Original Article

Mode of Presentation and Susceptibility to Treatment of Malaria in Children at Thal, a Remote Area of KP, Pakistan

Khawar Kamal*
Mahmood ur Rahman**
Farwa Rizvi****

**Combined Military Hospital (CMH) Thal, KP Pakistan*
***Prof. and HOD, Community Med., Army Medical College, Rawalpindi*
****Assistant Professor, Community Medicine, Islamabad Medical and Dental College, Bahria University, Islamabad*

ABSTRACT:

Objective: To determine the mode of presentation and susceptibility to treatment of malaria in children at Thal, a remote area of KP, Pakistan.

Study Design: A descriptive study.

Place and Duration: The study was carried out at Combined Military Hospital (CMH) Thal from Sep 2008 to Aug 2009.

Materials and Methods: A total of 202 children suffering from malaria (diagnosis confirmed by positive slide examination for malarial parasites by qualified hematologist) selected by consecutive sampling, were in the study including 138 (68%) males and 64 (32%) females with mean age of 7.2 years. Statistics regarding age, gender, fever duration, clinical signs and response to treatment were evaluated.

Results: Out of 202, Plasmodium falciparum was detected in 67 (33.2%) cases, Plasmodium vivax in 135 (66.8%) cases. Fever was present in 100% of cases and the mean duration prior to diagnosis was 6.7 days. Major symptoms included vomiting, headache and diarrhea. Splenomegaly was present in majority of cases (182 out of 202). Artemether was first line therapy in Plasmodium falciparum with 100% success. Chloroquine was given in Plasmodium vivax with 12% failure (all responded to subsequent Artemether).

Conclusion: Malaria is prevalent in children in Thal and response to standard treatment remains satisfactory.

Key words: Malaria, Plasmodium vivax, Plasmodium falciparum, Chloroquine, Artemether.

Address for Correspondence
Dr Farwa Rizvi, Assistant Professor, Community Medicine, Islamabad Medical and Dental College, Bahria University, Islamabad.
Email: farwa.riz@gmail.com

Introduction

Malaria is a protozoal disease caused by infection with parasites of the genus plasmodium and transmitted to man by certain species of infected female anopheline mosquito.[1] Malaria causes symptoms that typically include fever and headache, which in severe cases can progress to coma or death. The disease is widespread in tropical and subtropical regions in a broad band around the equator, including much of Sub-Saharan Africa, Asia, and the Americas.[2] In many settings of stable malaria transmission, the presence of asymptomatic malaria parasite carriers is common and the definition of clinical malaria remains uncertain.[3] The signs and symptoms of malaria typically begin 8–25 days following infection;[4] however, symptoms may occur later in those who have taken anti malarial medications as prevention.[5]Initial manifestations of the disease are similar to flu-like symptoms,[6] and can resemble other conditions such as septicemia, gastroenteritis, and viral diseases.[5] The presentation may include headache, fever, shivering, joint pain, vomiting, hemolytic anemia, jaundice, hemoglobin in the urine, retinal damage,[7] and convulsions. Malaria is the major health hazard in Pakistan. There is a lot of dormant water after heavy rains in the country, providing a perfect setting for mosquito reproduction. In Pakistan, malaria is prevalent from July to November.[8]

According to reports, an estimated 247 million malaria cases among 3.3 billion people were at risk in 2006, causing a million deaths, mostly children under 5 years and 109 countries were endemic for malaria in 2008. [9, 10]

In Indian sub continent the majority of malaria infections are contributed by *P. falciparum* and *P. Vivax*.[11, 12]
In Pakistan Southern Punjab, Baluchistan and Sind are endemic areas. This study was carried out to determine the mode of presentation and susceptibility to treatment of malaria in children at Thal.

Materials and Methods

This descriptive study was carried out from Sep 2008 to Aug 2009 at the Department of Pediatrics, Combined Military Hospital (CMH) Thal. Study population comprises of 202 children who were diagnosed as cases of malaria at children ward of our hospital. Informed consent was taken from parents of the children (patients). Principles of respect for the person, beneficence and justice were strictly observed. Detailed history from parents and patients especially history of fever, rigors and chills, vomiting, headache, generalized body aches, convulsions, cough and diarrhea was recorded on specifically designed Performa. The age range was 2-12 years with mean age of 7.2 years. After history and complete clinical examination, three consecutive blood samples for thick and thin peripheral blood smears were analyzed. Patients with positive results were included in the study. The thick smear was stained by Giemsa's stain and thin smear by Leishman's stain. The slide was then studied under oil immersion lens (x1000) of the microscope. The parasites were quantified by independently counting asexual and sexual stages of both P. falciparum and P. vivax parasites against 300 white blood cells (WBCs) on the thick smear. Parasite density was done to classify the patients as mild, moderate, high and very high parasite density. First line of treatment was Chloroquine in cases with Plasmodium vivax whereas Artemether in cases with Plasmodium falciparum. Response to treatment was also recorded meticulously, and a total of three a febrile days and disappearance of other symptoms were prerequisite of cure of malaria.

Results

Total 202 children were included in this study over a period of one calendar year. Study population comprised 68% male and 32% female with mean age of 7.2 (2-12) years. Plasmodium falciparum was detected in 67 (33.2%) cases whereas Plasmodium vivax in 135 (66.8%) cases. No case of mixed smear was detected. Fever was present in 100% of cases with mean duration before diagnosis was 6.7 days and range was 1-25 days. Chills and rigors were present in 77 (38.1%) cases. Other major symptoms included vomiting 44 (21.8%), headache 39 (19.3%), body aches 39 (19.3%) and diarrhea 35 (17.3%) cases. Only 5 (2.5%) cases presented with fever and fits, diagnosed subsequently as cases of cerebral malaria. Splenomegaly was clinically palpable in 182 (90%) cases whereas significant hepatomegaly was detected only in 32 (15.8%) cases. Clinically pallor was present in 73 (36%) cases (67 out of 67 falciparum infection and 6 out of 135 of vivax infections). Presence of Splenomegaly and pallor are graphically shown in Fig 1 and 2 respectively.

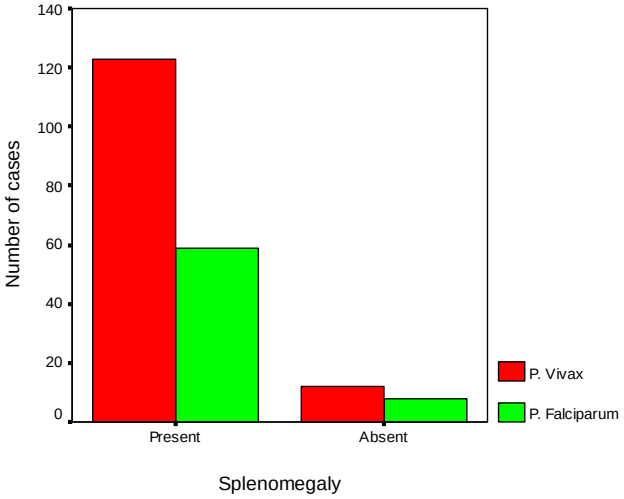

Figure 1: Splenomegaly in cases

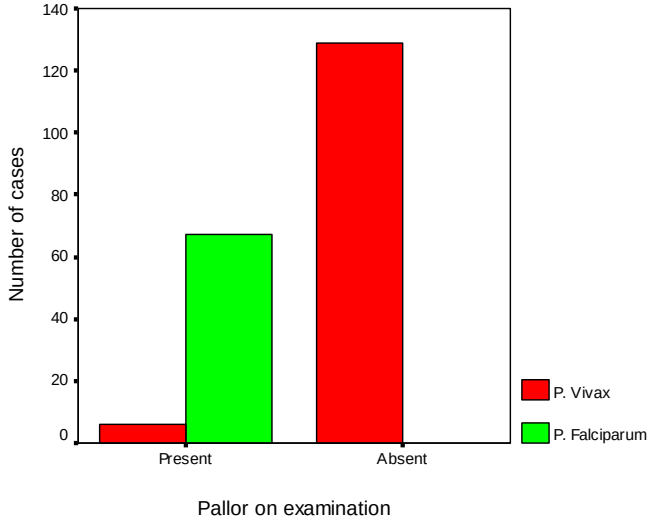

Figure 2: Presence of anemia in malaria cases

Anemia and thrombocytopenia were detected in majority of cases with P. falciparum as shown in table I. Artemether was given as first line therapy in cases with Plasmodium falciparum with 100% success. Chloroquine was given as first line drug in cases with Plasmodium vivax with 12% failure (all responded to subsequent Artemether). Fever, chills, and rigors were settled initially followed by vomiting, diarrhea, headache and body aches. The duration of response to treatment was short except in those cases that were resistant to chloroquine. There was no adverse effect of treatment observed.

Table I: Blood counts in cases

		Hb in g/dl	Platelets x 10^6/L
Plasmodium Vivax	Mean	9.49	198.57
	Number	135	135
	Std. Deviation	1.05	41.14
Plasmodium Falciparum	Mean	6.27	181.64
	Number	67	67
	Std. Deviation	1.13	299.73
Total	Mean	8.42	192.96
	Number	202	202
	Std. Deviation	1.86	175.19

Discussion

Malaria is a cause of mortality and morbidity in developing countries, where children and pregnant women are the primary target. Malaria is a mosquito-borne disease caused by the Plasmodium parasite [13]. Malaria is a major health problem in Pakistan and areas adjoining Afghanistan-Pakistan border due to inefficient use of anti-malarial drugs, misdiagnosis and inadequate follow up and drug resistance.

The study was carried out at Thal city, the last out post of settled area. The patients were received from khost province of Afghanistan, kurram, orakzai, South Waziristan agencies and district Hangu. A 12 month study was conducted based on positive blood slides for parasitemia. Plasmodium vivax was the predominant organism throughout the study period with no seasonal variation.

The studies carried out in Uganda, Ghana and other parts of the world revealed that the maximum hematological deterioration occurs in malaria caused by plasmodium falciparum[14] and the same was the result in our study. Chloroquine resistance was absolute in P. falciparum and emerging in vivax.

Each year 350-500 million cases of malaria occur worldwide and over one million people die, most of them are young children in Africa. [13]A study carried out by Snow RW etal revealed that in 2005, there were almost 515 million cases of P. falciparum malaria in 2002.[15]

Both Plasmodium vivax and falciparum are prevalent in Pakistan.[16] In this study P. falciparum was diagnosed in 67 (33.2%) cases and P. vivax was diagnosed in 135 (66.8%) cases. According to a recent report Chloroquine remains the drug of choice in P. vivax malaria in the region of south Asia. [17]In this study the cases of P. vivax malaria were treated by chloroquine as the drug of choice and the failure rate was only in 12% of cases who were treated with Artemether successfully.

Symptoms of malaria include fever, flu-like illness, chills, headache, muscle aches, and tiredness. Cough, nausea, vomiting, and diarrhea may also occur. The classic symptom of malaria is cyclical occurrence of sudden coldness followed by rigors, fever and sweating lasting four to six hours, occurring every two days in P. vivax and P. ovale infections, while every three days for P. malariae.[18] In this study fever was present in 100% of cases. Chills and rigors were present in 77 (38.1%) cases. Vomiting 44 (21.8%), headache 39 (19.3%), body aches 39 (19.3%) and diarrhea 35 (17.3%) cases. Only 5 (2.5%) cases presented with fever and fits, diagnosed subsequently as cases of cerebral malaria caused by P. falciparum. P falciparum can have recurrent fever every 36–48 hours or an almost continuous fever. Malaria causes hemolysis with anemia and jaundice. Plasmodium falciparum, may cause renal failure, seizures, mental confusion, coma, and death.[13]

A study in Uganda revealed that one in four children develop cognitive abnormalities after cerebral malaria.[14] The presentation of malaria is similar in endemic areas but there may be divergent symptoms in migrant people. This may lead to misdiagnosis when splenomegaly is not obvious, or when diarrhea, vomiting or cough is present with fever. [19]

Confirmed diagnosis of malaria is microscopic examination of blood films as each of the four major parasite species has distinguishing characteristics. Thin films allow species identification as the parasite's appearance is best preserved in this preparation. Thick films allow screening larger amount of blood and are eleven times more sensitive than the thin film, so picking up low levels of infection is easier on the thick film, but the appearance of the parasite is much more indistinct and therefore distinguishing between the different species can be trickier. It is vital to utilize both smears while making a definitive diagnosis. [20]

Of all anti malarial drugs, Chloroquine has been the drug of choice for many years in the world. However, resistance of Plasmodium falciparum to Chloroquine has spread from Asia to Africa, making it ineffective against the most hazardous Plasmodium strain in parts of the world. In areas where Chloroquine is still effective it remains the first choice. Extracts of Artemisia Annua, containing the compound artemisinin or semi-synthetic derivatives offer over 90% efficacy rates. We used Chloroquine as first line treatment in cases with P vivax (12% failure subsequently treated with Artemether) and Artemether in cases with P. falciparum with 100% success. Five cases of cerebral malaria were also successfully treated with intramuscular Artemether. Cerebral malaria is usually treated with IV Quinine or IM Artemether. A study carried out in Pakistan revealed that there was 11% mortality in cases of cerebral malaria, treated with IV quinine but in our study mortality rate was 0% as all the five cases of cerebral malaria were treated with IM Artemether.

Drug resistance, lack of compliance in children, multiple drug therapy, cross-resistance, positive selection and genetic influence of drugs are primary hurdles in treatment.[22] Artemether and Quinine are commonly used for treating severe malaria caused by P. falciparum. There was 100% success for Artemether in our study in treating P. falciparum malaria and as rescue therapy in P. vivax malaria. In view of its good performance by intramuscular injection, Artemether appears to be an excellent alternative for treatment of severe malaria and cerebral malaria in areas with poor medical facilities.

Conclusion

Presentation of malaria in this region is similar to other endemic areas and resistance to drugs is emerging

References

1. Park K. Park's text book of preventive and social medicine, Banarsidas Bhanot Publisher, Prem Nagar, Jabalpur,2010;222.
2. Nayyar GML, Breman JG, Newton PN, Herrington J (2012). "Poor-quality anti malarial drugs in southeast Asia and sub-Saharan Africa". *Lancet Infectious Diseases* 12 (6): 488–96.
3. Mabunda S, Aponte J J, Tiago A, Alonso P. A country-wide malaria survey in Mozambique. II. Malaria attributable proportion of fever and establishment of malaria case definition in children across different epidemiological settings. *Malaria Journal* 2009, 8:74.
4. Fairhurst RM, Wellems TE (2010). "Chapter 275. *Plasmodium* species (malaria)". In Mandell GL, Bennett JE, Dolin R (eds). *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases* 2 (7th ed.). Philadelphia, Pennsylvania: Churchill Livingstone/Elsevier. pp. 3437–3462.
5. Nadjm B, Behrens RH (2012). "Malaria: An update for physicians". *Infectious Disease Clinics of North America* 26 (2): 243–59.
6. Bartoloni A, Zammarchi L (2012). "Clinical aspects of uncomplicated and severe malaria". *Mediterranean Journal of Hematology and Infectious Diseases* 4 (1): 2012-026
7. Beare NA, Taylor TE, Harding SP, Lewallen S, Molyneux ME (2006). "Malarial retinopathy: A newly established diagnostic sign in severe malaria". *American Journal of Tropical Medicine and Hygiene* 75 (5): 790–7.
8. Khadim MT. Malaria a menace at Zhob Garrison. Pak Armed Forces Med J 2002:52;203-7
9. Farooq MA, Salamat A, Iqbal MA. Malaria – An Experience at CMH Khuzdar (Baluchistan). J Coll Physicians Surg Pak 2008; 18:257-8.
10. World Malaria report 2008. Available at http://www.who.int/malaria/publications/atoz/9789241563697/en/index.htm Cited on 06 March 2009
11. Dhiman S, Goswami D, Rabha B, Gopalakrishnan R, Baruah I, Singh L. Malaria epidemiology along Indo-Bangladesh border in Tripura state, India. Southeast Asian J Trop Med Public Health. 2010; 41(6):1279–1289.
12. Sharma SK, Chattopadhyay R, Chakrabarti K, Pati SS, Srivastava VK, Tyagi PK, Mahanty S, Mishra SK, Adak T, Das BS, Chitnis C. Epidemiology of malaria transmission and development of natural immunity in a malaria- endemic village, San Dulakudar, in Orissa state, India. Am J Trop Med Hyg. 2004; 71(4):457–465.
13. Malaria. Available at http://www.cdc.gov/Malaria. Cited on 28 feb 2009
14. Cserti-Gazdewich C, Dhabangi A, Musoke C, Nabukeera-Barungi N, Ddungu H, Mpimbaza A, Ssewanyana I et al. Hematologic Findings and Transfusion Therapy in Severe Pediatric Plasmodium Falciparum Malaria: Results from a Prospective Observational Study in Uganda. December 8, 2008, 50th ASH annual meeting and exposition, San Francisco.
15. Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI. The global distribution of clinical episodes of Plasmodium falciparum malaria. Nature 2005;434:214-7.
16. Khan MA, Smego RA, Rizvi ST, Beg MA. Emerging drug-resistance and guidelines for treatment of malaria. J Coll Physicians Surg Pak 2004;14:319-24.
17. Leslie T, Mayan MI, Hasan MA, Safi MA, Klinkenberg E, Whitty CJ et al. Sulfadoxine-Pyrimethamine, hlorproguanil-Dapsone, or Chloroquine for the Treatment of Plasmodium vivax Malaria in Afghanistan and Pakistan: A Randomized controlled Trial. JAMA 2007;297:2201-9
18. Malaria life cycle & pathogenesis. Malaria in Armenia. Available at. http://www.lumrix.net/health/Malaria.html Cited on December 2008.
19. Jamal MM, Ara J, Ali N. Malaria in pediatric age group: a study of 200 cases. Pak Armed Forces Med J:2005;55:74-7.
20. White NJ. Antimalarial drug resistance. J Clin Invest 2004;113:1084–92.
21. Din JU, Khan SA, Ally SH. Malaria in children: study of 160 cases at a private Clinic in Mansehra. Ayub Med Coll Abbottabad 2006;18:44-5
22. John CC, Bangirana P, Byarugaba J, Opoka RO, Idro R, Jurek AM et al. Cerebral Malaria in Children Is Associated With Long-term Cognitive Impairment. Pediatrics 2008:122;e92-e9