Short Communication

Impact of Artemisinin-Based Combination Therapy on Falciparum Malaria in Urban Kolkata: A Clinic-Based Report

Pabitra Saha1, Swagata Ganguly1*, Soma Dutta1, Pratip K. Kundu1, Dilip K. Bera1, Nandita Basu2, and Ardhendu K. Maji1

1Department of Microbiology, Calcutta School of Tropical Medicine, Kolkata; and 2Calcutta School of Tropical Medicine, Kolkata, India.

SUMMARY: In India, artemisinin-based combination therapy (ACT; specifically artesunate + sulfadoxine-pyrimethamine) has been implemented for uncomplicated falciparum malaria since 2010. But for vivax malaria drug policy remained unchanged i.e., chloroquine and primaquine. We observed the impact of this intervention in urban Kolkata by analyzing data from the Malaria Clinic from 2001 to 2013. In Kolkata, we observed that Plasmodium vivax was perennial, whereas P. falciparum infection was seasonal. Before ACT implementation, the proportion of P. falciparum was as high as 50% and it steadily decreased during 4 successive years post intervention. No change was observed in the number of P. vivax cases. ACT may be an effective measure in reducing falciparum malaria cases. Artemisinin-derivative combination therapies should be explored in vivax malaria to reduce the overall burden of malaria.

A total of 207 million diagnosed cases of malaria and 627,000 deaths globally were reported in 2012 (http://www.who.int/malaria/publications/world_malaria_report_2013/en/). Approximately one-third of the world’s population at risk for malaria lives in India, where Plasmodium falciparum accounts for about 50% of the total malaria cases (1). Since 2005, the National Vector Borne Disease Control Programme (NVBDCP) of India has introduced new interventions and undertaken several policy changes to improve malaria control (2). Artemisinin-based combination therapy (ACT), a combination of artesunate + sulfadoxine-pyrimethamine (AS + SP), was introduced in 2010 as a first-line agent to treat uncomplicated falciparum cases, but chloroquine (CQ) remains the drug of choice for vivax malaria. The introduction of ACT in different countries was associated with a decline in the incidence of falciparum malaria in successive years (3–5). Such data from India are scarce (6). The present report focuses on the impact of ACT on the total number of falciparum malaria cases in urban Kolkata, India.

The present study was a clinic-based study from the Malaria Clinic of the Protozoology Unit of Calcutta School of Tropical Medicine located in the central part of Kolkata. Symptomatic patients from surrounding wards of the Kolkata Municipal Corporation attend this clinic for malaria diagnosis and treatment.

This study retrospectively analyzed the data maintained in the Malaria Clinic of the host Institute. The period from 2001–2009 was considered our baseline, and the period from 2010–2013 was considered the post-intervention period because ACT was introduced in 2010. The majority of patients were from a nearby locality belonging to a lower socio-economic status. Most of the patients were originally residents of Jharkhand, Bihar, and were mainly migratory workers to Kolkata with frequent visits to their domicile states.

Consent was not obtained for each case detection and treatment administered for malaria as these are routine health system activities for clinical care and conducted according to NVBDCP guidelines.

All individuals who attended our clinic were examined clinically and blood was collected from a finger prick (thick and thin smears) for malarial parasite detection and species identification following Giemsa staining. Laboratory-confirmed P. falciparum, P. vivax, and mixed infections were treated according to the age-specific dosage guidelines of the National Drug Policy. Prior to ACT implementation, malaria cases were treated with CQ (25 mg/kg divided over 3 days) and primaquine (PQ) (0.25 mg/kg body weight daily for 14 days after estimating their glucose 6 phosphate dehydrogenase levels for vivax malaria and a single dose of 0.75 mg/kg body weight on day 2 for falciparum malaria).

In 2010, AS + SP replaced CQ for the treatment of uncomplicated P. falciparum cases with 4 mg/kg body weight of artesunate for 3 days, 25 mg/kg body weight of sulfadoxine on day 1, 1.25 mg/kg body weight of pyrimethamine on day 1 and a single dose of PQ at 0.75 mg/kg body weight on day 2.

All patients with falciparum malaria were advised to report to the clinic weekly for 6 weeks of follow-up.

We summarized the pre- and post-intervention malaria cases by tabulating standard yearly epidemiological indicators. We also assessed the seasonal variation in the incidence of each species.

Prior to ACT implementation, the average slide positivity rate was 35.94%, ranging from 29.91%–43.03% (Table 1). This rate declined over the 4 succes-
sive years of the post-intervention period (34.35%, 27.72%, 25.17%, and 27.38%, respectively) with an average of 29.43%. The percentage of *P. falciparum* cases ranged from 20.62%–46.73% reaching almost 50% in 2009 and declining steadily after the intervention (Table 1). The actual decrease in *falciparum* malaria cases in the post-intervention period can be better depicted by the slide falciparum rate (SFR) (Table 1). During 2001–2009, SFR ranged from 6.37%–20.01%, with an average of 13.12%. After ACT implementation, the SFR decreased to 6.23% ranging from 3.59%–9.40%. The number of vivax malaria cases remained almost constant throughout (Table 1).

Before ACT implementation patients with falciparum infection attended our clinic with repeated episodes of malaria that were due to recrudescence (7), thus increasing *P. falciparum* cases and acting as source of transmission. In our previous study (8), we showed that the combination of AS + SP was highly effective against falciparum malaria in urban Kolkata with a therapeutic efficacy rate of 100%. The efficacy of this combination is unknown against *P. vivax* malaria, as it has never been implemented. CQ and PQ are still in use for vivax malaria. A high rate of recurrent *P. vivax* infection has been reported during the 1-year post-treatment period with CQ alone (26.7%) and CQ + PQ for 14 days (16.5%) (9). In Kolkata, 2 interventions, namely insecticide treated net and indoor residual spray, were not found to be implemented. Since other parameters have remained unchanged, the reduction in *P. falciparum* cases was probably due to the drug policy change.

Similarly, observations have also been reported from West Bengal during the post-ACT implementation period (http://www.nvbdcp.gov.in/Doc/mal_situation_Apr2015.pdf) and other malaria-endemic countries (3–5). Several workers reported a decrease in *P. vivax* cases whose treatment remained unchanged (CQ + PQ) in areas receiving ACT for *P. falciparum* only (6). This decline was probably due to improved treatment with ACT in mixed or misdiagnosed infections (10). On the contrary, we observed that *P. vivax* burden remained almost constant in both the pre- and post-intervention periods, which might be due to the unchanged drug policy and a high rate of recurrent infection following treatment with CQ + PQ (9).

In urban Kolkata, microscopy is used as diagnostic tool for malaria, which minimizes the chance of misdiagnosis. In rural settings, malaria diagnosis is mainly based on rapid diagnostic test, leading to chances of misdiagnoses resulting in falciparum cases receiving CQ. A similar problem was addressed by Douglas et al, 2010 (10). Though we have not registered any cases of CQ-resistant *P. vivax* in our setting (11), any ACT that is effective against both malarial species will be convenient in treating all malaria cases irrespective of species identification.

We also assessed the seasonal changes in *P. falciparum* burden in the same study areas from 2006 by analyzing data from the 5 years prior to ACT implementation. Every year, *P. falciparum* cases declined beginning in the dry season (April), disappeared in May–June, increased during the monsoon season (July), and attained peak levels in the post-monsoon period (November–December), with a gradual decline after that. On the contrary, *P. vivax* cases persisted throughout the year; they increased beginning in the dry season (March), attained a plateau in the monsoon season (May–September), gradually decreased in winter, and maintained a constant level in the rest of the year. Interestingly, the 2 different peaks of *P. vivax* and *P. falciparum* never coincided with one another in any year from 2006–2013 (Fig. 1). This pattern of seasonal distribution was different from that reported in Delhi (12). It was also a hospital-based study, showing that *P. falciparum* occurred throughout the year and started increasing in July with a peak in September, then gradually declined. *P. vivax* appeared in June, peaked in August–September, and then showed a steady decline.

<table>
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<tr>
<th>Yr</th>
<th>BSE</th>
<th>Parasite species</th>
<th>Total positive</th>
<th>SPR</th>
<th>SFR</th>
<th>Pf %</th>
<th>Pv %</th>
<th>SVR</th>
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<td></td>
<td></td>
<td><em>Pv</em></td>
<td><em>Pf</em></td>
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**BSE = Blood slides examined.**

**Slide positivity rate (SPR) = Total positive × 100/Total slides examined.**

**Slide falciparum rate (SFR) = Total positive *P. falciparum* × 100/Slides examined.**

**Slide vivax rate (SVR) = Total positive *P. vivax* × 100/Slides examined.**

**Pf percentage (Pf %) = Total positive for *P. falciparum* × 100/Total positive for MP.**

**Pv percentage (Pv %) = Total positive for *P. vivax* × 100/Total positive for MP.**
in the October–November timeframe, disappearing in winter.

Our study had certain limitations. Because this was a clinic-based report, our findings may not be a true reflection of the entire population.

ACT implementation in urban Kolkata had a significant effect on total falciparum malaria cases during the 4 years after the intervention. Even so, a substantial falciparum malaria burden still persists and needs adequate attention. Since ACT is highly effective in treating falciparum malaria, a study of the effectiveness of ACT for treatment of vivax malaria is recommended.

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Conflict of interest None to declare.

REFERENCES