# A Study of Pharmacological Management of Hospitalized Patients of Malaria at A Tertiary Care Teaching Hospital

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**Abstract:** Aims & objectives: The present study was aimed to study usage pattern of drugs used in management of hospitalized patients of malaria and to monitor any adverse drug reactions occurring during the course of the given treatment in malaria patients. Methods: This prospective, observational, single centre study was carried out in 2 units of each Medicine and Paediatric Department of Civil Hospital, Ahmadabad. All the relevant details of hospitalized patients of malaria willing to participate in the study were recorded in a pre-decided case record form. Relevant statistical tests were employed wherever necessary. Results: A total of 87 hospitalized patients of malaria were studied during the period of one year. In our study, we found that type of malaria was P.vivax malaria in 49 (56.32 %) patients, P.falciparummalaria in 34 (39.08 %) patients and mixed infection malaria in 4 (4.59 %). Most commonly prescribed anti malarial in these patients was chloroquine (n=63, 72.4%). For prophylaxis, out of 87 patients, 72 (82.75%) patients were prescribed primaquine. Out of 87 patients, 21 ADRs were observed among 21 patients. The commonest ADRs were rash (n=9) and pruritus (n=6). Commonest suspected drug was chloroquine (n=12) followed by primaquine (n=6). Conclusion: Despite some limitations this study has made several important conclusions and useful suggestions can be made for future use of anti malarials. Prevention and treatment of malaria especially in Indian setup (limited resources, lack and cost of laboratory investigations, non availability of newer drugs) should be outlined in a rational manner. [C Dumatar, Natl J Integr Res Med, 2018; 9(2):39-43]

**Key Words**: P.falciparum, P.vivax, Chloroquine, ACT

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**Introduction:** Malaria occurs in over 90 countries worldwide.[1] Malaria is a major public health problem as around 40% of the global population are at risk of malaria especially thoseresiding in South-East Asia region.India has the largest population in the world at risk of malaria, with 85% living in malariouszones.[2]

Malaria is a systematic disease caused by infection of the red blood cells with intracellular protozoan parasites of the genus Plasmodium. The parasites are inoculated into the human host by a feeding female anopheles mosquito. Resistance of Plasmodium falciparum to chloroquine was first reported in 1973, and there is increase in antimalarial resistance, along with rapid urbanisation and labour migration. Although several institutions have done drugresistance monitoring in India, a complete analysis of countrywide data across institutions does not exist. Increasing drug resistance in P falciparum is a possible cause for the changing scenario in India.[3]

If resistance to artemisinins develops and spreads to other large geographical areas, the public health consequences could be dire, as no alternative antimalarial medicines will be available for at least five years. WHO recommends the routine monitoring of antimalarial drug resistance, and supports countries to strengthen their efforts in this important area of work.

More comprehensive recommendations are available in the Global Plan for Artemisinin Resistance Containment, which was launched in 2011 by WHO.[4] Thus, the present study was aimed to study usage pattern of drugs used in management of hospitalized patients of malaria and to monitor any adverse drug reactions occurring during the course of the given treatment in malaria patients.

**Methods:** A prospective, observational, single centre study was conducted at department of medicine and paediatrics over a period of one year (November 2012 to October, 2013) at a tertiary care teaching hospital in western India with a bed capacity of 2040 and average occupancy rate of 61 %. The institutional ethics committee approved the study protocol. During the study period, the investigator visited the medicine and paediatric ward of the concerned unit. The patients fulfilling the selection criteria were enrolled and informed written consent was taken from patients and / or patients' relatives. After enrolment, the following details were obtained from the patients and / or relatives and case papers and recorded in the CRF. The data collected was compiled, entered and analyzed in Microsoft Excel spreadsheet 2007. GraphPad Prism (demo version 6) software was used to calculate mean and standard deviation.

Analysis of the suspected adverse drug reactions and causality assessment was done by WHO-UMC scale (1992) and Naranjo's probability score.[5] Severity of ADRs was assessed by a scale described by Hartwig and Siegel (1992).

**Results:** A total of 87 hospitalized patients of malaria were studied during the period of one year from November 2012 to October 2013. We observed that most patients of malaria among adults were in the age group of 17-70 years and mean age was 32.5 ±15.2 years while children were in age group 6-12 years and mean age was 9.4± 1.8. In present study 57.5 % patients were males. More severe malaria was noted in male patients.

In present study, in all patients microscopy was used initially to detect Malaria. During follow up, patients were labeled as P.falciparum or P.vivax positive (Figure 1). In presentstudy, P.vivax malaria was observed in 49 (56.32 %) patients, P.falciparummalaria in 34 (39.08 %) patients and mixed infection malaria in 4 (4.59 %) patients.

Most commonly prescribed anti malarial in these patients was chloroquine (72.4 %, n=63). Chloroquine is still considered to be a drug of choice for P.vivax malaria. Most commonly prescribed anti-pyretic drug for fever management was paracetamol (100%, n=87). For prophylaxis, out of 87 patients, 72 (82.7 %) patients were prescribed primaquine. Additionally prescribers may also be aware of the higher cost of newer oral antimalarial. It is clear that a large experience in chloroquine and paracetamol use, relatively low cost and easier availability justify these prescription patterns.

Out of 87 hospitalized patients, 49 (56.32 %) patients were diagnosed malaria due to P.vivax infection, most common prescribed anti malarial drug was chloroquine in 40 (81.6 %) patients, 5 (10.2 %) patients were prescribed artesunate while 4 (8.2 %) patients were prescribed chloroquine and artesunate. Out of 87 patients, 34 (39.1 %) patients were diagnosed malaria due to P.falciparuminfection, 17 (50 %) patients were prescribed artemisinin based combined therapy (ACT), 6 (17.8 %) patients were prescribed chloroquine and ACT, 4 (11.8 %) patients were prescribed only chloroquine, 3 (8.8 %) patients were prescribed chloroquine and artesunate, 2 (5.8 %) patients were prescribed only artesunate while 2 (5.8

%) patients were prescribed chloroquine and sulfadoxine- pyrimethamine. 4 (4.59%) patients were diagnosed mixed infection malaria due to both P.vivax and P.falciparum infection and were prescribed ACT (Figure 2).

We observed that all patients were prescribed paracetamol; it was used as adult and paediatric dose as per patient and as when required.

We observed that total 129 anti malarial drugs were prescribed in 87 patients for treatment. Out of 129 drugs, 41 (31.7%) anti malarial drugs were prescribed by brand name while 88 (68.3%) drugs were prescribed by generic name. Out of 129 drugs, 100 (77.5 %) drugs prescribed were single formulation while 29 (22.5 %) drugs were fixed dose combination. All prescribed anti malarial drugs were supplied by the hospital drug store.

All antimalarial drugs were included in National List of Essential Medicines of India (2011) and Essential Medicines list of Gujarat (2011).

Out of 87 malaria patients, 7 (8 %) patients were preferred G-6 P D sensitivity test before primaquine administration was done. Out of 87 patients, 21 ADRs were observed among 21 patients (figure 3). The commonest ADRs were rash (n=9) and pruritus (n=6) as shown in table 1. Commonest suspected drug was chloroquine (n=12) followed by primaquine (n=6). None of patients died during follow up.

**Discussion:** A total of 87 hospitalized patients were enrolled, which included 50 (57.5%) males and 37 (42.5%) females. All enrolled patients (100%) completed the follow up till they got discharge. Gender distribution shows that 57.5 % (50) patients were males and 42.5 % (37) were females, with male: female ratio being 1.3:1.However, another study conducted in India showed 68.8% were male patients and 31.2% were female, with male: female ratio being 2.2:1[6,7]. Reasons are exactly not known but prevalence rate of malaria was more common in males. Even severity and fatality of malaria was noted to be more in male[8].

In present study, type of malaria was P. vivax malaria in 49 (56.32 %) patients, P.falciparummalaria in 34 (39.08 %) patients and mixed infection malaria in 4 (4.59 %) patients. One epidemiological study

conducted in India showed that 60 % patients had P.vivax malaria, 30 % had P.falciparum malaria and 10% had mixed infection malaria[8].In present study, microscopy (smear examination) was done to diagnose and to monitor progress of malaria in all patients as per guideline for NVBDCP 2011. This shows that national guidelines were strictly followed as present study was done in a tertiary care government hospital. Another reason could be that RDT (Rapid Diagnostic Test) was done in semi Government or private hospital which has high cost of investigations. In present study, G-6 PD sensitivity test before primaquine administration was done in 8 % of patients. G-6 PD deficiency can cause anemia and other hematological complications in primaquine treated patients. Other studies have shown that prevalence of G-6 PD deficiency are more common in some community (Muslim, Sindhi, Parasi etc.)[9].

As per WHO guideline 2013, Chloroquine is drug of choice for P.vivax malaria and ACT is first line therapy for P.falciparummalaria. In present study among patients of P.vivax malaria (n= 49), 81.6 % patients were prescribed chloroquine, 10.2 % patients were prescribed artesunate, 8.2 % patients were prescribed chloroquine and artesunate. Yet another study of India showed that 47 % patients of P.vivaxmalaria were prescribed chloroquine (Faheem M et al., 2013). In present study among patients of P.falciparuminfection (n=34), 17 (50 %) patients were prescribed artemisinin based combined therapy (ACT), 6 (17.64%) patients were prescribed chloroquine and ACT, 4 (11.76%) patients were prescribed only chloroquine, 3 (8.82%) patients were prescribed chloroquine and artesunate. However another study of India showed that 82 % patients of P.falciparum malaria were prescribed chloroquine[6]. In another study 65.8 % patients of P.falciparum malaria were prescribed ACT[10]. As per national malaria policy 2013 chloroquine resistance was found in P.falciparummalaria, so ACT is first line therapy. However, artesunate monotherapy was given in few patients, this is not preferred as it induces resistance. Artesunate is precious drug so always used with combination. In this study 6 paediatric patients were prescribed artesunate-lumifantrine in P.falciparummalaria. Another study suggests that this fixed dose combination is effective against P.falciparummalaria[11].

In present study, most drugs were prescribed by parenteral route. Reason could be that patients were hospitalized so parenteral route was preferred. Since majority drugs were prescribed by parenteral route, the ADRs like nausea vomiting were less compared to oral anti malarial therapy. A rational approach in selection of drug formulations was observed.

In present study 65.5 % (n=57) patients were treated as per national guidelines. In another study 57.5 % patients were treated as per national treatmentprotocol[12].

Out of 87 patients, 21 ADRs were observed among 21 patients (Table 2). The commonest ADRs were rash (n=9) and pruritus (n=6). All observed ADRs in present study were assessed by WHO- UMC score. All ADRs as per WHO-UMC Scale and Naranjo's score were labeled as possible. Commonest suspected drug was chloroquine (n=12) followed by primaquine (n=6). Similar results were seen in other studies as mentioned in Table 2.

**Conclusion:** This study has shown that treatment given to majority of patients was according to the recommended National guideline (NVBDCP 2013). Though malaria has high prevalence in India no mortality was seen in our study. All antimalarial drugs which were used in this study were included in essential medicine list of India.

**Table 1: Causality assessment of ADRs (n=21)**

| Sr. No. | Causality assessment | WHO-UMC scale number of ADRs | Naranjo's scale number of ADRs |
|---|---|---|---|
| 1 | Certain/ definite | 0 | 0 |
| 2 | Probable/ likely | 0 | 0 |
| 3 | Possible | 21 | 19 (+3 possible) 2 (+2 possible) |
| 4 | Unlikely/doubtful | 0 | 0 |
| 5 | Conditional/ unclassified | 0 | NA |
| 6 | Unassessible/unclassifiable | 0 | NA |

**Table 2: Comparison of adverse drug reaction profile**

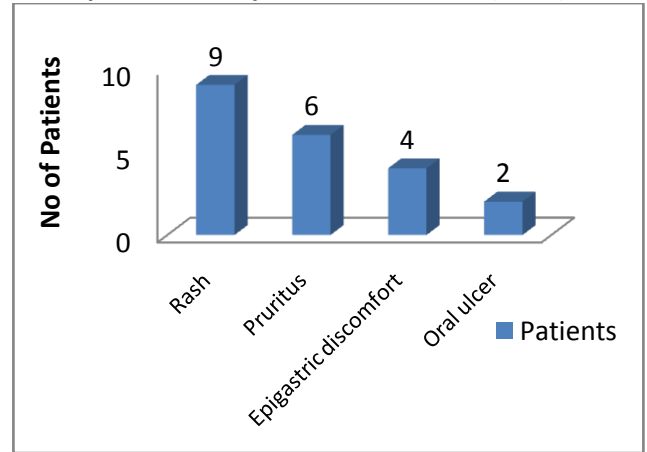| Adverse drug reaction | Present study (n=87) | Indian study (n=110) (Singh J et al., 2011) |
|---|---|---|
| Rash | 10.3 % | 12.6% |
| Pruritus | 6.9 % | 8.7% |
| Epigastric discomfort | 4.6 % | 4.1% |
| Oral ulcer | 2.3 % | - |

**Figure 1: Gender wise distribution as per speices of Plasmodium in hospitalized patients of malria (n=87)**
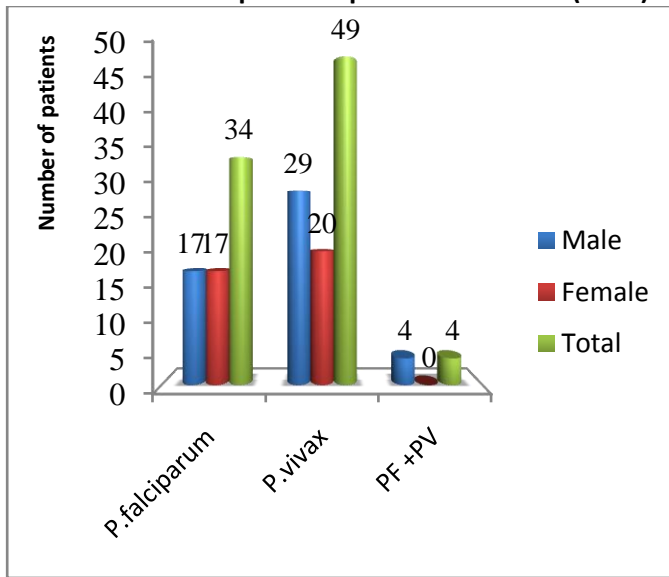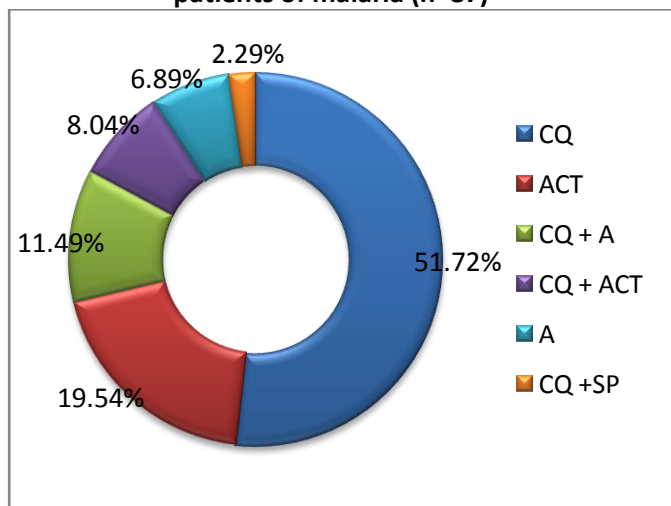


**Figure 2: Prescription pattern of antimalarial drugs in patients of malaria (n=87)**



CQ- Chloroquine
ACT- Artemisinin based combined therapy
A- Artesunate
SP- Sulfadoxine- Pyrimethamine

**Figure 3: Adverse drug reactions due to drugs prescribed in patients of malaria (n=21)**

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