Original Research Article

Assessment of anti-malarial drug prescribing pattern in pediatric and adult malaria patients in a tertiary care hospital in Eastern India

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ABSTRACT

Background: Kolkata, one of the major metropolitan cities of India, is also the capital of the state West Bengal, contributes largest number of malaria cases reported from West Bengal. The present study was undertaken to assess the anti-malarial prescribing pattern in a tertiary care teaching hospital in Kolkata.

Methods: This was an observational, prospective, cross-sectional study for a period of one year (from March 2017 to February 2018) in which prescriptions of diagnosed pediatric and adult malaria patients were scanned and reviewed for anti-malarial use pattern. Core drug use indicators were also analyzed to assess the rational prescribing pattern.

Results: During one-year study period, 122 adult and 24 child malaria patient encounters were screened. Among adult patients, 48(39.3%) patients had P. falciparum and 74(60.7%) patients had P. vivax malaria; in children, 9(37.5%) patients had P. falciparum and 15(62.5%) patients had P. vivax malaria. All adult and pediatric P. vivax malaria patients were treated with chloroquine. Artemisinin derivatives were prescribed to 91.67% of adults and 88.88% of pediatric falciparum malaria patients. 77.09% of adults and 66.67% of children received ACT. Artemether-lumefantrine was the most commonly prescribed ACT (33.34% in adults and 55.56% in children). Prescriptions were usually in generic name and from National EDL. Percentage of encounters with antibiotics was high in both age group but percentage of encounters with injections was low in adults and children.

Conclusion: Chloroquine was used rationally for treatment of P. vivax malaria patients. Artemether-lumefantrine was the most common ACT used for treatment of P.falciparum malaria cases though the National guideline for treatment of malaria does not recommend Artemether-lumefantrine for this state and region for treatment of falciparum cases.

Keywords: Anti-malarial drugs, Drug use survey, Prescribing indicators

INTRODUCTION

Malaria, one of the most important vector-borne diseases, is endemic throughout India. Due to high morbidity, mortality and economic loss, malaria is also one of the major public health problem in India. In 1947, when India achieved independence, 75 million people were infected with malaria, direct mortality due to malaria was 0.8 million per annum. In the following years, several programs were taken by the Indian Government to control the malaria situation in India. The National Malaria Control Program was launched in 1953, which
Evidence of the earliest malaria cases in West India, which have entered the northwestern India districts by 1958, suggests that malaria was prevalent in these areas. The strategic decision to eliminate malaria from the northwestern India districts by 1958, and later the adoption of malaria control programs in the Indian subcontinent, reflects a significant commitment to malaria control. The revision and update of the national Malaria guidelines in 2010 and 2014 reflects the continued effort to control and eliminate malaria in India. The national malaria policy recommends chloroquine and primaquine for treatment of \textit{P. vivax} cases. On the other hand, Artemisinin Combination Therapy (ACT) is recommended for confirmed \textit{P. falciparum} cases. ACT consists of an artemisinin derivative such as artesunate, arteether, or arteether combined with a long acting drug such as lumefantrine, mefloquine, amodiaquine, piperaquine or sulfadoxine-pyrimethamine. The national program recommended ACT in North Eastern states of India is artether-lumefantrine and in rest of India is artesunate-sulfadoxine-pyrimethamine. The other fixed dose ACT combinations registered for marketing in India are artesunate-amodiaquine, artesunate-mefloquine and arterolane-piperaquine. ACT is used for treatment of uncomplicated \textit{P. falciparum} or mixed infections. For treatment of severe \textit{falciparum} or \textit{vivax} malaria, intravenous quinine or artesunate, intramuscular arteether or arteether is recommended. Full course of oral ACT is given following parental artemisinin derivatives. Primaquine is given for fourteen days for \textit{P. vivax} cases whereas, single dose primaquine is recommended for \textit{P. falciparum} cases.

Drug utilization studies may reveal current prescribing practices and irrational prescribing practices; these studies may also identify associated problems with drug use and provide feedback to the prescriber regarding rational use of drugs. Supervision and monitoring of drug use practices particularly rational drug use practices may be assessed by WHO-INRUD developed core drug use indicators for health facilities.

As malaria is endemic and public health problem in Sub-Saharan Africa and South-East Asia, studies on anti-malarial use pattern is particularly reported from these regions of the globe. Anti-malarial prescribing pattern in Nigeria showed that most of the patients were treated without parasitological confirmation, which now is discouraged in guidelines, also poor adherence to National and WHO guidelines is a common practice in Nigeria. In rural Kenya, lack of adherence to malaria treatment guideline was associated with irrational prescribing. Data on anti-malarial use pattern in India are scanty. Studies in India have pointed out that ACTs are being used irrationally; in Moradabad, Uttar Pradesh, artemisinin derivatives were used rampant as the first line drug irrespective of the causative agent.

Another study from Odisha highlighted the anti-malarial use pattern in a tertiary care set-up. Malaria and other vector-borne diseases situation in Kolkata Municipal Corporation areas were analyzed in different studies, though anti-malarial use pattern was not assessed by...
This study pioneers to analyze the antimalarial prescribing practices from a tertiary care Medical College and Hospital in Kolkata, West Bengal.

METHODS

For the observational, cross-sectional, prospective study prescriptions of diagnosed (either by light microscopy or RDT) malaria patients who had attended General Medicine or Pediatrics out-patient department (OPD) and prescriptions in Bed-head tickets (BHTs) or clinical case notes of admitted patients in Medicine or Pediatrics department of Medical College and Hospital, Kolkata were obtained. Medical college and Hospital, is a tertiary care teaching hospital, situated in the central part of metropolitan city Kolkata, West Bengal.

For the study, scanned copies of prescriptions of OPD patients and scanned BHTs of admitted patients were collected and evaluated. Institutional Ethics Committee approval was obtained beforehand. Written informed consent was obtained from a patient or their legal guardian, with the provision of a witness when the guardian was illiterate.

Duration of study was one year (from March 2017 to February 2018). Data was recorded in a predesigned, structured case record form. Scanned documents were collected once on all working days as per convenience. No follow-up was scheduled. Information extracted from the prescriptions included patients’ age, sex, symptoms, signs, diagnostic tests, test for G6PD and use of antimalarial/other drugs. Patients were classified into mild and severe *P. falciparum* cases based on their clinical presentations.

Symptoms such as fever, chills and rigor, headache, leg cramps, nausea, vomiting and signs of severe malaria were noted. ‘Laboratory test done’ was classified when the results were recorded in the prescriptions /BHTs or separate laboratory report card was available. The laboratory tests considered in this study were those of malaria diagnosis (either by light microscopy or RDT) and test for G6PD estimation. The other parameters which were assessed also included WHO-INRUD core prescribing indicators such as: average number of drugs per encounter, percentage of prescriptions from EDL, percentage of drugs prescribed in generic name, percentage of encounters with an injection, percentage of encounters with an antibiotic.

Fixed-dose combination drugs such as amoxicillin-clavulanic acid, artemether-lumefantrine, artesunate-sulfadoxine-pyrimethamine etc. were considered as a single drug and counted as such during analysis of data.

The data have been summarized by routine descriptive statistics; mean and standard deviation for numerical variables, count and percentages for categorical variables. GraphPad Prism version 5 (GraphPad software Inc, San Diego, California, USA) software was used for analysis of data.

RESULTS

The total 146 patient encounters with malaria were recruited during one year study period. Among these 122 were adults and 24 were children. In the adult group, 71(58.19%) patients were male, 51(41.81%) patients were female; in the pediatrics group 18(75%) patients were male, 6(25%) were female (Table 1, Figure 1). The mean age of patients in adult and pediatric age group was 35.17±12.5 years and 7.7±3.24 years respectively (Figure 2). Among adult patients, 48(39.3%) patients had *P. falciparum* and 74(60.7%) patients had *P. vivax* malaria; in children, 9(37.5%) patients had *P. falciparum* and 15(62.5%) patients had *P. vivax* malaria. Eleven adults and 3 children were suffered from severe *P. falciparum* malaria (Table 1, Figure 3).

| Variables | Adult (N=122) | Children (N=24) |
|-----------|---------------|-----------------|
| Male      | 71(58.19%)    | 18 (75%)        |
| Female    | 51(41.81%)    | 6 (25%)         |
| Mean age  | 35.17±12.5    | 7.7±3.24        |
| Treated in OPD | 111 (91%) | 21 (87.5%)  |
| Treated in IPD | 11 (9%)     | 3 (12.5%)  |
| P. vivax  | 74 (60.7%)    | 15 (62.5%)      |
| P. falciparum | 48 (39.3%) | 9 (37.5%) |
| Severe    | 11 (9%)       | 3 (12.5%)       |
| Mild      | 111 (91%)     | 21 (87.5%)      |
| G6PD test done | 89 (73%) | 20 (83.3%) |
| Oral drugs | 111 (91%)    | 21 (87.5%)      |
| Parenteral drugs | 11 (9%) | 3 (12.5%) |
| Primaquine used | 101 (82.78%) | 22 (91.66%) |

**Figure 1: Sex distribution of malaria patients.**

All the *P. vivax* malaria patients (15 children and 74 adults) were treated with Chloroquine. Artemisinin derivatives were prescribed to 88.88% of pediatric
91.67% adult *falciparum* malaria patients; 66.67% of children and 77.09% of adults received ACT.

![Figure 2: Age distribution of malaria patients (Mean±Standard deviation).](image)

### Table 2: Prescribing pattern of anti-malarial drugs in *P. falciparum* patients.

| Drug regimen prescribed         | Adult (N=48) | Children (N=9) |
|---------------------------------|--------------|---------------|
| Artemether-lumefantrine         | 16 (33.34%)  | 5 (55.56%)    |
| Arsunate-sulfadoxine-pyrimethamine | 15 (31.25%) | 1 (11.11%)    |
| Artesunate-mefloquine           | 6 (12.50%)   | Nil           |
| Quinine                         | 4 (8.33%)    | 1 (11.11%)    |

Artemether-lumefantrine was the most commonly prescribed ACT (55.56% in children and 33.34% in adults) (Table 2). Severe *P. falciparum* malaria patients (3 children and 11 adults) were prescribed injection of quinine or artesunate. Primaquine was prescribed to 91.7% of children and 82.8% of adults; G6PD test was done in 20(83.3%) children and 89(73%) of adults (Table 1).

Amoxicillin-clavulanic acid (50%) in children and azithromycin (29.31%) in adults were the most common antibiotics prescribed. Other than anti-malarials, paracetamol was the most commonly prescribed drug both in children (26.37%) and in adults (17.53%), pantoprazole being the second commonest drug prescribed (9.11%) in adults only.

![Figure 3: Distribution *P. vivax* and *P. falciparum* malaria patients.](image)

### Table 3: Drug utilization on the basis of WHO core prescribing indicators.

| Indicators                              | Variables in adults (n/%) | Variables in children (n/%) |
|-----------------------------------------|---------------------------|-----------------------------|
| Average no. of drugs per encounter      | 3.59                      | 3.79                        |
| Drugs prescribed by generic name        | 350(79.72%)               | 78(85.71)                   |
| Drugs prescribed from EDL               | 380(86.56%)               | 81(89.01%)                  |
| Prescriptions with antibiotics          | 58(47.54%)                | 18(75%)                     |
| Prescriptions with injections           | 11(9.01%)                 | 3(12.5%)                    |

Total number drugs prescribed in children and adults respectively were 91 and 439. The average number of drugs per prescription was 3.79 in children and 3.59 in adults.

Percentage of drugs prescribed in generic name was 85.71% in children and 79.72% in adults; respectively 89.01% and 86.56% of drugs were from EDL in children and adults.

Percentage of encounters with antibiotics in children and adults were 75% and 47.54% respectively whereas percentage of encounters with injections in children and adults were 9.01% and 12.5% respectively (Table 3).
DISCUSSION

Kolkata, one of the major metropolitan cities in India, is also the capital of the state West Bengal. Kolkata harbors highest number of malaria cases of West Bengal. In 2016, total malaria cases of West Bengal were 35236, of which 16498 were contributed by Kolkata (KMC area) and rest of the malaria cases were contributed by 19 districts and private hospitals of West Bengal.8

In this study, the total number of patients diagnosed of malaria were146, 122 adult and 24 pediatric patients. In the adult group, 71(58.19) patients were male, 51 (41.81%) patients were female; in the pediatrics group 18 (75%) patients were male, 6(25%) were female. The mean age of patients affected with malaria in adults and children were 35.17±12.5 years and 7.7±3.24 years respectively (Table 1). Different studies have classified malaria patients according to age and sex, which is usually arbitrary. Studies in India have revealed that burden of malaria in all age groups is usually higher in male patients than in females.5,15,18

Among adult patients, 48(39.3%) patients had P. falciparum and 74(60.7%) patients had P. vivax, among pediatric patients, 9(37.5%) patients had P. falciparum and 15(62.5%) patients had P. vivax. P. falciparum percentages (PI%) reported from West Bengal in 2015 and 2016 were 23.9% and 16.8% respectively, while in Kolkata PI% was 7.73 in 2015.8 Data showed that PI% in India has steadily risen to 50% in the recent years, in Odisha PI% is more than 40%.9 Also studies from tertiary care Medical College and Hospitals from Uttar Pradesh and Karnataka reported 60.10% and 39.63% P. falciparum cases respectively.15,18 All the severe cases of malaria in this study were infected with P. falciparum (3 in pediatric age group and 11 in adult age group), were admitted and treated in the in-patient department. The mild cases were infected both with P. falciparum and P. vivax, were treated as Out-patient department patients. In a previous study, most of the cases of P. vivax and P. falciparum were treated in OPD, but the severe cases of P. falciparum were admitted and treated as indoor patients.15

In this study, Chloroquine was prescribed to all the patients (adult n=74, child n=15) suffering from P. vivax, 3 children and 9 adults with falciparum malaria initially received chloroquine which later was changed to ACT due to non-response to chloroquine and blood report confirmed P. falciparum infection. One study from Karnataka showed that chloroquine was not prescribed to any of the patients with P. falciparum infection.18

Another study from a tertiary care center in Odisha reported that chloroquine was prescribed to 23.1% of P. falciparum patients.16 Anti-malarial drug utilization studies in Nigeria in 2003 and 2004 reported use of chloroquine in 30.2% and 47% of P. vivax patients respectively.12,19 In studies in tertiary care set-ups in Karnataka and Uttar Pradesh, chloroquine mono-therapy was done in 60.37% and 18.51% respectively.15,18

In this study, 88.88% of children and 91.67% of adults with falciparum malaria received artemisinin derivatives; ACT were prescribed to 66.67% of children and 77.09% of adults. Among the ACT artemether with lumefantrine combination was the most commonly prescribed ACT (55.56% in children and 33.34% in adults). Artesunate-sulfadoxine-pyrimethamine (31.25%) and artemunate-mefloquine (12.50%) were the other ACT prescribed in adults whereas only one child received artemunate-sulfadoxine-pyrimethamine, none received artemunate-mefloquine. NVBDCP 2014 guideline recommends prescribing artemether-lumefantrine to North-eastern states of India and artemunate-sulfadoxine-pyrimethamine to other states for treatment of falciparum malaria cases.2

A study in KMC hospital in Mangalore, Karnataka by Mubeen F et al, reported that artemunate-sulfadoxine-pyrimethamine were prescribed to 46.1% patients, lumefantrine was the most commonly prescribed agent and was prescribed to 86.5% of patients; whereas another study from a tertiary care hospital in Uttar Pradesh reported that artemunate-sulfadoxine-pyrimethamine was prescribed to only 5.29% of cases but artemunate- lumefantrine was prescribed to 82.78% of cases.15,20 In one drug utilization study in Nigeria in 2003, when ACT was introduced in the National Program, it was found that artemisinin derivatives were prescribed to 15.8% of falciparum cases, only 3% of whom received ACT (artemether-lumefantrine being the commonest agent); another study in Nigeria in 2012 reported increase and appropriate use of ACT to over 60% of children with falciparum malaria.12,15 In this study, quinine (11.11% in children and 8.33% in adults) and artesunate (22.22% in children and 14.58% in adults) in injection formula were used in falciparum malaria patients who were suffering from severe malaria and were admitted in the hospital. In one study from a tertiary care hospital in Eastern India showed that artesunate (48.1%) and mefloquine (25.9%) were the most common anti-malarials for falciparum malaria.16 In another study from Karnataka reported quinine and artesunate mono-therapy in respectively 80% and 5% of falciparum malaria cases.18 In this study, Primaquine was prescribed to 91.7% of pediatric and to 82.8% of the adult patients; G6PD test was done in 83.3% of pediatric and 73% of adult patients. Similarly in another study conducted in another part of India by Mubeen F et al reported prescription of primaquine to all the patients, whereas Singh AK et al observed that primaquine was not prescribed to children suffering from falciparum malaria.15,20 Two other studies from India reported use of primaquine which varied from 12.5% to 56.7%.15,18

In the present study the average number of drugs per prescription was 3.79 in children and 3.59 in adults. According to World Health Organization guideline of rational use of medicine, the average number of drug per prescription should be 1.6-1.8. Two studies from India
reported respectively 2.32 and 3 average number of drugs per prescription.\textsuperscript{15,18}

In the present study, percentage of encounters with antibiotics was 75\% in children and 47.54\% in adults respectively; amoxicillin-clavulanic acid (50\%) in children and azithromycin (29.31\%) in adults were the most common antibiotics prescribed. In a study in Nigeria, Chedi BAZ et al, found that 65\% prescriptions of malaria had an antibiotic co-prescribed.\textsuperscript{19} In studies in Odisha and Karnataka reported respectively 43.3\% and 9.45\% encounters with antibiotics.\textsuperscript{16,18}

Other than anti-malarials, paracetamol was the most commonly prescribed drug in both children (26.37\%) and in adults (17.53\%), pantoprazole being the second commonest drug prescribed (9.11\%) in adults only. One study from Odisha reported that proton pump inhibitors (65.4\%) were the commonest co-prescribing other drug group.\textsuperscript{16}

WHO suggests 100\% of prescription encounters should be in generic name and from Essential Drug List. In the present study, 85.71\% encounters in pediatric age group and 79.72\% encounters in adult group, generic name were used. Studies in India showed that prescribing drugs in generic name is very low and varied in studies-4.50\%, 8.50\%, 16.9\%; whereas in Nigeria prescribing in generic name was more than 40\%. \textsuperscript{15,16,18-19} In the present study, respectively 89.01\% and 86.56\% drugs in pediatric and adult age group were from essential drug list. This study reveals that EDL prescribing is reaching to the mark. Two different studies from different parts of India reported satisfactory EDL prescribing which were 85\% and 92.56\% respectively.\textsuperscript{16,18}

**CONCLUSION**

The present study reveals the prescribing pattern of anti-malarial drugs in a tertiary care hospital and Medical College in India, in both children and adults. Chloroquine along with primaquine was used rationally for treatment of \textit{P. vivax} malaria cases. Artemether-lumefantrine followed by artesunate-sulfadoxine-pyrimethamine were the most common drugs used for treatment of \textit{P. falciparum} malaria cases.

The Guidelines for diagnosis and treatment of malaria in India (2014) recommends artemether-lumefantrine as the first-line drug for \textit{P. falciparum} malaria cases for the North-eastern States of India only, artesunate-sulfadoxine-pyramethamine is recommended for other states. So the National guideline was not followed for treatment of \textit{P. falciparum} cases. The study also reveals high average number of drugs and antibiotics per encounter, which reflects irrationality in prescribing. On the other-hand, high EDL prescribing, prescribing in generic name and minimum use of injection per encounter satisfactorily reflects the tendency of rational prescribing in a tertiary care teaching hospital.

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