*J Vector Borne Dis* 50, December 2013, pp. 271–277

# Insights following change in drug policy: A descriptive study for antimalarial prescription practices in children of public sector health facilities in Jharkhand state of India

Neelima Mishra[1], Ruchi Gupta[1], Sagya Singh[2], Roma Rana[1], Bhartendu Shahi[1], Manoj Kumar Das[2], Anupkumar R. Anvikar[1] & Neena Valecha[1]

[1]*ECR Division, National Institute of Malaria Research, New Delhi;* [2]*National Institute of Malaria Research (Field Unit), Ranchi, India*

## ABSTRACT

*Background & objectives:* Widespread resistance to chloroquine was the mainstay to implement artemisinin-based combination therapy (ACT) in the year 2007 in few malaria endemic states in India including Jharkhand as the first line of treatment for uncomplicated *Plasmodium falciparum* malaria. This study was conducted in Jharkhand state of the country just after the implementation of ACT to assess the prevailing antimalarial drug prescribing practices, availability of antimalarial drugs and the acceptability of the new policy by the health professionals for the treatment of uncomplicated *P. falciparum* malaria patients particularly in children ≤15 yr of age.

*Methods:* This is a cross-sectional study in children aged ≤15 yr with malaria or to whom antimalarial drug was prescribed. Main outcome measure was prescription of recommended ACT in children aged ≤15 yr with malaria in the selected areas of Jharkhand.

*Results:* In the year 2008, artemisinin-based combination therapy (ACT) was implemented in 12 districts of the studied state; however, the availability of ACT was confirmed only in five districts. Antimalarial prescription was prevalent amongst the undiagnosed (8.4%), malaria negative (64.3%) and unknown blood test result (1.2%) suggesting the prevalence of irrational treatment practices. ACT prescription was very low with only 3.2% of confirmed falciparum malaria patients receiving it while others received either non-artesunate (NA) treatment (88.1%) including chloroquine (CQ) alone, CQ + Primaquine (PQ)/other drugs, sulphadoxine-pyrimethamine (SP) alone, SP + other drugs or artemisinin monotherapy (AM) treatment (6.3%). Still others were given non-antimalarial treatment (NM) in both malaria positive (0.3%) and malaria negative (2.1%) cases.

*Interpretation & conclusion:* Despite the change in drug policy in the studied state the availability and implementation of ACT was a major concern. Nevertheless, the non-availability of blister packs for children aged ≤15 yr was the main hindrance in the implementation of the recommended antimalarial. Availability, training and participation of health professionals in decision-making are the key elements to improve adherence to new treatment guidelines. This study provided evidence for the requirement of age-specific blister packs in the country and the national programme has introduced age-specific blister packs in the country in 2010. This baseline information will be useful to monitor the progress in ACT implementation in the country.

**Key words** ACT; antimalarial prescription practices; implementation of drug policy; India

## INTRODUCTION

Artemisinin-based combination therapy (ACT), namely artesunate + sulphadoxine-pyrimethamine (AS+SP) is the first-line treatment for the uncomplicated *Plasmodium falciparum* malaria episodes throughout India[1]. The urgency for ACT roll-out was spurred by alarming levels of drug resistance to previously used monotherapies such as chloroquine (CQ) and sulphadoxine-pyrimethamine (SP) and rising morbidity and mortality[2]. India switched to ACT in 2005 in chloroquine resistant areas of the country, expanding ACT to more areas with >10% treatment failure in 2007 and later in 2008, ACT was adopted in 117 districts within the country, including Jharkhand[3]. In 2007, four districts of Jharkhand were identified as chloroquine resistant and later in 2008 this was expanded to 12 districts which were notified as chloroquine resistant[3]. The ACT recommended in the National Programme of India for chloroquine resistant areas was artesunate (4 mg/kg body weight) daily for 3-days and sulphadoxine (25 mg/kg body weight), pyrimethamine (1.25 mg/kg body weight) on Day 0 which was recommended to be given only to confirmed *P. falciparum* cases found positive by microscopy or RDK. Recommendations were also given for concomitant use of single dose of primaquine (0.75 mg/kg body weight) for effective gametocyte clearance thereby interrupting transmission[4].

The introduction of new policy does not get translated to its implementation immediately at the community level[5]. The key factors behind this may include lack of prescription by the health workers, its unavailability with the chemists, lack of production by the industries thereby affecting sale, lack of compliance by the patients and general acceptance by the community[5]. These factors promote irrational treatment practices and thereby contribute to the development of drug resistance[5].

It has been shown that the dearth in antimalarial drug supply and malaria diagnostics is the major shortcoming in effective implementation of the recommended policy and that the national ministries and the international community must address this issue to overcome this problem[6–7]. A five year study was conducted in seven malaria endemic countries to provide evidence to the policy makers on trends in availability, use and price of antimalarials further highlighting the importance of these factors in effective implementation of the recommended drug policy[8]. Although malaria misdiagnosis results from lack of basic infrastructure and logistics[7], there have been reports where improved diagnostics still resulted in inappropriate use of antimalarials suggesting prevalence of irrational treatment practices[9–14]. Despite improved malaria case management, the issues like policy ambiguities, underuse of diagnostics and distrust on malaria negative results were still problems, which resulted in misdiagnosis and incorrect treatments[7, 14–16]. Furthermore, the task of patient counseling, improved quality interventions and drug dispensing is important in malaria case management along with appropriate prescription and policy adherence[17–20].

The important pre-requisites which help in effective implementation of malaria case management practices are availability of recommended, genuine medicines with discontinued provision of obsolete therapies and the capacity of the health facility for malaria testing, in general with the provision of ACTs and diagnostics including a package of health systems' support activities for health workers, in particular, is a necessity[21].

In view of this, the present study was carried out to assess the availability of the recommended antimalarial and its prescription focusing on the prevalent treatment practices in children aged ≤15 yr following the change in drug policy from CQ to ACT (AS+SP) in selected areas of Jharkhand state of India.

## MATERIAL & METHODS

*Study site*

The study was carried out in Jharkhand state of India. Information was obtained from the Directorate of the National Vector Borne Disease Control Programme (NVBDCP) on districts/areas identified for use of ACT (AS+SP) for the treatment of *P. falciparum* malaria. Based on the above information, districts with the change in drug policy, where ACT was implemented were identified. In Jharkhand, ACT was implemented in two stages. In 2007, four districts in Jharkhand were identified as CQ resistant (Simdega, Ranchi, Gumla and Saraikela)[3]. However, in 2008, a total of 12 districts were notified for use of ACT (AS+SP) for the treatment of *P. falciparum* malaria[3]. Surveys were carried out in 2008–09 to obtain information on the availability of ACT drugs in the notified 12 districts and in addition, data from state malaria office were also collected on the supply of antimalarial drugs to the above districts. As per the records from state programme office, the availability of ACT was confirmed only in five districts, namely Gumla, Latehar, Ranchi, Saraikela and Simdega. Further, in these districts Primary Health Centres (PHCs) were selected on the basis of availability of ACT drugs (ACT combi blister pack or loose tablets). A total of 14 PHCs were identified where prescription practices and compliance with the prescribed drug policy was evaluated. Besides primary health care facilities, private hospitals, clinics, missionary hospitals, etc. were surveyed to document the prevailing prescription practices. However, the record keeping and support was inadequate and hence, only two such facilities were covered.

*Study design*

Both retrospective and prospective surveillance was done. The survey involved PHCs with ACT as the first line of treatment. Retrospective surveillance included auditing of records which was carried out for a period of one year from April 2007–March 2008 in selected PHCs of the studied districts. These cases were children aged ≤15 yr and the criterion for selection of records included patients to whom antimalarial drugs were prescribed. Attempt was made to collect data in a large number of hospitals and PHCs but due to inadequate record maintenance and unavailability of records, surveys were restricted to 14 PHCs in five districts in addition to, two private health facilities. A total of 6712 records were audited during the study period. Variables recorded include data on age, sex, signs and symptoms, diagnosis and the antimalarial medicines prescribed to the patients. The confidentiality of the data was ensured.

Prospective surveillance was done by exit interviews of patients attending outpatient department (OPD) in selected PHCs to study the compliance for artemisinin combination drugs in *P. falciparum* infected children and the serious adverse events, if any, with the usage of ACT. The selection criteria for exit interviews were to inter-

view patients having malaria confirmed either by microscopy or by rapid diagnostic kit (RDK) or patients to whom antimalarial medicine was prescribed. A total of 666 exit interviews were conducted during the study period (September–October 2009) to ascertain the prevailing prescription practices of antimalarials including ACT in children aged ≤15 yr.

*Questionnaire design and sample size*

The questionnaire was developed with the help of social scientists, epidemiologists and a statistician. To understand the prevailing prescription practice, audit of prescription record of OPD is a useful tool and has been used in a similar study like this[22]. Pre-testing of structured performa in the field was undertaken before initiating the study. A total of 20 questionnaires for the exit interview of the OPD patients in the PHC were tested in the field. Sample size was calculated with the help of senior statistician from National Institute of Medical Statistics, New Delhi, India and it was concluded that the audit of one year OPD record of PHCs with change in drug policy and exit interviews from 10% of the OPD load will be appropriate from each district.

*Ethical guidelines*

The Scientific Advisory Committee of the National Institute of Malaria Research approved the study design and questionnaires. Verbal consent was obtained from all interviewees, and the data were de-identified. The study was a public health program evaluation conducted at the request of WHO representative to India, New Delhi, and thus IRB exempt.

## RESULTS

*Availability of ACT drugs*

There are a total of 24 districts in Jharkhand state, out of which 12 were identified as chloroquine resistant and hence, ACT was implemented in these districts in 2008. However, the supply of ACT was limited to only five of them, namely Ranchi, Simdega, Saraikela, Latehar and Gumla. Furthermore, the availability of blister packs remained confined to only three of them (Ranchi, Latehar and Simdega). In the other two districts, ACT was available as loose tablets.

*Prescription of antimalarials and use of ACT*

*Prescription pattern from audit of records:* A total of 6712 records were audited. Details of audit of records are depicted in Fig. 1. Amongst the diagnosed (16.9%) cases, which were positive for *P. falciparum* malaria (44.4%), ACT prescription was only 4% while others were

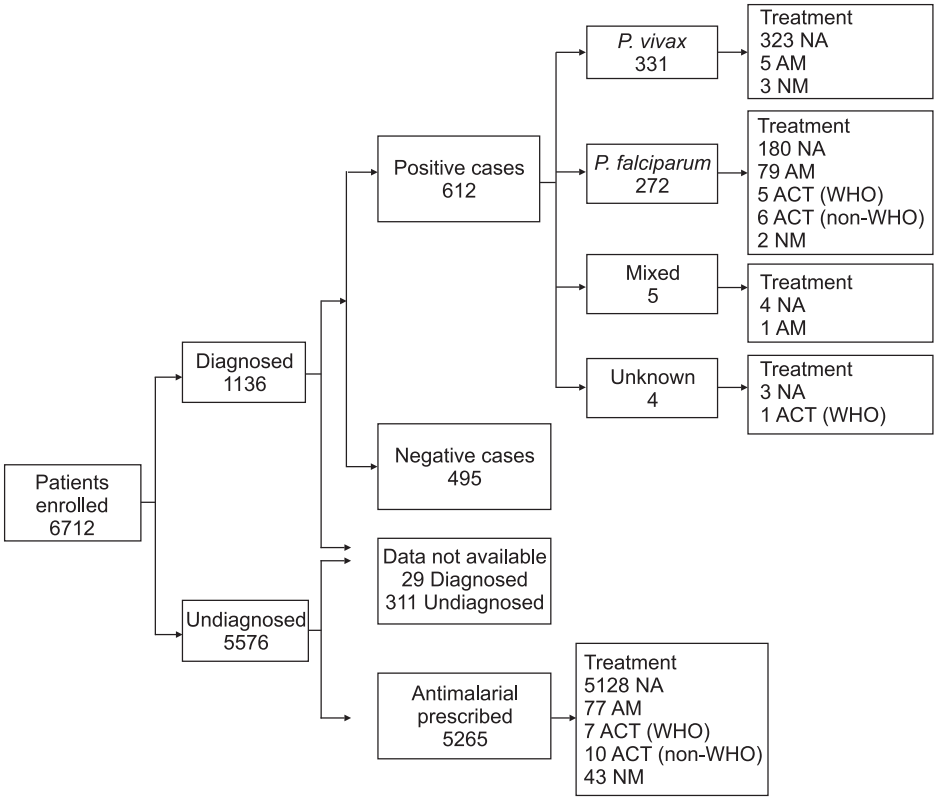


*Fig. 1:* Flow chart of patient case management from audit of records, Jharkhand, India, 2007–08. NA — Non-artesunate treatment; AM—Artesunate monotherapy; ACT (WHO) or ACT (non-WHO)— Artemisinin-based combination therapy WHO recommended or Artemisinin-based combination therapy other than WHO recommended; NM—Non-antimalarial.

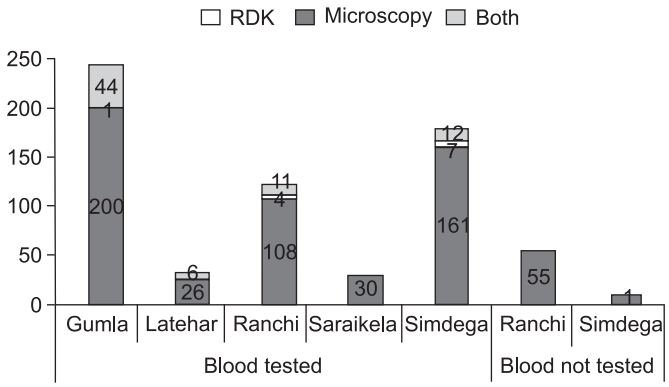


*Fig. 2:* District-wise diagnostic practices as evident from exit interviews, Jharkhand, India 2009.

given non-artesunate treatment (87.6%), artemisinin monotherapy (7.6%) and non-antimalarial (0.9%). *Plasmodium vivax* cases (54.1%) were given non-artesunate (97.6%), artesunate monotherapy (1.3%) and non-antimalarial (0.8%) treatment. The percentage of undiagnosed cases was 83.1% in which antimalarial prescription was prevalent in 94.4% cases while prescription of non-antimalarial was recorded in 5.6% of cases. There were others who were given non-WHO ACT (0.2%) which includes combination of artemisinin derivatives with CQ. Data were not available for 5.1% of cases in both diagnosed (0.4%) and undiagnosed (4.6%) categories.

*Prescription pattern from exit interview:* A total of 666 exit interviews were conducted in children attending OPD of the studied PHCs. Two hundred eighty nine exit interviews were done from the age group 0–5 yr, 219 were from 5–10 yr and 158 were from 10–15 yr age group of children. Microscopy remains the main diagnostic tool followed by RDK in all the studied districts (Fig. 2). Amongst the diagnosed cases (91.6%) which were either diagnosed microscopically (86.1%) or with RDK or both (13.9%), 26.2% were positive for malaria while others were negative (72.5%) and results were unknown in 1.3% cases as conclusions could not be made even after the diagnosis (Fig. 3). Furthermore, amongst the confirmed *P. falciparum* cases (26.2%), ACT prescription was documented in only 3.4% of cases while others were either treated with non-artesunate treatment (NA = 96.2%) which includes chloroquine alone, chloroquine with PQ/other drugs, SP alone or SP with other drugs

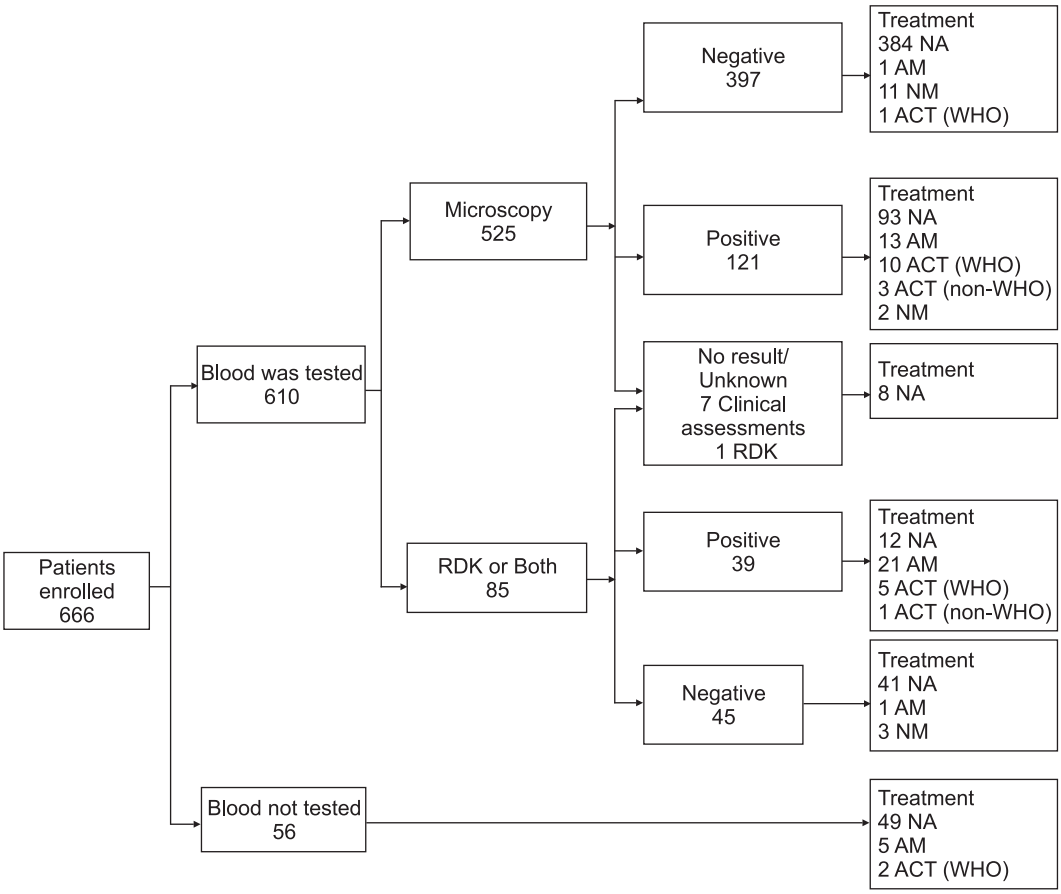


*Fig. 3:* Flow chart of patient case management from exit interviews, Jharkhand, India, 2009. NA — Non-artesunate treatment; AM—Artesunate monotherapy; ACT (WHO) or ACT (non-WHO)—Artemisinin-based combination therapy WHO recommended or Artemisinin-based combination therapy other than WHO recommended; NM—Non-antimalarial.

Table 1. Antimalarial groups and treatment prescribed to patients from exit interviews, India 2009

| Drug group/treatment | n | % | PQ* | Abx** | PCM†/ Other drugs |
|---|---|---|---|---|---|
| Artemisinin monotherapy | 41 | 6.3 | | 15 | 24 |
| Non-artesunate treatment | 587 | 88.1 | 108 | 361 | 452 |
| Chloroquine | 554 | | 108 | 332 | 429 |
| Primaquine | 30 | | | 29 | 21 |
| Sulphadoxine-pyrimethamine | 3 | | | | 2 |
| ACT (WHO) | 18 | 2.6 | | 5 | 14 |
| ACT | 9 | | | 2 | 7 |
| SP+ACT | 9 | | | 3 | 7 |
| ACT (non-WHO) | 4 | 0.6 | 1 | 1 | 3 |
| CQ+Arteether/Artemether/ Artesunate | 4 | | 1 | 1 | 3 |
| Non-antimalarial drug | 16 | 2.4 | | 8 | 13 |

*Primaquine; **Antibiotics; †Paracetamol.

(Table 1). Artemisinin monotherapy (AM) treatment was prevalent in 6.6% of diagnosed cases while others in the diagnosed category were treated with non-antimalarial (NM = 2.6%) in both malaria positive (0.3%) and malaria negative (2.3%) category. Amongst the undiagnosed cases (8.4%), patients were either given non-artesunate treatment (7.4%) or artemisinin monotherapy (0.8%). ACT prescription was also documented amongst the undiagnosed cases although at a low prevalence of 0.3% but still holds statistical significance ($p$ <0.05) when compared with diagnosed cases (Fig. 3).

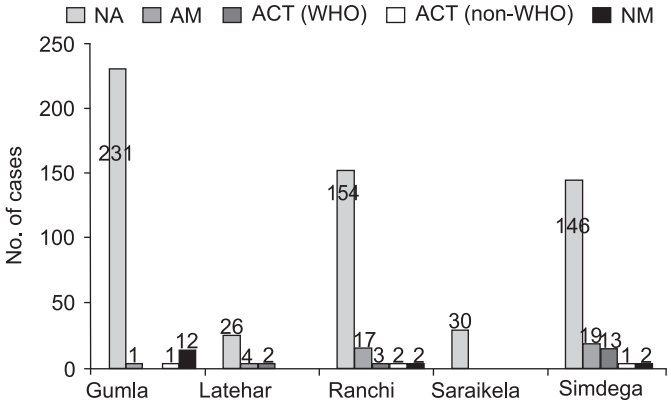


*Fig. 4:* District-wise treatment practices as evident from exit interviews, Jharkhand, India, 2009 [NA – Non-artesunate treatment; AM–Artesunate monotherapy; ACT (WHO) or ACT (non-WHO); NM–Non-antimalarial].

*Availability of blister packs and ACT prescription*

Attempts were made to understand if availability of blister packs is affecting ACT prescription and if at all there exists any correlation. The availability of ACT blister packs was confirmed in three out of the five districts, namely Ranchi, Simdega and Latehar. Although the total prevalence of ACT prescription was very low (n=18) but still it was confirmed only in the above mentioned three districts (Fig. 4). Also ACT prescription was strongly associated with the availability of ACT blister packs at the health facilities as the calculated value of chi-square ($\chi^2$=7.10) was found to be significant (3.841 at 1 d.f.) at 5% level of significance.

## DISCUSSION

The change in national drug policy of India led to the implementation of ACT in chloroquine resistant areas. In the year 2008, 12 districts of Jharkhand were identified as chloroquine resistant but the availability of ACT was confirmed by only five of them. Furthermore, translation of changed drug policy to its implementation could not be confirmed to a great extent as ACT prescription was very low. The unavailability of blister packs for children aged ≤15 yr was another reason which led physicians to prescribe inappropriate drugs and made implementation of ACT even more difficult. Moreover, physicians prescribed presumptive treatment of malaria with unjustifiable use of antimalarial drugs and antibiotics suggesting prevalence of irrational treatment practices as documented earlier[23].

Both retrospective (audit of records) and prospective (exit interview) data analyses were suggestive of non-implementation of recently introduced ACT although use of diagnosis improved within this period with 91.6% of patients being diagnosed during the period of exit data collection as compared to 16.9% suggested by audit of records. Antimalarial prescription was prevalent both in undiagnosed category and malaria negative category which exhort unregulated treatment practices. ACT prescription was very low with only 4 and 3.4% as per audit of records and exit interview respectively, again signifying non-acceptance of newly changed drug policy.

Furthermore, for effective implementation of changed drug policy it is necessary to adopt few measures like provision of basic infrastructure for diagnosis with availability of newly introduced drug and withdrawal of obsolete therapy from the market. Awareness amongst the physicians and the general community in terms of conducting basic training programmes and campaigns is another pre-requisite for regulated use of antimalarials and effective malaria case management.

## CONCLUSION

The study has helped to generate important information on the prevailing antimalarial drug prescription practices in children and the implementation of recently introduced ACT drugs in selected five districts. The study revealed that the physicians were less inclined to refer the laboratory diagnosis before prescribing antimalarial drugs. Awareness among the physicians and other health personnel for the use of ACT drugs needs to be created through adequate training. The use of ACT drugs for confirmed malaria cases is nominal. More health facility surveys are needed to understand the prevailing prescription practices and adoption of ACT in the community. Since, inappropriate use of drugs is known to increase drug pressure and so the development of drug resistance, therefore, this study also augments the prospects of studying drug resistance in these areas as the results suggest them to be more prone to threat.

*Limitations*

This study was carried out during 2008 at the time when ACT was initially implemented in the studied state and age-specific blister packs were also unavailable at the PHCs. Availability of loose tablets of artesunate and sulphadoxine-pyrimethamine was also limited at selected PHCs. This could have influenced the study results; however, as this study was a public health need, study provided evidence for the requirement of age-specific blister packs in the country and thereafter, the national programme has introduced age-specific blister packs throughout the country in 2010. Following this, there could be improved availability, however, the progress needs to be monitored from time to time to assess the availability across the facilities studied as well as in the larger areas in the country.

## ACKNOWLEDGEMENTS

This paper bears the NIMR publication screening committee's approval No. 018/2012. We thank the field teams, health professionals, pharmacists and the data entry team of NIMR. We acknowledge the financial support received from the Office of WHO Representative to India, New Delhi, India.

## REFERENCES

1. *Guidelines for diagnosis and treatment of malaria in India 2011*. Available from: *http://www.mrcindia.org/Guidelines%20for%20 Diagnosis 2011.pdf* (Accessed on December 3, 2011).
2. *Guidelines for diagnosis and treatment of malaria in India 2009*. Available from: *http://www.mrcindia.org/Guidelines_for_ Diagnosis_Treatment.pdf*
3. National Vector Borne Disease Control Programmme. Available from: *http://www.nvbdcp.org*
4. *National drug policy on malaria 2008*. Available from: *http:// www.whoindia.org/LinkFiles/Malaria_Malaria_drug-policy-08.pdf*
5. Godfrey MM, Miguel AG. Research influence on antimalarial drug policy change in Tanzania: Case study of replacing chloroquine with sulfadoxine-pyrimethamine as the first-line drug. *Malar J* 2005; *4:* 51.
6. Beth BK, Julius N, Beatrice W, Sarah VK, Dorothy NM, Catherine AG, *et al*. Short report. Malaria drug shortages in Kenya: A major failure to provide access to effective treatment. *Am J Trop Med Hyg* 2009; *80:* 737–8.
7. Nankabirwa J, Zurovac D, Njogu JN, Rwakimari JB, Counihan H, Snow RW, *et al*. Malaria misdiagnosis in Uganda: Implications for policy change. *Malar J* 2009; *8:* 66.
8. Actwatch.info [homepage on the Internet]. ACT watch: Evidence for malaria medicine policy. Available from: *http:// www.actwatch.info/downloads/results/7% 20 Country%20OS 1%20and%204%20Country%20HH1%20Results, %20MIM% 20Symposium,%20O%27Connell,%2003-11-09_FINAL.pdf.*
9. Hamer DH, Ndhlovu M, Zurovac D, Fox M, Antwi KY, Chanda P, *et al*. Improved diagnostic testing and malaria treatment practices in Zambia. *JAMA* 2007; *297:* 2227–31.
10. Zurovac D, Njogu J, Akhwale W, Hamer DH, Larson BA, Snow RW. Effects of revised diagnostic recommendations on malaria treatment practices across age groups in Kenya. *Trop Med Int Health* 2008; *13:* 784–7.
11. Barat L, Chipipa J, Kolczak M, Sukwa T. Does the availability of blood slide microscopy for malaria at health centers improve the management of persons with fever in Zambia? *Am J Trop Med Hyg* 1999; *60:* 1024–30.
12. Zurovac D, Midia B, Ochola SA, English M, Snow RW. Microscopy and outpatient malaria case management among older children and adults in Kenya. *Trop Med Int Health* 2006; *11:* 432–40.
13. Bisoffi Z, Sirima BS, Angheben A, Lodesani C, Gobbi F, Tinto H, *et al*. Rapid malaria diagnostic tests vs. clinical management of malaria in rural Burkina Faso: Safety and effect on clinical decisions. A randomized trial. *Trop Med Int Health* 2009; *14:* 491–98.
14. Ansah EK, Narh-Bana S, Epokor M, Akanpigbiam S, Quartey AA, Gyapong J, *et al*. Rapid testing for malaria in settings where microscopy is available and peripheral clinics where only presumptive treatment is available: A randomised controlled trial in Ghana. *BMJ* 2010; *340:* 930.
15. Chandler CI, Semkin C, Boniface G, Juma K, Reyburn H , Whitty CJ. The importance of context in malaria diagnosis and treatment decisions: A quantitative analysis of observed clinical encounters in Tanzania. *Trop Med Int Health* 2008; *13:* 1131–42.
16. Rowe AK, Ponce de León GF, Mihigo J, Santell AC, Miller NP, Van-Dúnem P. Quality of malaria case management at outpatient health facilities in Angola. *Malar J* 2009; *8:* 275.
17. Wasunna B, Zurovac D, Bruce J, Jones C, Webster J, Snow RW. Health worker performance in the management of paediatric fevers following in-service training and exposure to job aids in Kenya. *Malar J* 2010; *9:* 261.
18. Zurovac D, Njogu J, Akhwale W, Hamer DH, Snow RW. Translation of artemether-lumefantrine treatment policy into paediat-

ric clinical practice: An early experience from Kenya. *Trop Med Int Health* 2008; *13:* 99–107.
19. Zurovac D, Tibenderana JK, Nankabirwa J, Ssekitooleko J, Njogu J, Rwakimari JB, *et al*. Malaria case-management under artemether-lumefantrine treatment policy in Uganda. *Malar J* 2008; *7:* 181.
20. Kachur SP, Khatib RA, Kaizer E, Fox SS, Abdulla SM, Bloland PB. Adherence to antimalarial combination therapy with sulfadoxine-pyrimethamine and artesunate in rural Tanzania. *Am J Trop Med Hyg* 2004; *71:* 715–22.
21. Abdelgader TM, Ibrahim AM, Elmardi KA , Githinji S, Zurovac D, Snow RW, *et al*. Progress towards implementation of ACT malaria case-management in public health facilities in the Republic of Sudan: A cluster-sample. *BMC Public Health* 2012; *12:* 11.
22. Meremikwu M, Okomo U, Nwachukwu C, Oyo-Ita A, Eke-Njoku J, Okebe J, *et al*. Antimalarial drug prescribing practice in private and public health facilities in southeast Nigeria: A descriptive study. *Malar J* 2007; *6:* 55.
23. Bhatnagar T, Mishra CP, Mishra RN. Drug prescription practices: a household study in rural Varanasi. *Indian J Prev Soc Med* 2003; *34:* 33–9.

*Correspondence to:* Dr Neelima Mishra, Scientist 'E', National Institute of Malaria Research, Sector–8, Dwarka, New Delhi–110 077, India. E-mail: neelima@mrcindia.org

*Received:* 30 August 2012 *Accepted in revised form:* 16 July 2013