E:/Biomedica Vol.22 Jul. – Dec. 2006/Bio-14 (A)

A STUDY OF PREVALENCE OF MALARIA IN ADULT POPULATION OF D. I. KHAN, PAKISTAN

H. U. KHAN, AZIZ M. KHATTAK, M. H. KHAN, I. U. MAHSUD AND S. HUMAYUN SHAH Departments of Medicine, Microbiology, Community Medicine and Pathology, Gomal Medical College, D. I. Khan

Malaria is a serious global health challenge. It continues to be a threat to the developing countries. Epidemiological data from different regions of Pakistan is insufficient to exactly evaluate the incidence of various types of malaria. D. I. Khan is a hot area on the right bank of the river Indus, providing favourable circumstances for mosquito breeding. We conducted this study to see the prevalence and presentation of various types of malaria in adult patients presenting with fever, and its response to anti-malarial agents in this region. This cross-sectional study was conducted in the Department of Medicine, Gomal Medical College, D. I. Khan, from 28th August 2005 to 27th February 2006. All adult patients presenting to the outpatient clinic with fever were included in the study. A total of 490 patients presented with fever as a chief complaint. After detailed history and thorough clinical examination, Giemsa stained thick and thin blood films were examined. Species determination and parasite count were performed. Patients were grouped into two; Group A having Falciparum malaria and Group B any other type. Group A patients were randomly given either Quinine or Artemether. Group B patients were given Chloroquine, Quinine or Artemether in standard doses. MP and parasite count were repeated on day 7 and 14 and the presence of more than 25% parasitaemia as compared to pretreatment was taken as treatment failure. Out of 490 patients, ninety-eight (20%) were found positive for malaria, seventy-five males and 23 females. Comparing the symptoms in falciparum and vivax malaria, it was found that nausea/vomiting was twice as common in falciparum malaria. Comparing the anti-malarial drugs, Chloroquine and Quinine were found to be effective in all patients. On the other hand Artemether was found to be 100% effective in vivax malaria and poor response to therapy was observed in two (4%) patients with falciparum malaria. As a conclusion malaria is responsible for fever in every fifth adult patient in our setup. Males are three times more commonly affected than females. Plasmodium falciparum is 1.5 times more common than vivax. Nausea/vomiting and pallor are more common in falciparum, while splenomegaly is seen in vivax malaria. Commonly used anti-malarial drugs are effective in most of the cases.

Malaria is a serious global health challenge.¹ It continues to be a threat in the developing countries, with more than 3000 deaths every day.² Estimated figures of its burden vary between 400 and 600 million cases per year.¹³ Although the burden of malaria and the focus of its control is Africa, malaria is still an important public health problem in other tropical countries such as India, Indonesia, Papua New Guinea, and the Amazon region of Latin America. Of the four species of human malaria, Plasmodium falciparum (P. falciparum) and Plasmodium vivax (P. vivax) account for the vast majority of cases but P. falciparum causes substantial morbidity and almost all of the mortality due to malaria.¹³

Malaria is quite common in Pakistan. Epidemiological data from different regions of Pakistan is insufficient to exactly evaluate the incidence of various types of malaria.⁴⁻⁶ Dera Ismail Khan (D. I.

Khan) with a hot climate, situated on the right bank of the river Indus, in the North West Frontier Province (NWFP) of Pakistan. The presence of ponds and improper drainage provide favourable sites for mosquito breeding. Patients presenting with fever usually pose a diagnostic problem for the clinicians but need a prompt response. Although malaria is a common cause of fever in this district, other infectious diseases like enteric fever and tuberculosis are not very uncommon.

Proper and timely anti-malarial therapy will lead to the cure of this disease in a short duration. Resistance to anti-malarial agents is a worldwide problem.^{7,8} The increasing prevalence of multi-drug resistant P. falciparum malaria is a serious public health threat to the global control of malaria, especially in developing countries.⁹⁻¹² In many countries choloroquine-resistance is a huge problem, accounting for more than 90% of malaria

cases.¹³ In Pakistan, resistance to choloroquine is on the rise and is reported in 16-62% of P. falciparum.¹⁴ Four to 25% of P. falciparum is also reported to be resistant to sulfadoxine-pyrimethamine and several cases of delayed parasite clearance have been observed in patients with P. falciparum malaria treated with quinine.¹⁴ Due to the problem of resistance, some studies have suggested the use of quinine or Artemether as the first line of treatment in malaria with complications, avoiding other drugs.¹⁵ Other studies carried out in the nearby districts have shown that even cases with very high parasite index did not show any significant resistance and responded well to routine treatment.⁴

We conducted this study to observe the prevalence and presentation of various types of malaria in adult patients suffering from fever, and its response to anti-malarial agents in this region.

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Medicine, Gomal Medical College, D. I. Khan, from 28th August 2005 to 27th February 2006. All adult patients presenting to the outpatient clinic with fever as a chief complaint, were included in the study. A detailed history and thorough clinical examination was performed and recorded. All these patients were referred to laboratory for collection of peripheral blood to be investigated for malaria. All the samples were processed without delay. The gold standard method i.e. smear examination for malarial parasite¹⁶ (MP) was performed. A trained laboratory technologist was assigned to prepare the slides. Thick and thin blood films, after Giemsa staining, were examined by an experienced Microbiologist (Author No. 2). Species determination and parasite count was performed. The slides were stored for further examination. A Clinical Pathologist was asked to counter examine these reported slides.

Patients having malaria i.e. showing malarial parasites (MP) in smears, were grouped into two according to their laboratory results. Group A having falciparum malaria and Group B having malaria due to rest of the three species. Group A patients were randomly given either Quinine or Artemether in standard doses. Group B patients were randomly given Chloroquine, Quinine or Artemether in standard doses. These drugs were given parenterally if the patient was vomiting.

Chloroquine sulphate was given orally in a dose of 600 mg loading dose, followed by 300 mg after 6-8 hours and then 150 mg twice daily for two days. Quinine bisulfate was given orally in a

dose of 600 mg three times daily for seven days. Parenterally, it was started in a dose of 600 mg by infusion 8 hourly for 7 days. The dose was reduced to 12 hourly if the patient complained of tinnitus or deafness. Artemether was given orally in a dose of 800 mg twice daily on first day and then 400 mg twice daily for further 4 days. Parenterally, it was started in a dose of 800 mg intra-muscularly (I/M) the first day and then 400 mg I/M daily for further 4 days.

Smear examination for MP and parasite count was repeated on day 7 and 14. The presence of more than 25% parasitaemia as compared to pretreatment results, was taken as treatment failure i.e. resistance.

RESULTS

Four hundred and ninety patients presented with fever as a chief complaint during the study period. Out of these, 98 (20%) were found positive for malaria, seventy-five (76.53%) males and 23 (23.46%) females. The average age of positive cases was 27.28 years, with an average age of 26.52 years in case of males and 29.86 for females (Table 1, Fig. 1)

Table 1: Age and sex distribution of malaria positive patients.

Sex	Number of Patients	Average Age (Years)
Male	75 (76.53%)	26.52
Female	23 (23.46%)	29.86
Total	98	27.28

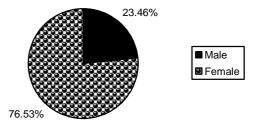


Fig. 1: Male to Female ratio of malaria patients.

Among 75 male patients, 44 (58.66%) were having P. falciparum, 30 (40%) P. vivax and only one (1.34%) P. malariae infection. In 23 female patients, 13 (56.52%) were having P. falciparum and 10 (43.48%) P. vivax (Table 2, Fig. 2).

The highest number of MP positive patients occurred during the month of September and the minimum in January, during this study period. The smear positivity for P. falciparum was highest during November and December (Table 3, Fig. 3).

The presenting symptoms apart from fever were headache in 79.59%, Rigors/chills in 52.04%, body aches in 47.96% and nausea/vomiting in 45.92% of cases. The commonest sign was splenomegaly found in 60.20% patients, while other signs were raised temperature at the time of examination 53.06% and pallor in 42.86% of cases (Table 4, Fig. 4, 5). Comparing the symptoms among falciparum and vivax malaria, it was found that nausea/vomiting was twice as common in falciparum malaria. Comparing the signs, splenomegaly was twice more common in patients with vivax malaria, while pallor in falciparum malaria (Table 5, Fig. 6).

Regarding the treatment by various antimalarial agents, fifty patients with falciparum malaria were given Artemether and seven patients were given Quinine, whereas 20 patients with vivax malaria were given Chloroquine, 11 Arte-

mether and 9 Quinine. Chloroquine was not given to falciparum malaria infected in our study¹⁷ and it was found to be effective in all patients with vivax malaria. Quinine was found to be effective in all patients of both falciparum and vivax malaria. On the other hand Artemether was found to be 100% effective in vivax malaria and poor response to therapy was observed in two (4%) patients with

falciparum malaria taking Artemether (Table 6, Fig. 7).

DISCUSSION

Epidemiological data from different regions of Pakistan is insufficient to exactly evaluate the incidence of various types of malaria.⁴ Our study will contribute to the data regarding the epidemiology of this disease.

The predominance of males in our study can be due to various factors. Males are the working and out going population in our society, hence they have more chances of being bitten by infected mosquitoes. Also they have early and easy approach to the health care facilities as compared to females, because of our traditional hindrances for females in this respect.

Table 2: Species distribution of Plasmodium in relation to sex of patients.

Sex	Plasmodium vivax	Plasmodium falciparum	Plasmodium malariae
Male	30 (40%)	44 (58.66%)	1 (1.34)
Female	10 (43.48%)	13 (56.52%)	0
Total	40 (40.81%)	57 (58.17%)	1

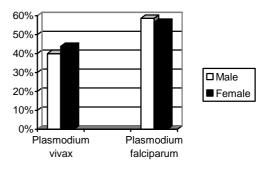


Fig. 2: Species distribution of Plasmodium in relation to sex of patients.

Table 3: Prevalence of various types of malaria during six months of study.

Mosquito	Sept	Oct	Nov	Dec	Jan	Feb
P. falciparum	12	12	16	14	2	8
P. vivax	12	3	2	4	2	10
P. malariae	-	-	-	1	-	-
Total	24	15	18	19	4	18

Comparing our results regarding age, prevalence of disease, species distribution of malaria and symptomatology, to that of the study by Sheikh et al¹⁷ (2005) in Quetta, our results are dissimilar to that study. The reason may be that in our study only adult patients were included, while all age group of subjects were included in their study. The average of age in our study was 27.28 years as compared to the range of 10-60 years in their study. The prevalence of malaria in febrile patients was 20% in our study as compared to 34.85% in that study. Prevalence of P. falciparum was 58.17% and P. vivax 40.81% in our study as compared to 30.72 and 66.87% respectively in their study. The reason behind may be confined age limit in our study, geographical difference like hot, plain area (of D. I. Khan) as compared to the extended age range and cold hilly area in their study.

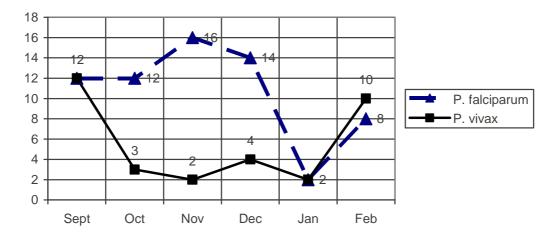


Fig. 3: Prevalence of various types of malaria during six months of study.

Table 4: Frequency of sign and symptoms in patients with malaria.

Symptoms		Signs		
Fever	98 (100%)	Temperature Normal		46 (46.94%)
			99-102	32 (32.65%)
			103-105	16 (16.33%)
			>105	4 (4.08%)
Headache	78 (79.59%)	Splenomegaly 59 (6		59 (60.20%)
Rigors / chills	51 (52.04%)	Pallor		42 (42.86%)
Body aches	47 (47.96%)	Jaundice		3 (3.06%)
Nausea / vomiting	45 (45.92%)	Hepatomegaly		2 (2.04%)

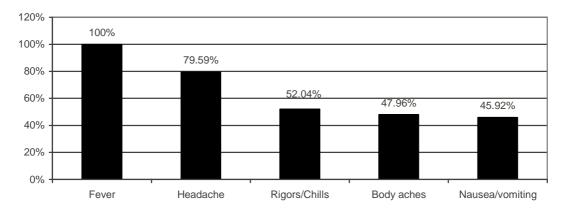


Fig. 4: Frequency of symptoms in patients with malaria.

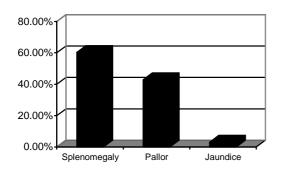
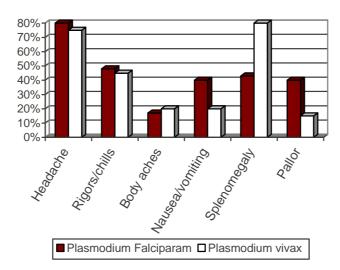


Fig. 5: Frequency of sign in patients with malaria.

Table 5: Comparison of presenting features between malaria due to Plasmodium falciparum and vivax.

Signs and Symptoms	Plasmodium falciparum	Plasmodium vivax	
Headache	80%	75%	
Rigors/chills	48%	45%	
Body aches	17%	20%	
Nausea/vomiting	40%	20%	
Splenomegaly	43%	80%	
Pallor	40%	15%	

Fig. 6: Comparison of presenting features between malaria due to P. falciparum and P. vivax.



In a study by Hozhabri et al¹⁸ (2000) in Jhangara Sindh, the prevalence of malaria was found to be 5.9% of febrile patients, P. falciparum 65% and P. vivax 35% in patients with median age range of 24 months. Fever as chief complaint was similar to our study. In the present study as compared to Sheikh et al¹⁷, fever at the

time of examination was noticed in 53% of patients. Pallor was more prominent sign in patients with P. falciparum while splenomegaly in patients with P. vivax in our study. In our patients having malaria, we gave Quinine or Artemether in P. falciparum and Chloroquine, Quinine or Artemether in P. vivax. The treatment response observed by follow up was favorable, similar to the findings of the study by Khadim et al⁴. There was a good response to Quinine while delayed clearance of P. falciparum in patients treated with Arte-

Table 6: Response to anti-malarials used in various species of Plasmodium.

	Chloroquine	Quinine	Artemether
P. falciparum	-	100%	96%
P. vivax	100%	100%	100%

mether in 4% of cases in our study. These findings are dissimilar to the report by Khan et al¹⁴, a study in Karachi, showing good response to Artemether while delayed clearance by Quinine in several cases

Due to Chloroquine resistance in the treatment of P. falciparum as reported by Djaman et al¹⁹ and Khan et al¹⁴, was not used and tried for the treatment of P. vivax only. The results were successful as shown by follow up smears.

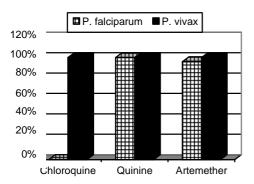


Fig. 7: Response of P. falciparum and P. vivax to antimalarials used.

It was **Concluded** that malaria is responsible for fever in every fifth adult patient in our setup. Males are three times more commonly affected than females. P. falciparum is 1.5 times more common than P. vivax. Nausea / vomiting and pallor are more common in falciparum, while splenomegaly in vivax malaria. Commonly used antimalarial drugs, Chloroquine, Quinine and Artemether in case of vivax and Quinine or Artemether in falciparum malaria are effective in most of the cases.

ACKNOWLEDGEMENT

We are grateful to Mr. Niamat-ullah lab technologist and Mr. Kamal-ud-din lab technician for their cooperation and help in carrying out this study.

REFERENCES

- World malaria situation in 1994. Part I. Population at risk. Wkl Epidemiol Rec 1997; 72: 269-76.
- Rathore D, McCutchman TE, Sullivan M, Kumar S. Antimalarial drugs: current status and new developments. Expert Opin Investig Drugs 2005; 14: 871-83.
- Snow RN, Craig M, Deichmann U, Marsh K. Estimating mortality, morbidity and disability due to malaria among Africa's non-pregnant population. Bull World Health Organ 1999; 77: 624-40.
- Khadim MT. Malaria a menace at Zhob Garrison. Pak Armed Forces Med J 2002; 52: 203-7.
- Muhammad N, Hussain A. Prevalence of malaria in general population of district Bunir. J postgrad Med Inst 2003; 17: 75-80.

- Murtaza G, Memon IA, Noorani AK. Malaria prevalence in Sindh. Med Channel 2004; 10: 41-2.
- 7. Fryauff DJ, Lexana B, Masbar S, et al. The drug sensitivity and transmission dynamics of human malaria on Nias Island, North Samarta, Indonesia. Ann Trop Med Parasitol 2002; 96: 447-62.
- 8. Bras JL, Durand R. The mechanism of resistance to antimalarial drugs in Plasmodium falciparum. Fundamental & Clinical Pharmacology 2003; 17: 147.
- 9. White NJ, Why is it that antimalaria drug treatments do not always work? Ann Trop Med Parasitol 1998; 92: 449-58.
- McGrady R, Cho T, Keo NK, et al. Artimesinin antimalarials in pregnancy: a prospective study of 539 episodes of multidrug-resistant Plasmodium falciparum. Clin Infect Dis 2001; 33: 2009-16.
- 11. Pradines B, Orlandi-Pradines E, Henry M, et al. Metallocenes and malaria: a new therapeutic approach. Ann Pharm Fr 2005; 63: 284-94.
- 12. Socheat D, Denis MB, Fandeur T, et al. Mekong malaria II. Update of malaria, multi-drug resistance and economic development in the Mekong region of Southeast Asia. Southeast Asian J trop Med Public Health 2003; 34 Suppl 4: 1-102.
- Aronsson B, Bengtsson E, Bjorkman A, et al. Chloroquine-resistant falciparum malaria in Madagaskar and Kenya. Ann Trop Med Parasitol 1981; 75: 367-73.
- Khan MA, Smego RA, Razi ST, Beg MA. Emerging drug - resistance and Guidelines for treatment of malaria. J Coll Physicians Surg Pak 2004; 14: 319-24.
- Murtaza G, Memon IA. Clinical Update Antimalarial Drugs in Plasmodium Falciparum Malaria. J Coll Physicians Surg Pak 2000; 10: 484-8.
- Zaman V, Beg A. Laboratory diagnosis of Malaria. Infect Dis J 2004; 13: 47-8.
- Sheikh AS, Sheikh AA, Sheikh NS, Paracha SM. Endemicity of malaria in Quetta. Pakistan J Med Res 2005; 44: 41-5.
- 18. Hozhabri S, Akhtar S, Rahbar M, Lubi S. Prevalence of plasmodium slide positivity among the children treated for malaria, Jhangara, Sindh. J Pak Med Assoc 2000; 50: 401-5.
- 19. Djaman AJ, Basco LK, Mazabraud A. Monitoring the chemoresistance of Plasmodium falciparum malaria in Yopougon (Abidjan): in vivo study of chloroquine sensitivity and evaluation of pyrimethamine resistance following the analysis of point mutation in the dihydrofolate reductase gene. Sante 2002: 12: 363-7.