Prevalence of substandard quality artemether-lumefantrine antimalarial agents in Uganda

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Research Article

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Abstract

Background: Substandard antimalarial agents are a key challenge to effective malaria control and elimination efforts especially in sub-Saharan Africa. The quality of antimalarial agents in most low-and-middle income countries (LMICs) is affected by several factors including inadequate regulation and limited resources. In this study, we assessed the pharmacopeial quality of Artemether-Lumefantrine (AL) in low and high malaria transmission settings in Uganda.

Methods: This was a cross-sectional study conducted among randomly selected drug outlets (pharmacies/drug shops). The AL antimalarial agents available in drug outlets were purchased using overt method. The samples were screened for quality using visual inspection, weight uniformity and content assay tests. The assay test was done using Liquid chromatography-mass spectrometry (LC-MS) following International and Unites States Pharmacopoeia (USP) method. The samples were considered substandard if the Active Pharmaceutical Ingredient (API) content was outside 90-110% range of the label claim. Data was analysed using descriptive statistics and presented as means with standard deviations, frequencies, and proportions. Correlation between medicine quality and independent variables was determined using fisher's exact test of independence at 95% level of significance.

Results: A total of 74 AL antimalarial samples were purchased from high (49/74; 66.2%) and low (25/74; 33.8%) malaria transmission settings. The most common batch of AL was LONART, 32.4% (24/74), with 33.8% (25/74) having a 'Green leaf logo'. Overall, prevalence of substandard quality artemether-lumefantrine was 18.9% (14/74; 95%CI: 11.4-29.7). Substandard quality AL was significantly associated with setting (p=0.002). A total of 10 samples (13.5%) failed artemether content assay while, 4 samples (5.4%, 4/74) had substandard lumefantrine content. One sample from a high malaria transmission setting failed both Artemether and Lumefantrine assay test. Of the samples that failed artemether assay test, majority, 90% had low (<90%) artemether content.

Conclusion: Substandard quality AL, the recommended first-line antimalarial agent in treatment of uncomplicated malaria is common especially in high malaria transmission settings. There is need for regular surveillance and monitoring of the quality of artemisinin based antimalarial agents across the country.

Introduction

The World Health Organization (WHO) currently recommends use of RTS, S/AS01 vaccine in malaria prevention [1]. This preventive strategy in addition to Artemisinin based antimalarial agents which have remained highly efficacious for malaria treatment, will strengthen malaria eradication efforts [2]. Globally, Artemisinin agents are the cornerstone of malaria treatment and have contributed to the gains in the fight against malaria [1]. However, malaria treatment especially in sub-Saharan Africa faces several challenges including widespread distribution and use of substandard and falsified antimalarial agents [3]. Use of

substandard and falsified artemisinin-based agents may however jeopardize gains in the fight against malaria [4, 5].

Substandard medicines are authorized medical products that fail to meet either quality standards, specifications, or both while falsified medicines are medical products that deliberately or fraudulently misrepresent their identity, composition, or source [6]. Substandard antimalarials are a common problem especially in malaria endemic regions. A recent meta-analysis revealed that 19% of antimalarials in low- and middle-income countries (LMICs) were substandard or falsified [7]. A report by WHO showed that 28.5% of antimalarial agents sampled from six sub-Saharan African countries were non-compliant with quality specifications [6]. In Uganda, a previous study by Bate et al., [8] found over a third, (35%) of antimalarial agents were of substandard quality.

In sub-Saharan Africa, a previous study reported that 3.8–8.9% deaths from malaria were due to use of substandard and falsified antimalarial agents [9]. In Uganda and Nigeria, substandard and falsified antimalarials contribute to substantial malaria burden especially in children under five years [10, 11]. A study by Renschler et al., [12] found that approximately 122,000 deaths among children under-five years in Africa were associated with consumption of poor-quality antimalarials. Effective malaria treatment requires use of good quality medicines [13]. Substandard and falsified agents may result in needless morbidity and mortality and can facilitate emergence of drug resistance [14]. Use of substandard ACTs in the treatment of malaria common in sub-Saharan Africa is likely to increase the risk of local emergence of artemisinin resistance [14, 15].

Substandard antimalarial agents are a recurrent problem especially in low-and-middle income countries (LMICs) due largely to the inadequate capacity to monitor and control medicine quality [3]. The limited laboratory infrastructure coupled with lack of political will further hinders effective regulation of medicine quality. Our study thus sought to assess the pharmacopoeia quality of Artemether-Lumefantrine antimalarial agents in low and high malaria transmission settings in Uganda.

Methods

Study design and setting

This was a cross-sectional study conducted in low (Kabale and Mbarara districts) and high (Apac and Tororo districts) malaria transmission settings between June-December 2021. Artemether-Lumefantrine drug samples were purchased over the counter from the drug outlets (pharmacies and drug shops). The study samples were analysed from February-March 2022 at the Infectious Disease Institute Clinical Pharmacology laboratory, Makerere University College of Health Sciences.

Sample size, drug outlet selection and sampling

The AL samples were collected from private drug outlets in high and low malaria transmission settings. Private drug outlets in this study are defined as for-profit licensed establishments that dispense

medicines. In each district (Tororo, Apac, Mbarara and Kabale), a comprehensive list of the available private drug outlets was compiled using the National drug authority register of drug outlets. We included both retail and wholesale private drug outlets. Two research assistants, a pharmacist and nurse were trained on the study protocol and collected drug samples for the study. Each of the research assistants separately visited different drug outlets in the study districts. The research assistants then inquired at each drug outlet whether there were any AL antimalarial agents explaining the study and providing approval letters from the Ethics committee, UNCST and district authorities. All the drug outlets that reported stocking AL antimalarial agents were purposively enrolled into the study and samples purchased. In each drug outlet, AL samples were selected from a batch that had not been sampled from previous drug outlets. In addition, AL samples had to have at least one year of shelf-life (time to expiry). In each study district, the research assistants moved from one drug outlet to the next until they could no longer get a batch of AL antimalarial that was not already sampled. For each batch, a minimum of 50 tablets (units) were collected in their original packaging and stored in polythene bags marked with unique code. A drug collection checklist was then filled to capture information on the date of data collection, location of drug outlet, drug outlet type, batch number, brand name, strength (dose), 'Green leaf logo', manufacturer, label claim, generic name, and package size. The samples were then transported to the Clinical Pharmacology laboratory at Infectious Disease Institute, Makerere University College of Health Sciences for content assay.

Visual inspection of packaging materials and tablets

The packaging, insert and individual tablets on each sample were visually inspected and a detailed description recorded on a Microsoft Excel spreadsheet. A modified checklist for Visual Inspection of Medicine (TVIM) provided by the International Council of Nurses in partnership with the United States Pharmacopeia (USP) and Military and Emergency Pharmacists Section of the International Pharmaceutical Federation (FIP) was used for inspection. The description included, stated active ingredients, date of purchase from drug outlets, name of manufacturer, country of origin, batch number, expiry date, number of tablets per packet, brand name, strength (mg/tablet), dosage statement and storage information. The individual tablets for each sample were also visually inspected for deterioration in colour, texture, size, uniformity of shape, contamination (embedded spots) and smell, markings (scoring and letters), breaks/ cracks/ splits. However, we did not have the original package from the manufacturers for comparison.

The registration status of each sample brand was checked using online human drug register of the national drug regulator (www.nda.org.ug/register). The samples that were not registered for use in the country were classified as substandard quality regardless of the assay test.

Weight uniformity determination

Twenty randomly selected tablets from each AL batch were weighed and recorded in excel spreadsheet. The standard deviation and percentage relative standard deviation (RSD) of the weight of each tablet was calculated. The sample passed weight uniformity test if the percentage relative standard deviation per batch was within ±5% [16, 17].

Content analysis of Artemether and Lumefantrine

The content of Active pharmaceutical Ingredient (API) in each AL sample was determined using liquid chromatography-mass spectrometry (LC/MS) following a method by IP and USP. Spectrometric analysis was carried out using ThermoScientific LCQ Fleet ion trap Liquid chromatography-mass spectrometry (LC/MS^n) model (Thermo Fisher Scientific Inc. *355 River Oaks Pkwy*, *San Jose*, *CA 95134)* operated by Xcalibur™ software. Briefly, twenty tablets in each sample were pulverised, powder dissolved in solvent depending on the stated API. For the artemether, the powder was dissolved in methanol (MERCK 1060182500) while for lumefantrine it was dissolved in 10 % acetic acid. For each API, samples for analysis were prepared in duplicate. Solvent extracts were sonicated followed by centrifuging, and the supernatant obtained using a pipette. The supernatant was then used in the analysis to quantify the APIs, Artemether and Lumefantrine in each sample.

The analysis was conducted using Xcalibur LCQ Fleet ion trap system LC/MS system (Thermo Scientific) and separation achieved using Uptisphere 5µm column (C18-ODB 125 x 2.1mm, Interchim technology, USA). The column temperature was maintained at 25°C. The mobile phase was a gradient of eluent A (10mM; 50:50 Ammonium acetate in methanol and acetonitrile) and eluent B (10mM; ammonium acetate). The column was conditioned with 70% of eluent A and 30% eluent B before sample injection. A photo-diode array unit (UV-PDA; DAD 3000) was set at 204 nm for artemether and 360 nm for lumefantrine. In all cases, the flow rate used was 1.0 ml/min. The injection volume was 10µL and the sample run was set at a flow rate of 500 µL/minute for a total run time of 9 minutes. A gradient of 70% eluent A (2 minutes), 100% (1 minutes) eluent B then back to 70% eluent A (6 minutes) to elute the sample through the column.

The calibration curves were generated using known concentrations of artemether and lumefantrine standards. The concentrations of artemether and lumefantrine in each sample were calculated from linear regression analysis of the peak area ratios versus concentration curve. The mean was taken as final API concentration for each batch. The linearity was verified using estimates of correlation coefficient (r^2). Two levels of quality control samples (QCLow=3000µg/L and QCHigh=6000µg/L for artemether and QCLow=1500µg/L and QCHigh=3000µg/L for lumefantrine) were included in each run and analyzed using standard curves of calibrators. Artemether and Lumefantrine standards were spiked in 0.5% formic acid and run-in duplicate alongside study samples. The average concentration of the standards was used in final content assessment of the APIs. For accuracy and precision, the magnitude of expected percentage standard deviation of 15% in quality control results was considered according to the Food and Drug Authority (FDA, USA) guidelines and 10% in expected concentration of pharmaceutical drug tablet according to the international pharmacopoeia recommendations for content analysis. After all the

sample runs, in addition to all samples with substandard API content, we further randomly selected 10% of all AL samples and re-run following the same conditions.

Artemether and Lumefantrine United States Pharmacopeia reference standards were purchased from USP (Twinbrook Parkway, MD 20852-1790, USA). Results were expressed as a percentage of the stated amounts of API on the sample label claim. Quality of ACT was assessed by comparing the amount of API detected with the stated label claim and indicated as a percentage of the stated value. We adopted a range between 90% and 110 % of the stated API content for both Artemether and Lumefantrine to classify samples as being of acceptable quality as recommended by USP and WHO [17].

Data management and analysis

Data was entered in Microsoft excel and transferred to STATA ver 14.0 for analysis. Data on weight uniformity was analyzed using mean, relative standard deviation (RSD) and percentage RSD (%RSD). Sample characteristics were summarized using frequencies and proportions. Prevalence of substandard quality was determined using proportions. Correlation between AL quality and independent variables was determined using Fisher's exact test of independence at 95% level of significance.

Results

Description of the Artemether-Lumefantrine samples collected from low and high malaria transmission settings in Uganda

A total of 74 different batches of Artemether-lumefantrine (AL) samples were collected. Most, 66.2% (49/74) of the samples were collected from high malaria transmission settings (Tororo district, 44.6% (33/74) and Apac district, 21.6% (16/74). All batches of AL except one, (PA0839K3) collected from Tororo district were registered for use in the country. Majority, 93.2% (69/74) of the samples were from India. Only two samples, 2.7% (2/74) were locally manufactured from Uganda. LONART, 32.4% (24/74) and ARTEFAN, 20.3% (15/74) were the most common brands of Artemether-Lumefantrine antimalarial agents (Table 1). Most of the samples, 89.2% (66/74) had standard strength, 20 mg (Artemether) and 120mg (Lumefantrine) of the active pharmaceutical ingredients (APIs). Of the nine samples, 12.2% (9/74) that contained a higher strength of APIs, one had three times the standard strength, 60mg (Artemether) and 360mg (Lumefantrine). A third, 33.8% (25/74) of the AL samples had a 'Green leaf logo'.

Table 1: Characteristics of Artemether-Lumefantrine samples collected from high and low malaria transmission settings in Uganda, June-December 2021 (N=74)

S/N	Brand name	No. of samples n (%)	Malaria transmission Setting	No. of batches	Label claim (AL/mg) 20/120	40/240	Manufacturer, country of origin
1.	LONART[a]	25 (33.8%)	Low	8	8	0	BLISS GVS Pharma Ltd, India
			High	17	13	1	
2.	ARTEFAN[b]	15 (20.3%)	Low	5	5	0	AJANTA Pharma Ltd, India
			High	10	7	1	
3.	LUMARTEM[c]	3(4.1%)	Low	1	1	0	CIPLA Ltd, India
			High	2	1	0	
4.	CO-METHER	5 (6.8%)	Low	2	2	0	AGOG Pharma Ltd, India
			High	3	3	0	
5.	KOMEFAN 140	1(1.4%)	Low	0	0	0	MYLAN Laboratories Ltd, India
			High	1	1	0	
6.	COMBIART	5(6.8%)	Low	0	0	0	STRIDES SHASUN Ltd, India
			High	5	5	0	
7.	LONART-DS[d]	1(1.4%)	Low	0	0	0	BLISS GVS Pharma Ltd, India
			High	1	0	0	
8.	LUMERAX	1(1.4%)	Low	0	0	0	IPCA laboratories Ltd, India
			High	1	1	0	
9.	LARIACT	3(4.1%)	Low	0	0	0	SKANT Healthcare Ltd, India
			High	3	3	0	
10.	Cach-ART	2(2.7%)	Low	0	0	0	CACHET Pharma PVT Ltd, India
			High	2	2	0	
11.	LUMAREN	2(2.7%)	Low	2	2	0	RENE Industries Ltd, Uganda
			High	0	0	0	
12.	COARTEM	1(1.4%)	Low	1	1	0	NOVARTIS PHARMA AG, Switzerland
			High	0	0	0	
13.	KOMEFAN	1(1.4%)	Low	0	0	0	MYLAN Laboratories Ltd, India
			High	1	1	0	

14.	Not indicated	4(5.4%)	Low	4	4	0	IPCA laboratories Ltd, India
			High	1	1	0	
15.	LUMITER	6(8.1%)	Low	3	3	0	MACLEODS Pharma Ltd, India
			High	3	3	0	

AL: Artemether-Lumefantrine; mg: milligrams.

[a]The brand had 3 samples all from high malaria transmission setting with the label claim of 80/480mg (AL)

[b]The brand had two samples all from high malaria transmission setting each with label claim of 80/480mg and 60/360mg (AL)

[c]The brand had one sample from a high malaria transmission setting with label claim of 80/480mg (AL)

[d]The sample had a label claim of 80/480mg (AL)

Visual inspection, physical assessment, and weight uniformity test

All samples passed visual inspection of the labels (as per USP guidelines) however, we could not confirm this due to lack of original packaging material from the manufacturers. From physical examination of the tablets, there was no evidence of disintegration and all samples passed physical assessment. The majority, 98.6% (73/74) of samples passed weight uniformity test. Only one sample (1.4%, 1/74) collected from a low malaria transmission setting (Kabale district) failed weight uniformity test with percentage relative standard deviation of 5.3%.

Prevalence of substandard Artemether-Lumefantrine antimalarial agents collected from high and low malaria transmission settings in Uganda

Overall, 18.9% (14/74; 95%CI: 11.4-29.7) of Artemether-Lumefantrine were of substandard quality. Of the 74 Artemether-Lumefantrine (AL) samples, 13.5% (10/74) failed artemether assay test. Of these, 9 samples had low (<90%) while one had higher (>110%) Artemether content (Additional file 1). Four samples, 5.4% (4/74) failed lumefantrine assay test. Of these, 2 samples each had low (<90%) and high (>110%) lumefantrine content (Additional file 2). All samples that failed either artemether or lumefantrine assay tests were from high malaria transmission settings (Tororo and Apac districts). One sample with the batch, CHRT21001E collected from Apac district failed both Artemether and Lumefantrine content assay test. Over half, 57.1% (8/14) of the brands of AL antimalarial agents failed either Artemether or Lumefantrine assay test (Table 2). One sample was not registered for use in the country and was considered as substandard quality regardless of the assay test.

Table 2: Assay test results of Artemether-Lumefantrine samples (N=74) collected from low and high malaria transmission settings in Uganda, June-December 2021

Brand name	Artemether label claim (mg)	Number of samples tested n/N (%)	Number of samples with Artemether content outside pharmacopeial* range (90-110%), n/N (%)	Number of samples with Lumefantrine content outside pharmacopeial* range (90-110%), n (%)
LONART	20/120	20 (27)	4 (5.4)	2 (2.7)
	40/240	1 (1.4)	0	0
	80/480	3 (4.1)	0	0
LONART-DS	80/480	1 (1.4)	0	0
ARTEFAN	20/120	12 (16.2)	0	0
	40/240	1 (1.4)	0	0
	60/360	1(1.4)	0	0
	80/480[f]	1(1.4)	1(1.4)	1 (1.4)
LUMARTEM	20/120	2 (2.7)	0	0
	80/480	1 (1.4)	0	0
CO-METHER	20/120	5 (6.8)	1 (1.4)	0
KOMEFAN-140	20/120	1 (1.4)	1(1.4)	0
COMBIART	20/120	5 (6.8)	0	0
LUMERAX	20/120	1 (1.4)	1 (1.4)	0
LARIACT	20/120	3 (4.1)	0	1 (1.4)
Cach-ART[e]	20/120	2 (2.7)	2 (2.7)	1 (1.4)
LUMAREN	20/120	2 (2.7)	0	0
COARTEM	20/120	1 (1.4)	0	0
KOMEFAN	20/120	1 (1.4)	0	0
LUMITER	20/120	6 (8.1)	1 (1.4)	0
Not Indicated	20/120	4 (5.4)	0	0
Total number		**74 (100)**	**11 (14.9)**	**5(6.8)**

[*]IP and US Pharmacopeia (90-110%)

[e]One batch (CHRT21001E) of this brand failed both Artemether and Lumefantrine assay test

[f]The sample was not registered for use in the country by the National drug regulator and was classified as substandard regardless of assay results as per the WHO guidelines

n: sample size, N: Total number of samples, %: Percentage

Correlation between substandard quality artemisinin-lumefantrine and independent variables

Of the AL samples having a 'Green leaf logo', 16% (4/25; 95%CI: 5.9-36.6) failed assay test. Most, 25% (6/24; 95%CI: 11.3-46.5) of the substandard quality AL samples were LONART brand. Substandard quality AL was significantly associated with setting (p=0.002). Majority, 28.6% (14/49; 95%CI: 17.5-43.1) of the samples from high malaria transmission setting were of substandard quality (Table 3).

Table 3: Relationship between substandard AL quality and independent variables

Characteristic	Description	Number of samples, n (%)	Proportion of substandard quality n (%)	95% CI	Fisher's exact test
Green leaf AL	No	49 (66.2)	10 (20.4)	11.2-34.4	0.761
	Yes	25 (33.8)	4 (16.0)	5.9-36.6	
Brand name	LONART	24 (32.4)	6 (25.0)	11.3-46.5	0.664
	ARTEFAN	15 (20.3)	1 (6.7)	0.8-37.7	
	CO-METHER	5 (6.8)	1 (20.0)	2.0-75.1	
	LUMITER	6 (8.1)	1 (16.7)	1.8-68.6	
	LARIACT	3 (4.1)	1 (33.3)	2.5-90.9	
	Others	21 (28.4)	4 (19.1)	7.0-42.3	
Setting	High malaria transmission setting	49 (66.2)	14 (28.6)	17.5-43.1	0.002
	Low malaria transmission setting	25 (33.8)	0 (0.0)	-	
AL standard strength (20/120mg)	No	9 (12.2)	1 (11.1)	1.3-54.1	1.000
	Yes	65 (87.8)	13 (20.0)	11.8-31.8	

Discussion

The findings of our study demonstrate that one fifth of Artemether-Lumefantrine (AL) agents contained APIs which were outside the recommended pharmacopeial range. Majority of the AL samples with substandard quality failed assay test of a single active pharmaceutical ingredient (API) in the combination. However, one sample had the content of both Artemether and Lumefantrine outside recommended pharmacopeial range. This is like findings of a review on prevalence of substandard antimalarial agents in sub-Saharan Africa done by Ozawa et al., 2022. Substandard antimalarial agents remain a key problem in the fight against malaria [18]. However, little attention is given to the burden and effects of these agents in the fight against malaria [19]. In most low-and-middle income countries

inadequate drug regulation, lack of political will and limited resources are common risk factors for substandard quality antimalarial agents [20, 21].

Four of fourteen substandard AL antimalarial agents found in our study were among the quality assured artemisinin-based combination therapies (QAACT) and had a 'Green leaf logo'. These agents are distributed under the co-payment mechanism which was developed following large-scale piloting of Affordable Medicines Facility-Malaria (AMFm) from 2010-2011 [22]. The co-payment mechanism was intended to ensure continued provision of subsidies and thus potentially increase access and use of quality assured ACTs in malaria treatment [22]. However, our study found one in every six AL antimalarial agents with a 'Green leaf logo' to be of substandard quality. This is an indicator of the challenges in assuring quality under the co-payment mechanism. Investing in improving capacity of the national drug regulator to monitor manufacture and distribution of ACTs under the co-payment mechanism is key in ensuring quality of ACTs with a 'Green leaf logo' (QAACTs) in the market.

The findings of our study show that all substandard AL antimalarial agents were from high malaria transmission settings in the country. This is like findings of a previous study by Hajjou et al., [21] done in sub-Saharan Africa. High demand coupled with ease of access over the counter of antimalarial agents in the private sector in these settings potentially drive distribution of falsified agents [23, 24]. Additionally, porous borders common in most low- and middle-income countries may contribute to entry and distribution of medicines of unknown quality [24]. This highlights the need to strengthen antimalarial medicine quality surveillance in the private sector especially in malaria endemic countries.

Artemisinin resistance was recently reported in Uganda in a study by Balikagala et al., [25]. Other studies also confirmed presence of K13 molecular markers of artemisinin resistance among *Plasmodium falciparum* parasites in Uganda [26] and in Rwanda [27]. Since its emergence in different regions within Southeast Asia, delayed artemisinin parasite clearance has not spread to other malaria affected areas [1]. This is an indicator of the role local factors unique to specific geographical regions play in driving development of artemisinin resistance among malaria parasites [28]. For the current reported artemisinin resistance in Uganda, understanding the local drivers for its development is key in establishing interventions to mitigate widespread emergence across the country. The findings of the current study demonstrate that seven in every ten substandard AL failed the artemether assay test with 90% of the failed samples having a low API content (<90%). This is like the findings of a previous study done in Ghana and Togo by Osei-Safo et al., [29]. The low artemether content in the AL agents found in this study could be contributing to the current emergence of artemisinin resistance among *Plasmodium falciparum* parasites [30]. This may be worsened by the potential monotherapy due to low content of some APIs in the ACT combination.

In this study, half of the AL samples that failed lumefantrine assay test had a low lumefantrine content (<90%). In the ACT combination, lumefantrine has a longer half-life than artemisinin [31, 32] and thus helps in clearing parasites that survive artemisinin exposure [33]. Use of ACTs with low content of the API is likely to result in exposure of the parasites to sub-therapeutic drug concentrations. The concentration

of the antimalarial agent to which the parasites get exposed to is a key determinant of cure [15]. Although there has not been any reported malaria parasite resistance to lumefantrine. If resistant parasites encounter sub-lethal concentrations of a slowly eliminated antimalarial, they will have a survival advantage and multiply faster than sensitive parasites [34]. This is especially important for poor quality ACTs as they risk the spread of resistance to both the affected API and the unprotected partner API [35]. The long half-life of lumefantrine coupled with substandard quality found in our study may drive emergence of resistance among malaria parasites in the country[34].

The study had some limitations, we used overt sampling where we informed the pharmacy staff of the purpose of the study and obtained a written informed consent prior to purchasing the drug samples. This is likely to present a risk of bias as some of the outlets refused to be sampled. However, this was minimal as only one drug outlet refused to be sampled in Tororo district. Additionally, if drug outlets knew the drug samples which are of poor quality, this would be hidden from the study team. This is unlikely to have affected our study as all the drug outlets provided the stock cards showing all the antimalarial agents that were present in stock at the time of the study.

Conclusion

Artemether-Lumefantrine antimalarials that do not meet pharmacopeial quality specifications are prevalent especially in high malaria transmission settings in Uganda. With the recent discovery of artemisinin resistance in the country, there is need for regular surveillance and monitoring of the quality of artemisinin based antimalarial agents, the cornerstone of malaria treatment.

Abbreviations

ACT: Artemisinin Combination Therapies

API: Active Pharmaceutical Ingredient

AL: Artemether-Lumefantrine

K13: *Kelch13* propeller gene

QAACT: Quality Assured Artemisinin Combination Therapies

AMFm: Affordable Medicines Facility-Malaria

IP: International Pharmacopeia

USP: Unites States Pharmacopeia

UNCST: Uganda National Council of Science and Technology

WHO: World Health Organization

LMICs: Low-and middle-income countries

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by Makerere University School of Biomedical Sciences Research Ethics Committee (SBS 803). The protocol was further reviewed and cleared by Uganda National Council of Science and Technology (UNCST), (HS1169ES). Administrative clearance was also obtained from the local district authorities in the study. In each drug outlet, a written informed consent was obtained from the pharmacist prior to data collection.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interest

The authors declare that they have no competing interests

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Author's contribution

Conceptualization was done by OM, and SN. Acquisition of data was done by OM, LN, DO and AB. The analysis of the data was done by OM and CO. Initial drafting of the manuscript was done by OM and the revisions done by LN, CO, DO, WN, and SN. All authors read and approved the final version of the manuscript.

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