence among children under five down from 42% in 2009 to 9% in 2019. Some regions such as Kigezi and Kampala City recorded very low parasite prevalence to less than 1% [3, 4]. This historical success motivated the country to shift its paradigm from mere control to an aggressive elimination agenda, culminating in the drafting of the Uganda Malaria Elimination Strategic Plan (UMESP) 2026–2030, which aims to achieve a 75% reduction in malaria cases and reach pre-elimination status in at least 19 districts by 2030 and across the country by 2035 [1].

Despite these strategic frameworks, clear political commitments and structural roadmaps, the epidemiological landscape presents severe challenges. Data from the recently disseminated 2025 Uganda Malaria Indicator Survey (UMIS) confirmed that the previous downward trajectory has stalled, with the national parasite prevalence among children aged 6 to 59 months reversing to 13% [5]. Crucially, this burden is not uniform but highly heterogeneous across regions. The survey revealed staggering regional disparities; hyper-endemic zones such as the Lango, Acholi and Karamoja sub-region recording parasite prevalence as high as 32%, 23% and 26% respectively by blood smear Microscopy (and 44%, 32%, 32% by real time PCR), while urban centers and traditionally low transmission areas like Kampala and Kigezi reported less than 1% prevalence [1, 5]. Concurrently, programmatic gaps persist. For example, while household ownership of at least one insecticide-treated net (ITN) stands relatively high at

84%, actual consistent usage drops to 65% among household members, signaling a mismatch between commodity distribution and behavioral adoption [5].

To optimize the implementation of the UMESP 2026–2030, a granular understanding of the factors influencing high parasite prevalence at sub-national level context is a key priority. While macro-level factors such as changing weather patterns and insecticide resistance play a broader role, micro-level individual, socioeconomic, household, and community level determinants ultimately dictate an individual child's risk of malaria infection [6, 7]. Relying on aggregate national statistics risks masking important factors that could break or make local elimination frameworks. Although initial reports from the 2025 MIS provide an essential descriptive overview of the disease burden and distribution, they lack the multi-variable statistical modeling required to isolate independent risk factors of malaria parasitemia using the same datasets collected during the survey. To fill this gap, a comprehensive secondary analysis of the 2025 MIS datasets was conducted to identify the specific factors associated with malaria parasite positivity that could provide localized malaria context, actionable evidence and sub-national level realities across different transmission zones in Uganda.

Methods

A secondary data analysis of the 2025 MIS datasets was conducted to assess the factors associated with malaria parasitemia. `Additional analysis was conducted to assess the difference in point prevalence of malaria parasitemia between the 2019 and 2015 MIS estimates

Design and setting of the 2025 National Malaria Indicator Survey (MIS)

The MIS was conducted from November 2024 to January 2025 coinciding with the second peak malaria transmission season in Uganda. Details on selection of clusters, households, children, consent and testing procedures at the selected households are contained in the 2025 MIS report [8]. Briefly, the MIS used a two-sampling approach. The first stage involved selecting clusters from the census enumeration areas (that acted as a sampling frame) delineated from the National Population and Housing Census (NPHC). Based on probability proportional to size approach, a total of 322 clusters were selected with 130 from urban and 192 from rural areas. The second stage of sampling involved random selection of a total of 10,011 households from all clusters for inclusion in the survey from where children were selected for malaria testing.

Study variables

The dependent variable is malaria parasite positivity by blood smear microscopy among children under 5 years of age. The independent variables analyzed included; age, residence (urban vs rural), use of a ITNs, IRS of household, caretakers' highest education level, household wealth status and geographical region.

Laboratory testing for malaria

Thick blood smears were prepared in the field. Each blood smear slide was given a duplicate barcode label affixed both on the microscope slide and the slide transmittal form to help track the smears from the field to the laboratory. Blood smear slides were dried in a dust-free environment and stored in slide boxes. The thick smear slides were collected regularly from the field and transported to the Central Public Health Laboratories (CPHL) for accessioning, staining, and microscopic reading. Thick blood smears were stained with 2% Giemsa stain and examined to determine the presence or absence of *Plasmodium* parasites and to determine parasite density based on the standard WHO recommended method for blood smear microscopy [9, 10]. Blood smears were considered negative if no parasites were found after 100 high-powered fields had been examined. All stained slides were read by two independent WHO-certified microscopists. Discrepant slides were re-analyzed by a third WHO certified microscopist to determine the final result.

Data Analysis

Variables of interest were extracted from the MIS 2025 primary datasets and MIS 2019 as necessary. Both MIS 2019 and 2025 surveys were conducted around the same time of the year /during the second peak transmission that runs from November to December within exact administrative and geographical survey boundaries (the traditional UBOS census boundaries) ensuring comparability. The demographics and household datasets were merged with biomarker (parasitemia) datasets. All estimates contained in the survey datasets were weighted by the statisticians (SB and AK) at the Uganda Bureau of statistics. Details of how the weighting was done is contained in the MIS 2019 and 2025 reports [8]. Baseline participant characteristics presented as frequencies and percentages with their corresponding 95% confidence intervals. To compare point prevalence of parasitaemia between the 2019 and 2025 MIS, data was abstracted from the respective datasets. The difference was then calculated and the confidence intervals estimated using the provided standard errors in each dataset using the formular; 95% CI of the difference = difference ± $1.96 \times \sqrt{(SE_1^2 + SE_2^2)}$. To determine the statistical difference between the two proportions (malaria positivity in 2019 and 2025 MIS), a two-sided z-test for a difference between two independent proportions and the corresponding p-value was calculated using the design-based standard errors using the formula; $z = (p_2 - p_1) / \sqrt{(SE_1^2 + SE_2^2)}$. Survey-weighted multivariable logistic regression was done to assess the factors associated with malaria parasitemia. Independent variables included in the adjusted model were: age of participants, residence (urban or rural), ITN use, IRS use, geographical region and household wealth. Caretaker's education level was not added to the adjusted model because it had a lot of missing observations (1,596/6,324; 25.2%), so would reduce the power of the model. A p-value of < 0.05 was taken as statistically significant. The analysis used design-based adjusted standard errors, to account for clustering, stratification and weighting.

Ethical Considerations

Caretakers or guardians provided written informed consent prior to participation in the study. All data and other information collected were kept confidential. The study protocol was reviewed and approved by Vector Control Division Research and Ethics Committee. Clearance to conduct the study was obtained from Uganda National Council for Science and Technology (UNCST). All participants interviewed consented to granting permission that information from survey can be published or samples used for future studies. The data used in this analysis were anonymous with no individual names of participants captured.

Results

A total of 6,324 children with valid malaria diagnostic test results by microscopy from 322 clusters or enumeration areas were included in this secondary data analysis of the MIS 2025. The 2019 MIS datasets from where point parasite prevalence data were extracted for comparison had been estimated based on 6,626 children with valid malaria diagnostic test results by microscopy from 320 clusters or enumeration areas [4]. The distribution of sampled clusters (EAs) where households are located and from where children were tested was mapped for each survey region using ArchGIS Fig. 1

Figure 1 legend: Location and distribution of clusters (EAs) from where households and samples came from for in each survey region during the 2025 MIS [5]

Baseline Characteristics of Participants

The age of children ranged from 6–59 months, however the 36–47 months old constituted the majority of the children tested (n = 1,473; 23.3%). In terms of residence, most of the children were from clusters located in rural-based survey regions (n = 4,060; 64.2%). Other than Kampala city (1.5%) and Kigezi (3.8%) that had relatively fewer numbers, the number of children was approximately evenly distributed across the survey regions. Most of the children had mothers who had completed primary education (n = 2,702; 42.7%), from the poorest households (n = 1,499; 23.7%) and had slept under the ITN (n = 4,331; 68.5%). Most of the children were from housing structures that were not sprayed (n = 5,503; 87.0%) (Table 1).

Table 1: Baseline characteristics of children aged 6 – 59 months tested for malaria in Uganda 2025 MIS

Variable	Frequency (N)	Percentage (%, 95 CI)
Age Group (months)		
6 to 8	325	5.1 (4.6 - 5.7)
9 to 11	333	5.3 (4.7 - 5.8)
12 to 17	707	11.2 (10.4 - 12.0)
18-23	617	9.8 (9.0 - 10.5)
24-35	1410	22.3 (21.3 - 23.3)
36-47	1473	23.3 (22.3 - 24.3)
48-59	1458	23.1 (22.0 - 24.1)
Residence		
Rural	4060	64.2 (63.0 - 65.4)
Urban	2263	35.8 (34.6 - 37.0)
Geographic Region (MIS Zones)		
Bukedi	436	6.9 (6.3 - 7.5)
Acholi	269	4.3 (3.8 - 4.8)
Ankole	434	6.9 (6.2 - 7.5)
Bunyoro	482	7.6 (7.0 - 8.3)
Busoga	571	9.0 (8.3 - 9.7)
Elgon	321	5.1 (4.5 - 5.6)
Kampala	98	1.5 (1.2 - 1.9)
Karamoja	261	4.1 (3.6 - 4.6)
Kigezi	239	3.8 (3.3 - 4.2)
Lango	366	5.8 (5.2 - 6.4)
North Buganda	685	10.8 (10.1 - 11.6)
South Buganda	912	14.4 (13.6 - 15.3)
Teso	369	5.8 (5.3 - 6.4)
Toro	465	7.4 (6.7 - 8.0)
West Nile	415	6.6 (6.0 - 7.2)
Caretaker education		
No education	511	8.1(7.4 - 8.8)
Primary	2702	42.7(41.5 - 43.9)
Secondary	1224	19.4(18.4 - 20.3)
Higher	291	4.6(4.1 - 5.1)
Wealth Index Quintile		
Poorest	1499	23.7 (22.7 - 24.8)
Poorer	1356	21.4 (20.4 - 22.5)
Middle	1262	20.0 (19.0 - 20.9)
Richer	1189	18.8 (17.8 - 19.8)
Richest	1018	16.1 (15.2% - 17.0)
Slept Under an ITN Last Night		
No	1994	31.5(30.4 - 32.7)
Yes	4331	68.5 (67.3 - 69.6)
IRS Use		
No	5503	87.0 (86.2 - 87.8)
Yes	782	12.4 (11.6 - 13.2)

ITN: Insecticide Treated Net; MIS: Malaria Indicator Survey; IRS: Indoor Residual Spraying;

Increasing proportions of malaria Parasitemia

Based on the MIS report of 2025 a total of 791 out of 6,324 children from the 15 sub-regions tested positive for malaria parasitemia by blood smear microscopy, representing a national weighted parasite prevalence of 12.5% (95% CI: 10.9% – 14.1%). When compared to the 2019 MIS, there was a statistically significant increase in the prevalence of parasite prevalence in the 2019 MIS [9.1% (95% CI = 7.3–10.9)] when compared to the 2025 MIS [12.5% (95% CI = 10.9–14.1)]; Difference = + 3.4 (95% CI = + 10 to + 5.8; p-value = 0.005, indicating an overall significant increase in prevalence across the country. At a sub-region level, the changes varied significantly by region. Significant differences were observed in Bunyoro, Acholi, Lango and Teso having an increase and West Nile being the only one with a significant decrease. Lango experienced the sharpest rise in parasitemia, jumping by + 18.3 percentage points between 2019 and 2025. Teso saw a substantial increase of + 14.7 percentage points. Acholi also increased by + 11

percentage points. West Nile achieved the most notable decline, dropping by -13.8 points which can be explained by the on-going IRS in that sub-region. Karamoja dropped by -8.1 points although it remains one of the highest malaria burden areas overall despite receiving major investments including the special interventions such as Seasonal Malaria Chemoprevention (SMC). Busoga (21%), Kampala (1%) and Kigezi (1%) had no differences in parasite prevalence between the two survey time points (Table 2).

Table 2
Malaria prevalence by microscopy among children under five, by survey region: Uganda MIS 2018–19 vs 2024–25

Survey region	MIS 2018–19		MIS 2024–25		Difference, 2025 – 2019 (95% CI), % points	p-value (z-test)
	No. tested	Prevalence % (95% CI)	No. tested	Prevalence % (95% CI)		
West Nile	459	21.8 (16.8–26.9)	416	8.0 (4.6–11.4)	−13.8 (− 19.7 to − 7.9)	< 0.001
Bunyoro	307	9.2 (4.8–13.6)	481	17.6 (12.0–23.1)	+ 8.4 (+ 1.4 to + 15.4)	0.018
Tooro / Toro	380	4.7 (1.9–7.6)	463	9.2 (1.9–16.5)	+ 4.5 (− 3.3 to + 12.3)	0.255
Ankole	413	2.6 (0.0–6.3)	435	1.5 (0.0–2.9)	−1.1 (− 5.1 to + 2.9)	0.587
Acholi	254	11.9 (7.6–16.2)	268	23.3 (16.3–30.3)	+ 11.4 (+ 3.4 to + 19.4)	0.005
South Buganda	948	0.6 (0.0–1.1)	907	2.3 (0.6–4.0)	+ 1.7 (− 0.2 to + 3.6)	0.073
Busoga	646	21.1 (11.7–30.6)	573	20.9 (11.5–30.2)	−0.2 (− 13.2 to + 12.8)	0.976
Lango	335	13.3 (6.3–20.4)	368	31.6 (23.8–39.3)	+ 18.3 (+ 8.0 to + 28.6)	< 0.001
North Buganda	1,069	8.8 (2.0–15.6)	684	11.4 (7.3–15.5)	+ 2.6 (− 5.1 to + 10.3)	0.510
Kampala	177	0.2 (0.0–0.6)	98	0.4 (0.0–1.2)	+ 0.2 (− 0.7 to + 1.1)	0.655
Bukedi	355	3.3 (0.0–6.6)	434	11.9 (3.5–20.3)	+ 8.6 (− 0.3 to + 17.5)	0.058
Bugisu / Elgon	422	4.8 (0.1–9.6)	318	6.1 (1.8–10.5)	+ 1.3 (− 5.1 to + 7.7)	0.690
Teso	382	8.2 (2.7–13.8)	368	22.9 (19.8–26.0)	+ 14.7 (+ 8.5 to + 20.9)	< 0.001
Karamoja	208	34.3 (24.8–43.7)	258	26.2 (15.7–36.8)	−8.1 (− 22.0 to + 5.8)	0.253
Kigezi	270	0.3 (0.0–0.8)	238	0.6 (0.0–1.8)	+ 0.3 (− 1.0 to + 1.6)	0.655
National	**6,626**	**9.1 (7.3–10.9)**	**6,309**	**12.5 (10.9–14.1)**	**+ 3.4 (+ 1.0 to + 5.8)**	**0.005**

Factors associated with malaria parasitemia

A multivariable logistic regression analysis revealed that individual-level demographics, household socioeconomic status, caregiver education, and distinct geographic regions were significantly associated with malaria parasitemia. In contrast, standard vector control interventions, including the utilization of ITNs and household IRS, did not demonstrate statistically significant protective effects against parasite positivity in this model. With regards to age, malaria risk scales significantly and progressively as a child gets older peaking at age (4 years +) or 48–59 months [aOR 3.34 (95% CI: 1.81–6.16), p = 0.001]. Analysis suggests an Urban Protective Effect. Urban children have 36% lower odds of testing positive for malaria compared to rural children (aOR: 0.64, 95% CI: 0.47–0.88, p = 0.007) suggesting that where a child lives strongly influences their exposure to malaria infection. In terms of regional epidemiological differences, the odds of malaria infections varied with the Lango sub-region a statistically significant association with malaria infection (aOR: 2.45, 95% CI: 1.05–5.67, p = 0.037). Kigezi (aOR: 0.04), Kampala (aOR: 0.11), Ankole (aOR: 0.12), and South Buganda (aOR: 0.26) exhibited highly significant, lower independent odds of malaria infection. In terms of socioeconomics, wealth provided powerful protection or buffer against malaria infection. Moving up the wealth index drastically minimizes odds of being malaria parasitemia positive. Compared to the poorest quintile, children in the middle quintile have 44% lower odds (aOR: 0.56), richer have 65% lower odds (aOR: 0.35), and the richest quintile sees a massive 83% reduction in risk (aOR: 0.17, 95% CI: 0.09–0.32, p = 0.001). Notably, IRS and bed net usage did not show a statistically significant independent correlation with lower parasitaemia (aOR: 0.67, 95% CI: 0.44–1.01, p = 0.058) and (aOR: 0.93, p = 0.509) respectively (Table 3).

Table 3
Factors associated with malaria parasitemia by blood smear microscopy based on MIS 2025 datasets

Variable	Malaria Parasitaemia		Unadjusted OR		Adjusted OR	
	Positive (n = 791)	Negative (n = 5533)	cOR (95% CI)	P-value	aOR (95% CI)	P-value
Age in months						
6 to 8	18 (2.3%)	307 (5.6%)	Reference		Reference	
9 to 11	23 (2.9%)	310 (5.6%)	1.29 (0.61–2.74)	0.504	1.41 (0.64–3.10)	0.388
12 to 17	71 (9.0%)	636 (11.5%)	1.93 (1.06–3.52)	0.032	1.92 (1.02–3.60)	0.043
18–23	62 (7.9%)	555 (10.0%)	1.93 (1.05–3.55)	0.035	1.92 (1.01–3.67)	0.048
24–35	168 (21.3%)	1242 (22.4%)	2.33 (1.29–4.23)	0.005	2.45 (1.32–4.57)	0.005
36–47	217 (27.5%)	1256 (22.7%)	2.98 (1.65–5.38)	0.001	3.18 (1.72–5.89)	0.001
48–59	230 (29.1%)	1228 (22.2%)	3.23 (1.80–5.80)	0.001	3.34 (1.81–6.16)	0.001
Residence						
Rural	638 (80.7%)	3422 (61.8%)	Reference		Reference	
Urban	152 (19.3%)	2111 (38.2%)	0.39 (0.27–0.54)	0.001	0.64 (0.47–0.88)	0.007
Sub-region						
Bukedi	52 (6.5%)	384 (6.9%)	Reference			
Acholi	63 (7.9%)	206 (3.7%)	2.27 (0.94–5.46)	0.068	1.47 (0.61–3.52)	0.385
Ankole	6 (0.8%)	428 (7.7%)	0.11 (0.03–0.39)	0.001	0.12 (0.04–0.39)	0.001
Bunyoro	85 (10.8%)	397 (7.2%)	1.60 (0.67–3.84)	0.290	1.23 (0.52–2.90)	0.638
Busoga	119 (15.1%)	452 (8.2%)	1.97 (0.75–5.17)	0.170	1.78 (0.74–4.28)	0.199
Elgon	20 (2.5%)	301 (5.4%)	0.48 (0.16–1.43)	0.188	0.34 (0.11–1.04)	0.059
Kampala	0 (0.1%)	98 (1.8%)	0.03 (0.00-0.24)	0.001	0.11 (0.01–0.90)	0.039

Variable	Malaria Parasitaemia		Unadjusted OR		Adjusted OR	
	Positive (n = 791)	Negative (n = 5533)	cOR (95% CI)	P-value	aOR (95% CI)	P-value
Age in months						
Karamoja	69 (8.7%)	192 (3.5%)	2.68 (1.03–6.97)	0.044	1.41 (0.54–3.69)	0.477
Kigezi	1 (0.2%)	238 (4.3%)	0.04 (0.01–0.38)	0.004	0.04 (0.00-0.30)	0.002
Lango	116 (14.7%)	250 (4.5%)	3.45 (1.45–8.21)	0.005	2.45 (1.05–5.67)	0.037
North Buganda	78 (9.8%)	607 (11.0%)	0.95 (0.39–2.31)	0.916	1.03 (0.43–2.45)	0.946
South Buganda	21 (2.6%)	891 (16.1%)	0.17 (0.06–0.52)	0.002	0.26 (0.09–0.77)	0.015
Teso	84 (10.7%)	285 (5.1%)	2.20 (0.98–4.95)	0.055	1.32 (0.59–2.96)	0.500
Toro	42 (5.4%)	423 (7.6%)	0.75 (0.23–2.40)	0.624	0.57 (0.17–1.84)	0.345
West Nile	33 (4.2%)	382 (6.9%)	0.65 (0.26–1.61)	0.348	0.46 (0.19–1.08)	0.075
Caretaker education						
No education	87 (15.8%)	424 (10.2%)	Reference			
Primary	373 (67.9%)	2329 (55.7%)	0.78 (0.56–1.11)	0.168		
Secondary	86 (15.6%)	1138 (27.2%)	0.37 (0.25–0.55)	0.001		
Higher	4 (0.7%)	287 (6.9%)	0.07 (0.02–0.20)	0.001		
Wealth Index						
Poorest	347 (43.9%)	1152 (20.8%)	Reference		Reference	
Poorer	223 (28.1%)	1133 (20.5%)	0.65 (0.49–0.87)	0.004	0.92 (0.71–1.21)	0.561
Middle	131 (16.6%)	1131 (20.4%)	0.38 (0.28–0.53)	0.001	0.56 (0.41–0.75)	0.001
Richer	71 (9.0%)	1118 (20.2%)	0.21 (0.15–0.30)	0.001	0.35 (0.25–0.49)	0.001

Variable	Malaria Parasitaemia		Unadjusted OR		Adjusted OR	
	Positive (n = 791)	Negative (n = 5533)	cOR (95% CI)	P-value	aOR (95% CI)	P-value
Age in months						
Richest	19 (2.4%)	999 (18.1%)	0.06 (0.04–0.11)	0.001	0.17 (0.09–0.32)	0.001
ITN use						
No	252 (31.9%)	1742 (31.5%)	Reference		Reference	
Yes	539 (68.1%)	3792 (68.5%)	0.98 (0.82–1.17)	0.843	0.93 (0.76–1.15)	0.509
IRS Use						
No	692 (87.9%)	4811 (87.5%)	Reference		Reference	
Yes	95 (12.1%)	687 (12.5%)	0.96 (0.63–1.47)	0.861	0.67 (0.44–1.01)	0.058

Discussion

The Uganda MIS 2025 reveals a troubling trajectory for malaria control, demonstrating a national parasite prevalence of 12.5% among children under five years a notable increase from the 9.1% reported in the 2019 MIS. This signifies a critical epidemiological regression and highlights the potential challenges of malaria control in the country [11, 12]. While malaria elimination would realistically require systematic decline and getting malaria cases towards zero, the country is currently moving in the opposite direction based on the 2019 and 2025 MIS. Launching an elimination plan for 2026–2030 while prevalence is actively rising creates a reality and structural gap. This evidence of epidemiological reversal underscores the profound challenge likely to face the newly launched National Malaria Elimination Strategic Plan (UMESP) 2026–2030, which aims to transition at least 19 districts and eventually all districts from control to elimination districts by 2030 and 2035 respectively. The importance of this secondary analysis of MIS data is premised in the fact that MIS provides an essential descriptive overview of the disease burden and distribution, but lacks the multi-variable statistical modeling required to isolate independent factors of malaria parasitemia such as micro-level individual, household, and community determinants which ultimately dictate an individual child's risk of infection. Our findings indicate that the burden of malaria parasitemia is not uniform but heavily stratified by socio-demographic vulnerabilities, caregiver education, geographic clusters and poverty levels, while traditional blanket interventions like ITNs and IRS showed diminished epidemiological protection.

Interestingly, neither Insecticide-Treated Nets nor IRS provided statistically significant protection against malaria parasitemia consistent with what was reported previously in a large cohort in Tororo in Eastern Uganda, a district that had received both IRS and ITNs for many years [13]. Based on the current

preference of these two vector control tools, this is probably one of the most alarming findings of the study; two primary pillars of Uganda's national malaria control strategy failing to provide significant protection for children < 5 years against malaria parasitemia. This could be explained by current levels and widely spread insecticide resistance [14]. Mosquitoes in Uganda have likely developed widespread physiological resistance to pyrethroids which has been a core component of insecticides used on standard nets and in IRS [14, 15]. The second plausible explanation is related to the changing mosquitoes biting habits and pattern (such as biting earlier in the evening before children go to bed, or biting outdoors), rendering indoor interventions less effective [16, 17]. There has been emerging net fatigue and misuse. While nets may be distributed to high coverage and ownership, they might not be fitted/hunged properly, are used for other purposes (like fishing or fencing), have physical holes that diminish physical protection or may not be used [18–20]. All these provide important avenues for mosquito bites and parasite transmission.

In this secondary analysis, children aged 48–59 months had over 3 times higher odds of malaria parasitemia compared to younger infants. However, every age bracket above 12 months shows a statistically significant increase in odds of malaria parasite positivity. The increase in odds of parasitemia with increasing age seen in this study is consistent with what was reported in previous studies in Eastern Uganda that found that older children were the primary carriers of parasite pool [13] and may be explained by the fact that immunity shifts and behavioral changes are exposing older toddlers to higher risks. Historically, malaria interventions heavily target pregnant mothers and neonates/young infants. As children reach 4 to 5 years old, parents may become less vigilant about ensuring they sleep under bed nets [21]. Furthermore, younger infants may still carry passive maternal immunity or receive prompt medical attention, whereas older children spend more time playing outdoors in the evenings during peak mosquito biting hours compared to infants, exposing them to early-biting mosquitoes [21, 22].

The analysis revealed significant association between malaria parasitemia and the socioeconomic and educational inequalities, though education level was only assessed at bivariable given the high levels of missing observations. The richest individuals and children of caretakers with secondary education or higher had dramatically lower odds of malaria infection suggesting that malaria remains fundamentally a disease of poverty and structural vulnerability. This can be explained by the fact that wealthier households usually have better-built housing (screens on windows, ceiled roofs and no eaves) that physically blocks mosquitoes, and they can afford supplementary protection (coils, sprays, commercial repellents) [6, 23, 24]. On the other hand, educated caretakers generally possess higher health literacy, meaning they recognize early symptoms faster, seek prompt diagnosis and treatment, and strictly adhere to treatment courses. The potential implication is that malaria control should integrate socio-economic development, poverty eradication, housing improvements, and targeted community health education for uneducated or impoverished caretakers [23–25].

Urban residents were less likely to have malaria while rural areas remain the primary reservoirs of high malaria transmission. This may be explained by the fact that rural settlements in Uganda feature higher

vegetation density, stagnant water bodies from agriculture, and poorer housing structures all of which provide ideal breeding grounds for malaria vector Anopheles mosquitoes. While urban areas are safer due to concrete structures and less standing water, the borderline significance shows that urban malaria is still a threat (likely driven by rapid, unplanned peri-urban slums) [25–28].

Results from this secondary analysis shows extreme geographic divergence particularly between high transmission regions of Lango, Acholi, Teso and Karamoka vs low transmission of Kigezi, Ankole and Kampala. Lango region saw a massive surge in risk of malaria parasitemia, while Kigezi, Ankole, and Kampala showed highly protective, near-negligible odds of malaria parasitemia. This shows that Uganda's malaria landscape is highly heterogenous rendering the current “one-size-fits -all” national strategy highly inefficient. These results further confirm that Lango, Acholi and Teso regions remain a malaria transmission hot spot [21]. The failure of previous IRS programs including premature withdraw of the intervention, changing environmental, vector and parasite related factors may be primary triggers responsible for persistence of high malaria parasitemia in this region [11, 13, 29]. On the contrary the cold, high-altitude geography of Southwestern Uganda naturally limits mosquito breeding and parasite development in Kigezi & Ankole [30–33]. In Kampala capital city, urbanization, better housing and readily accessible private healthcare suppress malaria parasitemia and transmission [34].

Findings of this secondary analysis of MIS datasets may be limited by the following;

The malaria indicator surveys use a cross-sectional design meaning data on exposure factors (e.g., net usage, socioeconomic status) and the outcome (malaria positivity) are collected at the exact same time only permitting analysis of statistical associations but making establishment of temporal sequence or definitive causal relationships impossible. Malaria transmission in Uganda exhibits two peak transmission seasons and heavily dependent on rainfall patterns making seasonality and timing of data collection fundamental for valid parasitemia data. However, all MIS in Uganda are conducted and aligned to the second peak transmission season November to December across all survey regions to ensure comparability of data. Data regarding the utilization of ITNs and IRS rely heavily on caretaker recall. This may introduce recall bias or social desirability bias (where caretakers report higher net usage than actual behavior because they know it is the expected answer), potentially masking the true efficacy of these interventions. Because of the massive malaria variables related to the parasites, vectors, human host, environment and interventions, MIS cannot exhaustively collect and analyse all of them in entirety. Unmeasured biological and environmental confounders missing in the MIS dataset could have influence malaria risk, leading to residual confounding. While blood smear microscopy is the gold standard for epidemiological surveys, its accuracy is highly dependent on the skill of the laboratory technician. Low-density parasitemia can sometimes be missed, potentially leading to an underestimation of the true prevalence, particularly in areas approaching near-elimination like Kampala or Kigezi. Microscopy cannot detect very low-level asymptomatic reservoirs therefore exclusion of sub-microscopic infections due to poor diagnostic tools particularly in areas where significant portion of the population carries low-density infections may lead to omission of crucial drivers of transmission dynamics that threatens the National Malaria Elimination Strategic Plan. By design, the MIS focuses strictly on children under five years old.

While we identified a stark vulnerability in the 48–59-month cohort (aOR 3.34), the dataset MIS misses the school-aged children (5–15 years). This older group often acts as a massive, untreated asymptomatic reservoir for malaria transmission in the community but cannot be quantified using this dataset.

However, the MIS data sets present exceptional statistical power and national representativeness with large, scientifically sampled Cohort. With a sample size of 6,324 children under five years old, the study possesses immense statistical power. This large sample size minimizes the margin of error and ensures that the identified associations are not statistical anomalies or products of chance. Secondly, the MIS utilizes a rigorous, multi-stage stratified cluster sampling design mapped directly to national census frames. Because it is nationally representative, the findings can be generalized across the entire country, unlike localized clinical trials or small-scale hospital-based data or sentinel sites. Thirdly, the use of blood smear malaria microscopy (the WHO recommended gold standard) and WHO certified slide readers rather than Rapid Diagnostic Tests (RDTs) provides diagnostic rigor for parasitemia estimation eliminating the risk of false positives caused by circulating *HRP2* antigens from historical infections that have already been cleared. Fourthly, MIS historically yields incredibly high household response rates (typically exceeding 90 – 95%). This minimizes selection bias and ensures that vulnerable, hard-to-reach rural populations are accurately represented in the datasets. Fifthly, even though self-reported data has limitations, the finding that ITNs and IRS yielded no statistically significant protection against malaria parasitemia across more than 6,000 children is a profoundly important signal. It provides strong epidemiological justification for the malaria program to accelerate the deployment of next-generation piperonyl butoxide (PBO) or dual-active ingredient nets. Lastly, the analysis unmasked important spatial fragmentation clearly defining the extreme sub-national variation, contrasting near-elimination clusters (Kampala, Ankole, Kigezi) against the surging crisis in the Lango region. This geographic granularity allows policymakers to abandon wasteful, blanket national interventions and switch to high-efficiency, targeted and context-specific sub-national resource allocation.

Although MIS provides robust datasets collected across the country based on a nationally representative sample, statistical testing was applied to point prevalence of 2019 and 2025 MIS to assess the difference in the two proportions. The epidemiological, entomological climatic and intervention related dynamics that were happening between the two-point prevalence at which parasitemia was measured were not factored into the model. Nevertheless comparison of two-point prevalence estimates are methodologically acceptable and provides important insight on Ugandas malaria control roadmap.

Conclusion

The significant resurgence of malaria parasitemia between 2019 and 2025 MIS point prevalence across all survey sub-regions reveals a critical epidemiological regression in Uganda's malaria control milestones potentially highlighting the fragile nature of the previous gains in malaria control in the country. Our findings indicate a breakdown in primary defenses, as traditional vector controls ITNs and IRS failed to provide clearly statistically significant protection against asymptomatic malaria

parasitemia. Furthermore, malaria burden remains heavily influenced by structural inequalities and socioeconomic vulnerabilities disproportionately affecting older children > 4 years, economically impoverished as well as children living in rural households. Geographically, malaria parasitemia was highly heterogenous, characterized by increasing malaria parasitemia in the Lango sub-region contrasted with near-elimination levels in Kigezi, Ankole, and Kampala suggesting the need for sub-regional specific malaria interventions based on local context. These findings also support the need for establishment of context specific innovative malaria control approaches which integrate malaria prevention into poverty-reduction programs to addresses both malaria transmission and underlying socioeconomic disparities and vulnerabilities particularly in rural households where the lowest wealth quintile and the highest burden of malaria parasitemia were reported

Abbreviations

ACT
Artemisinin Based Combination Therapy
DBS
Dried blood spots
DNA
Deoxyribonucleic Acid
GIS
Geographical Information System
HMIS
Information Management System
IRS
Indoor Residual Spraying
PCR
Polymerase chain reaction
RDT
Rapid Diagnostic Tests
SMC
Seasonal Malaria Chemoprevention
UNCST
Uganda National Council for Science and Technology
WHO
World Health Organization

Declarations

Ethics approval and consent to participate

Approval was obtained from the Vector Control Division Research and Ethics Committee (VCD REC) and the Uganda National Council of Science and Technology ensuring that the study and procedures adhered to the declaration of Helsinki. All participants provided written informed consent before recruitment into the survey.

Consent for publication

Not applicable

Availability of data and materials

This manuscript is generated from secondary analysis of the Uganda Malaria Indicator Survey raw datasets for which the first author (also the corresponding author) is the principal investigator. The entire complete dataset is available from the corresponding author on request. The datasets together with the original MIS reports are also being deposited on online for public access on the demographic health survey website.

Competing interests

The authors declare no competing interests

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Authors' contributions

BBA is the PI of the MIS from which the analyzed datasets originated and designed the study. BBA, TK, CM, ST, AA, IS did sample collection and testing during MIS. BBA, TK, CM, EA supported the data analysis. BBA drafted the manuscript. BBA, EA, JO, SLS, MO, EK, AM, MK, PK reviewed the manuscript. All authors read and approved the final.

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Figures

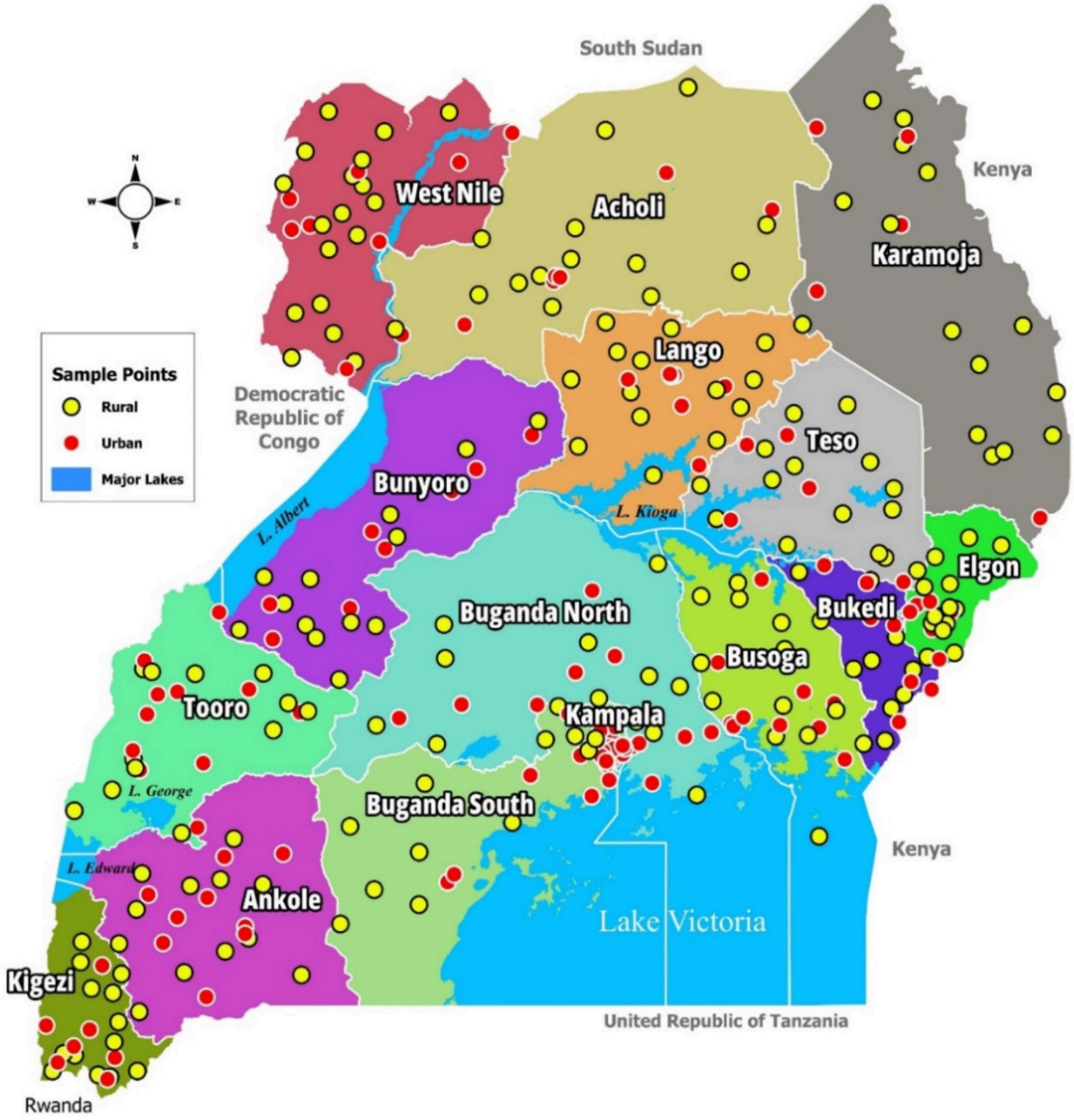

Figure 1

Location and distribution of clusters (EAs) from where households and samples came from for in each survey region during the 2025 MIS [5]