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Short communication

Molecular surveillance of antimalarial drug resistance related genes in *Plasmodium falciparum* isolates from Eritrea

Michela Menegon[a], Abduselam M. Nurahmed[b], Albadawi A. Talha[b], Bakri Y.M. Nour[c], Carlo Severini[a,*]

[a] Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanità, Viale Regina Elena, 299, 00161 Rome, Italy
[b] Faculty of Medical Laboratory Sciences, University of Gezira, P.O. Box 20, Wad Medani, Sudan
[c] Blue Nile Research National Institute for Communicable Diseases, University of Gezira, P.O. Box 20, Wad Medani, Sudan

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ABSTRACT

The introduction of artemisinin-based combination therapy has led to extraordinary results in malaria control, however the recent emergence of partial resistance to artemisinin therapy in Southeast Asia jeopardizes these successes. This study aimed at investigating resistance to the antimalarial drugs by evaluating the polymorphisms in the *PfK13*, *Pfcrt* and *Pfmdr1* genes in *Plasmodium falciparum* isolates obtained from patients in Eritrea.

1. Introduction

After the emergence and spread of *Plasmodium falciparum* multi-drug resistant isolates insensitive to most of the available antimalarials, the introduction of artemisinin-based combination therapy (ACT) as a first-line drug treatment for non-complicated malaria has opened a new horizon in the fight against malaria, with extraordinary results: in practical terms, over the last decade, a dramatic reduction of mortality due to malaria in children, especially in sub-Saharan Africa, has been achieved and the total malaria cases dropped by 40% worldwide (Bhatt et al., 2015). Unfortunately, two studies carried out in 2008 and 2009 in Western Cambodia showed unequivocally that *P. falciparum* was developing resistance to artemisinin (Noedl et al., 2008; Dondorp et al., 2009), and to date, partial artemisinin resistance is spreading across mainland Southeast Asia (Ashley et al., 2014). The possible extent of resistance to artemisinin in Africa would have a devastating effect on child mortality and could wipe out the successes achieved in this decade in the fight against malaria. The recent identification of Kelch 13 propeller (*PfK13*) gene as a marker of artemisinin resistance (Ariey et al., 2014) has provided the international scientific community with a molecular marker to track in real time the emergence of resistant *falciparum* isolates before the artemisinin resistance spread in Africa. The *PfK13* gene codes for a Kelch protein, characterized by a C-terminal six-blade propeller region. Three point mutations (C580Y – R539T – Y493H) in the propeller region have been associated with *in vitro* artemisinin resistance and prolonged parasite half-life after treatment in Cambodian field isolates (Ariey et al., 2014). Furthermore, so far, several SNPs have been identified in this gene in *P. falciparum* isolates from Asia and Africa (Ashley et al., 2014; Conrad et al., 2014; Mohon et al., 2014; Takala-Harrison et al., 2015; Taylor et al., 2015; Tun et al., 2015).

Artesunate-amodiaquine (AS-AQ) was introduced in Eritrea in 2007 as first-line treatment for uncomplicated malaria. In 2010, a study, conducted in five sentinel sites in Gash Barka region by the National Malaria Control Programme to evaluate the therapeutic efficacy of AS-AQ in this area, showed treatment failure in 7.6% of patients treated with AS-AQ (Malaria Update, 2011). This ratio is close to the cut-off limit suggested by WHO, *i.e.* 10%, to take into consideration a change in the local malaria treatment policy.

The objective of the present study was to investigate the presence of point mutations in the *PfK13* gene to monitor the pos-

* Corresponding author.
E-mail addresses: michela.menegon@iss.it (M. Menegon), peace.abdu@gmail.com (A.M. Nurahmed), badawiat@yahoo.com (A.A. Talha), bakrinour@gmail.com (B.Y.M. Nour), carlo.severini@iss.it (C. Severini).

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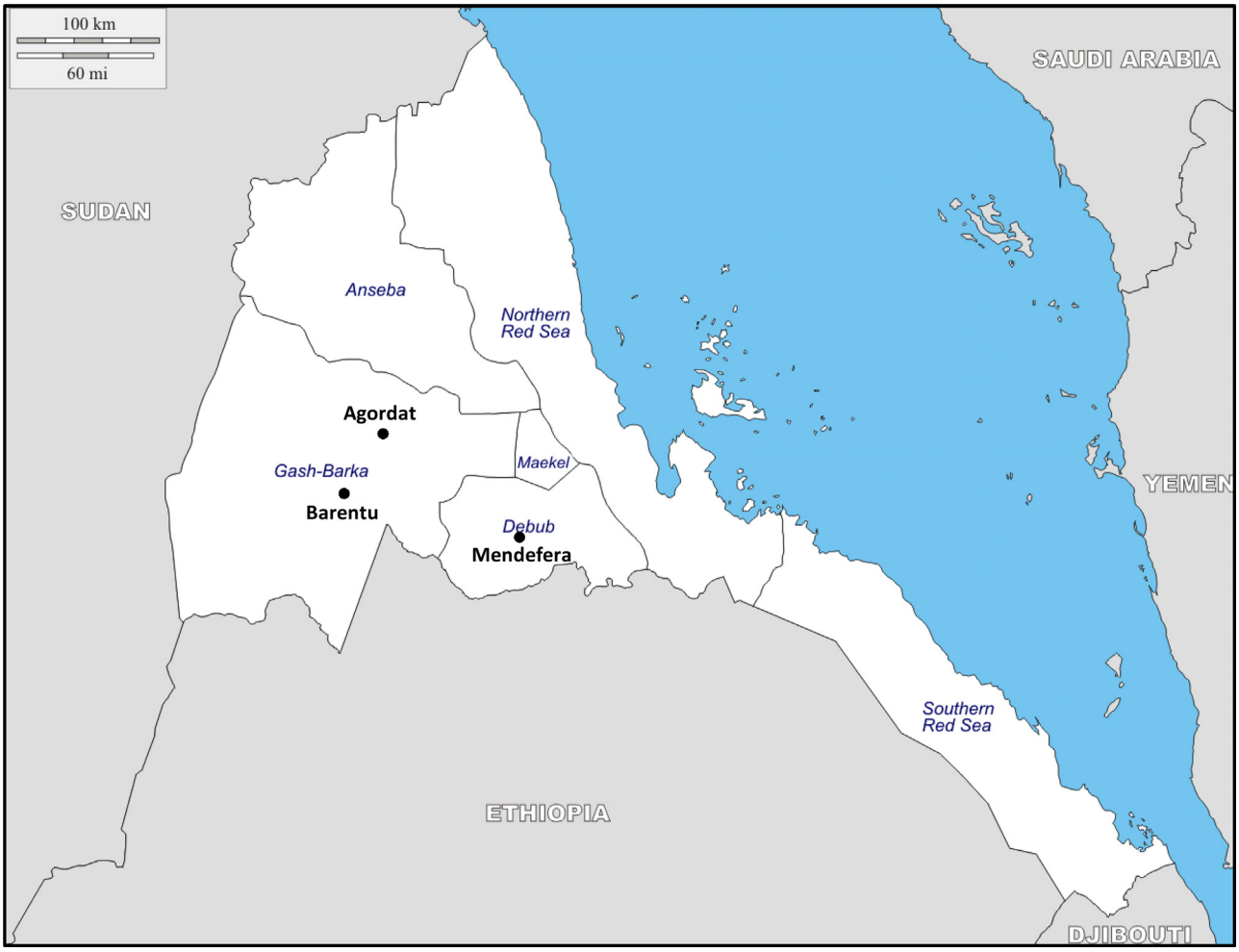

Fig. 1. Study sites for present investigation in Eritrea.

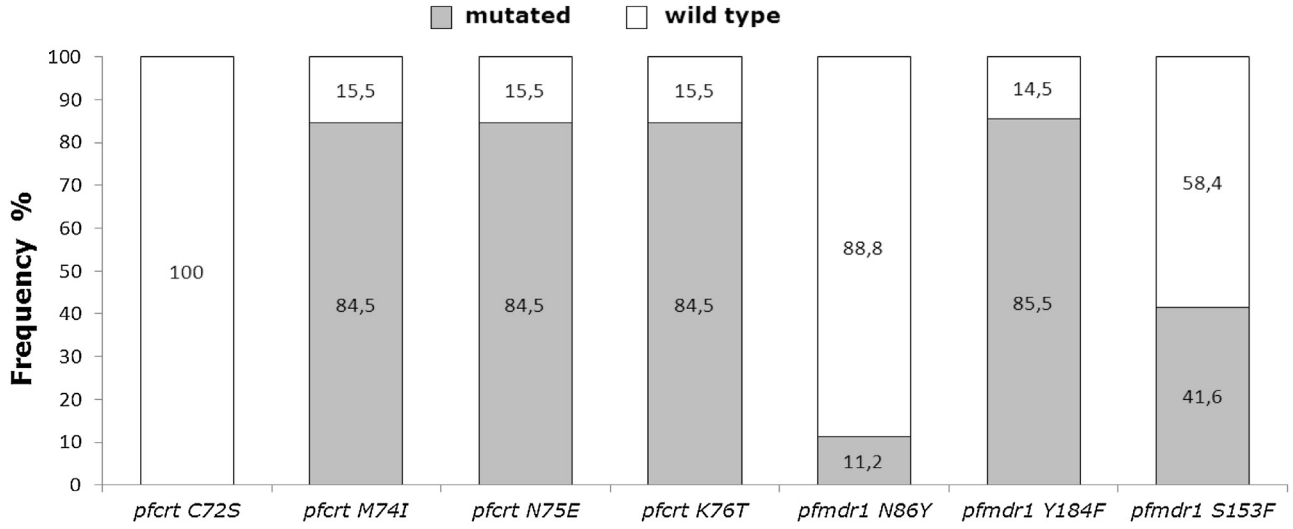

Fig. 2. Frequencies of SNPs in *Pfcrt* codons 72–76 and in *Pfmdr*1 codons 86,153,184 in *P. falciparum* isolates from Eritrea.

sible emergence of resistance to the artesunate drug in Eritrea. Mutations in *Pfmdr1* and *Pfcrt* genes as markers of resistance to amodiaquine, the partner drug in the ACT in Eritrea, were also investigated.

2. Materials and methods

Between November 2013 and November 2014, a total of 209 malaria infected blood samples were collected in Eritrea from three study sites: 200 samples from Barentu and Agordat, in the