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High and persistent circulation of *Plasmodium falciparum* drug resistant isolates in Nigeria

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Dear Editor,

The return of *Plasmodium falciparum* strains that are sensitive to chloroquine (CQ) in some parts of Africa and the simultaneous development of its resistance to artemisinin and artemisinin combination therapy (ACT) in some south east Asian countries is prompting researchers to reevaluate probable evidence for the re-introduction of these former antimalarial drugs should *P. falciparum* parasite develop resistance to ACTs in Africa. This becomes much more the glaring option (re-introduction of former antimalarials) since there is no alternative first-line drug against *P. falciparum*, although so many are in different clinical trial phase.

In Nigeria, despite the fact that CQ and sulphadoxine-pyrimethamine (SP), formerly used in the treatment of uncomplicated *P. falciparum* infections, have been proscribed for use as first-line antimalarial therapies for more than a decade [1], various troubling reports of very high circulation of *P. falciparum* drug resistant isolates in different parts of the country [2–4] keeps surfacing. This includes our recent study on mutations in the *Pfcrt* and *Pfdhps*/*Pfdfr* genes responsible for CQ and SP resistance, analysed by capillary electrophoresis. In this study which involved more than a hundred and fifty sequenced isolates from two different endemic regions, a significant number (61% for *Pfcrt* and 96% *Pfdhps*/*Pfdfr*) of the isolates were carrying *P. falciparum* drug resistant alleles [5].

This disturbing records is accompanied by the recent World Health Organization report where Nigeria was the highest contributor of malaria cases (25%) and mortality (19%) in the region and worldwide [6]. Such findings provoke series of questions, some of which might have adequate responses. One of such question is if there is indiscriminate use of these drugs (CQ and SP) in the country unknown to malaria control managers and policy makers. This is supported by various epidemiological findings where both drugs have been found to be prescribed and sold as monotherapy in some parts of the country [7,8], needless to mention the unregulated drug entry into Nigeria. Another probable question specifically to CQ would be that perhaps the use of amodiaquine (AQ), a drug with a similar mode of action, in combination with artesunate (AS) is cross selecting for the persistent occurrence of the *P. falciparum* chloroquine resistant transporter gene among the populace, however the ASAQ combination therapy is the second choice ACT therapy in areas where artemether/lumefantrine is not readily available. While this may likely support the current observation, it might not hold true for all parts of Nigeria

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and even if such is the case for *Pfcrt*, what then can we say about the continuous detection of *Pfdhfr* and *Pdhps* mutant alleles?

Now more than ever where, *P. falciparum* sensitive strains are being reported in various parts of Africa, from Ethiopia [9] and Kenya in East Africa [10] Malawi in Southeast Africa [11,12] and even Senegal in West Africa prompting advocacy by the authors for the reintroduction of CQ following the return of sensitive strains [13] in their study. But can this present advocacy be extended to Nigeria and other countries in sub-Saharan Africa? To adequately provide answer to this question and critically look at the way forward, Africans, – especially those in countries where the health system is weak or with high malaria burden such as the Democratic Republic of the Congo [6] and specifically Nigerian researchers must on one hand carry out *in vitro* and molecular analysis study to evaluate each country's profile of *P. falciparum* resistant strains to the different antimalarials and on the other hand, the importation, distribution and drug prescription pattern should be deliberately monitored to unearth any unofficial use of monotherapy should there be any. The later part of this "to do list" is particularly specific to Nigeria, as a very recent study indicates that about 91% of patent and propriety medicine vendors (PPMV) still think that non-artemisinine combination therapies (ACTs) were also certified for use by the Ministry of Health [14]. To this end, while effective routine training for PPMVs in different regions of the country and population education on current antimalarial drugs used should be prioritised, only ACTs antimalarial drugs should be allowed and distributed to different parts of the country, those found defaulting by importation of non-ACTs should be seriously reprimanded.

Conflict of interest

The authors declare that they have no conflict of interest

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.sciaf.2019.e00095.

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