Epidemiological profile of malaria in a University Hospital in the Eastern Region of Saudi Arabia

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ABSTRACT

Objectives: To study the epidemiological, clinical and hematological profile of laboratory-diagnosed malaria cases at King Fahd Hospital of the University, Al-Khobar, Saudi Arabia, during the period from January 1990 to December 1999, and to provide suitable recommendations accordingly.

Methods: This was a clinical case series study of confirmed cases presenting to King Fahd Hospital of the Univeristy during the period from January 1990 to December 1999. A specially designed form was used for data collection and 602, laboratory-confirmed cases of malaria were retrospectively analyzed.

Results: There were 602 cases with a mean age of 25.8 ± 14.3 and a male to female ratio of 2.9:1. Less than half the cases were Saudis (42%), most of whom (93%) reported a history of travel to the Southwestern part of the Kingdom. The highest frequency of cases was observed in the years 1992, 1994 and 1998 and 40% of the cases were diagnosed during the months of February, March and September. *Plasmodium falciparum* was the most common species among Saudi (83%), Sudanese (72%) and Yemeni (64%) patients, while *Plasmodium vivax* was predominant among others. Most of these cases (75%) had a history of travel to their home countries (endemic areas). The most common clinical presentation was fever (97%), while the most common clinical signs were splenomegaly (9%) and jaundice (8%). Anemia (60%) and thrombocytopenia (53%) were the most common hematological findings.

Conclusions: Although it appears that the Eastern Province is still free of indigenous malaria transmission, this could not be confirmed by the data. Imported cases, however represent a continuous threat due to the existence of such vectors as *Anopheles stephensi*, *Anopheles fluviatilis*, *Anopheles sergentii* and *Anopheles superpictus* and a large number of non-immune persons. It is recommended that malaria be always considered in the differential diagnosis of all acute fevers, especially among those with a history of travel to an endemic area. Prompt diagnosis and treatment is necessary. Chemoprophylaxis, when traveling to endemic areas is mandatory, as well as the use of other primary preventive measures to protect against mosquito bites.

Keywords: Malaria, epidemiology.

Saudi Medical Journal 2001; Vol. 22 (2): 133-138

Malaria remains a major public health problem in many parts of the world. Over 40% of the world's population are at risk, and it is endemic in 91 countries, mostly developing.[1] Despite being the oldest parasitic disease facing mankind, its continued association with morbidity and mortality is considerable. The World Health Organization (WHO) estimates that there are 300 million to 500 million people infected with malaria.[2] Malaria has an even larger impact on disability-adjusted life

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Received 8th July 2000. Accepted for publication in final form 14th October 2000.

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years (DALYs),[3] an indicator developed to estimate the disease burden for purposes of evaluating the cost-effectiveness of interventions. Globally, malaria is responsible for the loss of 35,728,000 DALYs,[3] compared with those for tuberculosis (46,450,000), all cancers (80,015,000) or hypertension (936,000), this demonstrates the relative importance of malaria's contribution to the global burden of disease.[4] In the Kingdom of Saudi Arabia, malaria endemicity is localized to the Southwestern part of the country, with the highest number of cases reported from Gizan and Asir regions.[5-7] However there has been no local transmission in the Eastern Province since 1978,[7] as a result of control programs that were initiated, as early as 1948.[7-9] The main objectives of this study were to examine the demographic, clinical and some hematological features of reported malaria cases at King Fahd Hospital of the University (KFHU) Al-Khobar, Saudi Arabia from the period January 1990 to December 1999. To assess frequency of suspected risk factors among the cases, and provide suitable recommendations, accordingly.

Methods. This was a clinical case-series study. The medical charts of all confirmed cases that presented to KFHU during the period from January 1990 to December 1999 were included in the study sample. A case was defined as a positive thin, thick, or both, blood film recorded in the KFHU Hematology Department records during the study-period. A specially designed form of 3 sections was used for data collection. Section A (basic demographic data) included such variables as age, sex, residence, education, occupation and history of travel to an endemic area. Section B (clinical data) inquired about fever pattern, presence of jaundice, organomegaly and lymphadenopathy. Section C (hematological data) recorded information on blood counts, plasmodium species and parasite level. Anemia was defined as a hemoglobin level less than 150 $\pm$ 20 g/L in males above 12 years of age, and below 135 $\pm$ 15 g/L in females. For children (below 12 years of age) it was defined as a hemoglobin level less than 135 $\pm$ 20 g/L.[10] The forms were completed by abstracting the relevant information from the medical records of the malaria cases diagnosed at KFHU, during the specified period. Data was entered using a d-Base program, and analyzed using SPSS version 7.5 software.[11] Statistical analysis included descriptive statistics, as well as analysis of variance (ANOVA). Tests of significance (t-test, Chi-square) were also used, as appropriate. The level of significance was set at < 0.05 throughout the study.

Results. ***Demographic profile. Age and sex distribution.*** A total of 602 patients fulfilled the criteria for diagnosis of malaria during the period of study. Their average age was 25.8 $\pm$ 14.3 years, with a wide range from just 2 months to 72 years of age. There were more males than females, giving a sex ratio of 2.9:1 (Table 1).

Nationalities. Less than half the patients were Saudis (42%), while 58% were non-Saudis. The non-Saudi patients included many different nationalities, as observed in Table 1.

Types of plasmodium species. *Plasmodium falciparum* (*P.falciparum*) was observed in more than half of the cases, followed by *Plasmodium vivax* (*P.vivax*). Both types were seen in 2% of cases, while in 5% of cases the type was not identified. In these cases only rare occasional ring forms were seen (Table 1). Table 2 shows the distribution of the type of malaria in relation to nationality. Among the Saudi, Yemeni and Sudanese patients, *P.falciparum* was the predominant species, while among Indians and Pakistanis, *P.vivax* was predominant. Mixed infections ranged from 1-9% among the different nationalities. The nationality of most of the patients was the same as that from which the malaria was acquired.

Yearly and monthly distribution. The frequency of cases varied with the years, but a lot more cases were seen in 1992, 1994, 1998, than in other years (Table 3). The monthly distribution showed that most of the cases were seen in February, March, and September (Table 4). A comparison was made between the frequency of cases seen at KFHU and the malaria cases reported by the Ministry of Health

Table 1 - Distribution of cases by demographic variables, malaria type and travel history.*

Variable	Number	Percentage
Age		
<10	124	21.0
10 - 19	50	8.5
19 - 20	170	29.0
20 - 29	150	25.0
30 - 39	65	11.0
40 - 49	23	4.0
50 - 59	8	1.0
Sex		
Male	449	74.5
Female	153	25.0
Nationality		
Saudi	253	42.0
Indian	120	20.0
Pakistani	63	10.5
Sudanese	83	14.0
Sri Lankan	24	4.0
Yeminese	22	4.0
Others	37	6.0
Type of Malaria		
P.falciparum	327	54.0
P.vivax	233	39.0
Both	14	2.0
Unknown	28	5.0

*Some of the figures will not add up to the total sample, due to missing values.

Table 2 - Distribution of cases by Plasmodium species for Nationalities, King Fahd Hospital of the University, 1990-1999.

Nationality	Type of malaria									p-value
	P. Falciparum		*P. Vivax*		Both		Unknown		Total	
	No.	%	No.	%	No.	%	No.	%	No.	
Saudi	210	83	23	9	3	1.0	17	7.0	253	0.0001
Pakistani	12	19	46	73	2	3.0	3	5.0	63	0.0001
Sudanese	59	72	19	23	-	-	4	5.0	82	0.0001
Indian	13	11	98	82	7	6.0	2	2.0	120	0.0001
Yemenese	14	64	6	27	2	9.0	-	-	22	<0.0001

No - Number

Table 3 - Yearly distribution of malaria cases, King Fahd Hospital of the University, 1990 - 1999.

Year	Number of malaria cases	Percentage
1990	55	9.0
1991	53	9.0
1992	85	14.0
1993	54	9.0
1994	70	12.0
1995	59	10.0
1996	61	10.0
1997	45	7.5
1998	86	14.0
1999	32	5.0

Table 4 - Monthly distribution of malaria cases, King Fahd Hospital of the University, 1990 - 1999.

Month	Number of cases	Percentage
January	54	9.0
February	88	15.0
March	69	11.5
April	41	7.0
May	33	5.5
June	43	7.0
July	46	8.0
August	42	7.0
September	77	13.0
October	43	7.0
November	26	4.0
December	40	7.0

Table 5 - Comparison of the percentage of cases at King Fahd Hospital of the University and Ministry of Health Malaria Center of the Eastern Province, 1990-1999.

Year	KFHU	MOH Malaria Center
1990	9.0	6.0
1991	9.0	8.0
1992	14.0	12.0
1993	9.0	12.0
1994	12.0	13.0
1995	10.0	12.0
1996	10.0	11.0
1997	7.5	10.0
1998	14.0	10.0
1999	5.0	6.0

KFHU - King Fahd Hospital of the University; MOH - Ministry of Health

Table 6 - Distribution of cases by Plasmodium species and travel history.*

Travel History	Type of malaria									
	P. Falciparum		*P. Vivax*		Both		Unknown		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Yes	274	61	150	33	14	3.0	10	2.0	448	77
No	44	34	72	55	11	8.0	4	3.0	131	23
	318	55	222	38	25	4.0	14	2.0	579	

No - Number; p-value <0.0001; *Unknown travel history and missing cases were removed.

(MOH) Malaria Center for the Eastern Province of Saudi Arabia (Table 5). The results are almost comparable. Both data-sets reflect increased occurrence during the years 1992 and 1994. The peak observed at KFHU during 1998 is not reflected in the MOH data. However, both data-sets showed a decrease in 1999. With respect to reported travel history, 75% of the studied cases had a positive travel history, 22% had no history of travel, while in another 3.5%, history of travel was not available. Table 6 shows the distribution of cases by Plasmodium species and travel history. According to family and past history of malaria, 23% of all cases reported a personal previous history of malaria, while 7% of all cases had a positive family history.

Clinical profile. The most common clinical presentation among cases was fever (97%). Table 7 summarizes the fever pattern observed in these patients. Typical paroxysms of fever were seldom seen. The p-value was 0.29, indicating lack of correlation of fever pattern and Plasmodium species (insignificant). The most common elicited clinical signs were splenomegaly (9%) and jaundice (8%). Hepatomegaly was less common (6%), while lymphadenopathy was very rare (0.2%). The majority of patients (87%) were treated with chloroquine as outpatients in the emergency room, while 5% were hospitalized on account of different complications.

Table 7 - Distribution of cases by Plasmodium species and fever pattern, King Fahd Hospital of the University, 1990 - 1999.**

Fever pattern	*P. Falciparum*		*P. Vivax*	
	No.	%	No.	%
Every day	218	73	144	66
Every other day	37	12	33	15
Every 3 days	27	9	29	13
Every 4 days	18	6	13	6

** Percentages from the total column
p-value = 0.29; No. = number

Selected hematological profile. The most common hematological findings were normocytic normochromic anemia (60%) and thrombocytopenia (53%). The level of parasitemia was not always available, but in the 80 cases (13%) where it was reported, the range was between 0.2% to 5%.

Discussion. This study has shown that population travel has maintained a considerable level of reported cases in malaria-free areas, including the Eastern Province of Saudi Arabia. Although malaria has been largely controlled in the Province, transmission and endemicity still occurs in the Southwestern part of the country. Malaria cases were diagnosed throughout the year during the study period, with the years 1992, 1994 and 1998 showing the highest frequency of reporting. A great majority of cases (77%) may be attributed to increased travel, especially for the year 1992, after the Gulf war. Another possible explanation of fluctuation may be due to different levels of reporting during the study period (over-reporting; under-reporting). However, this possibility was not investigated in this work. The peaks during the months of February and March may also have been due to increased travel, as these months sometimes coincide with Eid vacations during the study period, while the peak during September would be expected as everyone returns from vacation, for school and work. These results are especially interesting as such months of increased peaks, fall within the same periods reported from studies in endemic areas i.e. October-April[7] (in this study, the present status, epidemiology and control of malaria was discussed) December-May,[5] (where a 5 year prospective study was carried out to determine the pattern of malaria in children in a tertiary health care institution in the Asir region 1988-1993), February and June,[12] (which was a 5 year; 1991-1995, retrospective study of all malaria cases seen in Asir Central Hospital, Abha) and December-April[13] (a review of 242 malaria patients seen in 2 hospitals in Jeddah in 1985). The average age of 25.8 ± 14 years in this study was higher than that reported by a previous study[12] in the Asir region, where the average age was 15.9 ± 17.2. Since the latter study was

carried out in an endemic area, its findings reflect the fact that the disease is more common among children, and young adults who are non-immune. There was also a predominance of *P.falciparum*, especially among Saudi patients, while *P.vivax* was more commonly found among non-Saudi cases, especially those from the Indian Subcontinent. These results also agree with observations of previous studies.[7,13,14] Males were affected more than females, but this is probably due to the movement of large numbers of male expatriates to work in the Kingdom from endemic areas, and also due to their outdoor work. Another possibility in relation to increased male cases from the Southwestern region, is that since women are traditionally veiled, and wear clothes which cover the entire body, they are protected from mosquito bites. This sex pattern has also been described in other studies in the Kingdom.[12,13] More than 3 fourths of the cases (75%) reported a history of travel to an endemic area, lasting days to weeks before the symptoms, which stresses the importance of travel history in patients with fever. It should be emphasized that in 3.5% of the patients, information concerning travel was not available, while in 22% there was no history of travel. It must be noted that it may be difficult to confirm such information in a retrospective study like this, which depends on abstraction of already collected data. It is noteworthy, however, that in cases with no history of travel the predominant type of malaria was *P.vivax* (55%), and most were non-Saudi. The interpretation of this finding after reviewing many of the files, could be that many of these cases had recently arrived in the Kingdom, and had been here for periods ranging between a few months to 18 months only. The symptoms may have been due to *P.vivax* malaria relapse, most likely the temperate strain of *P.vivax*, which is most frequently imported from North India, and could have an incubation period of 9-12 months.[15] Patients may also have misinterpreted the question on travel to assume that it had to be outside of the Kingdom. Other studies have also shown correlation with travel history.[14] In this study also,[14] many patients were already resident in Kuwait for a variable period before clinical presentation, and were diagnosed with *P.vivax* malaria. Almost all Saudi cases (93%) had visited the endemic Southwestern part of the Kingdom, while others visited other endemic countries such as parts of India, Turkey, and Afghanistan. Although there is strong evidence that transmission in the Eastern Province has been interrupted since 1978, this cannot be confirmed from the results of the study as a good percentage of the cases had no history of travel as recorded in their files. Imported cases, however, represent a continuous threat due to the existence of such vectors as *Anopheles stephensi* (*A.stephensi*), *Anopheles sergentii* (*A.sergentii*), *Anopheles fluviatilis* (*A.fluviatilis*) and *Anopheles superpictus* (*A.superpictus*) and a large number of non-immune persons.[7] Approximately one quarter of the cases (23%) had a previous personal history of malaria, within the same year or in the past, stressing the need for adequate treatment. The family history of malaria was positive in a minority of cases (7%), either parents or siblings having been affected. This was mostly observed among Sudanese and Saudi cases. Again, stressing the importance of travel history in patients presenting with fever.

The clinical presentation of our case is similar to that described in other studies from the Kingdom, with fever >38ºC being the most common clinical presentation. Fever was associated with chills in 91% of the patients, rigors in 20%, vomiting in 8%, diarrhea in 4%, headache in 5%, and photophobia in 2% of the patients. It would seem that the fever pattern may not have been well described by the patients, and the pattern observed in the case files, was different from that described in classical textbooks of medicine or parasitology i.e. typical paroxysms of fever were seldom seen, and periodic fever was distinctly uncommon. One possible explanation is that these cases may not be representative of all cases of malaria. The classical cases are more likely to have been seen and treated in primary health care centers and specialized fever hospitals. The study also confirmed the usual irregular fever pattern described in *P.falciparum*. The most common elicited physical signs were: splenomegaly (9%) and jaundice (8%). In comparison to 2 other similar studies, Malik et al's[12] study in Asir region reported tachycardia (76%), hypotension (41%), splenomegaly (45%) and hepatomegaly (35%), as the most common clinical findings. While, Banzal et al's[6] study of severe malaria in Gizan reported pallor (39%), splenomegaly (26%) and jaundice (23.5%) as the most common clinical findings. There was only one fatality (attributed to spontaneous splenic rupture), which reflects a very low mortality rate during the study period, which maybe attributed to the high level of health care services provided by KFHU. In addition one case of *P.falciparum* malaria presented as acute renal failure, and another presented with features suggestive of cerebral malaria. Those were the only recorded major complications among the cases in our series. Other complications (requiring admission), which occurred in 40 patients (7%) included thrombocytopenia (less than 50 x 10^9/L), anemia requiring blood transfusion, and persistent fever. Of the hematological findings, anemia and thrombocytopenia were the most common complications. A low platelet count is usually seen in approximately 85% of patients with uncomplicated malaria, as well as all patients with severe falciparum malaria.[16] This is also considered a classical feature, the cause of which is multifactorial.[16,17] In contrast to

leucopenia being reported as a common finding in malaria, most of the patients in our study had a total white blood cell count within the normal range. The anemia was normocytic normochromic in a majority of the cases however microcytic hypochromic anemia was also seen, in 80 patients (22%), especially in children. In the latter cases, there was documented concurrent iron deficiency and hemoglobinopathy, or both, which maybe contributing factors. The majority of patients (87%) were treated with chloroquine, except in those who had features of complications, i.e. persistent fever, or in patients coming from countries with known chloroquine resistance, where treatment with alternative drugs like quinine, sulfadoxine/pyrimethamine, doxycycline or mefloquine were administered. There have been reports from the Kingdom of possible chloroquine resistance.[18-20] In a retrospective study of this type, it would be difficult to evaluate the frequency of chloroquine resistance among these patients, and to correlate the clinical findings with parasite counts. However, approximately 14 Saudi patients from the south of the Kingdom, out of 75 Saudi patients, (19%) noticed during 1998 and 1999 did not improve clinically until a drug other than chloroquine was used. Reports of such resistance need to be substantiated by well-designed prospective studies.

In conclusion, malaria is still diagnosed in the Eastern Province, mostly due to imported cases from endemic areas. *Plasmodium falciparum* was diagnosed more than *P.vivax*. In Saudi, Sudanese and Yemeni patients the predominant species was *P.falciparum*, while among Indian and Pakistani patients, *P.vivax* was the predominant species. From the results of this study, certain recommendations to the public and to health professionals are suggested. Keeping malaria in the differential diagnosis of all acute fevers is necessary. Malaria should always be suspected in any febrile patient who has traveled to an endemic area, or received a blood transfusion. There could even be other less common routes of infection, requiring prompt diagnosis and treatment. Chemoprophylaxis which tends to be ignored and neglected by some health professionals needs not be emphasized, and from the results of this study it was clear that many patients have traveled to endemic areas. So, there should be adequate health education for patients living in and travelling to endemic areas. In addition, there should be awareness of the possibility of chloroquine resistance in patients who fail to improve clinically, on chloroquine, and correlate this with levels of parasitemia. Alternative drugs may be used in such cases.

Acknowledgment. The authors would like to thank Dr. E. Larbi for his valuable comments.

References

1. World Health Organization. World Health Director General's Report. Fighting disease, fostering development. Geneva: WHO; 1996.
2. World Health Organization. Control of Tropical Diseases (CTD): Malaria Control. Geneva, Switzerland: WHO Office of Information; 1995.
3. Murray CJL. Quantifying the burden of disease: the technical basis for disability-adjusted life years. Bull World Health Organ 1994; 72: 429-445.
4. Murray CJL, Lopez AD, Jamison DT. The global burden of disease in 1990: Summary results, sensitivity analysis and future directions. Bull World Health Organ 1994; 72: 495-509.
5. Annobil SH, Okeahialam TC, Jamjoom GA, Bassuni WA. Malaria in children: Experience from Asir Region, Saudi Arabia. Annals of Saudi Medicine 1994; 14: 467-470.
6. Banzal S, Ayoola EA, El-Sammani EE. The Clinical Pattern and Complications of Severe Malaria in the Gizan Region of Saudi Arabia. Annals of Saudi Medicine 1999; 19: 378-380.
7. Al-Seghayer SM, Kenawy MA, Ali OTE. Malaria in the Kingdom of Saudi Arabia epidemiology and control. Scientific Journal of King Faisal University 1999; [Febuary Special issue]: 6-20.
8. Sebai ZA. Malaria in Saudi Arabia. Trop Doct 1988; 18: 83-188.
9. Warrell DA. Leishmaniasis, malaria and schistosomiasis in Saudi Arabia. Saudi Med J 1993; 14: 203-208.
10. Dacie SJV, Lewis SM. Reference Ranges and Normal values. In: Practical Hematology. 8th ed. UK: Churchill Livingstone; 1994. p. 9-19.
11. Statistical Package for Social sciences – Personal Computers (SPSS-PC). Version 7.5 SPSS Co. (444 N. Michigan Avenue, Chicago, Illinois, U.S.A.) 1998.
12. Malik GM, Seidi O, El-Taher AM, Mohammed AS. Clinical aspects of malaria in the Asir Region, Saudi Arabia. Annals of Saudi Medicine 1998; 18: 15-17.
13. Vassallo L, Khan MA, Edeson JFB. Epidemiological aspects of clinical implications of malaria as seen in Jeddah, Saudi Arabia. Ann Trop Med Parasitol 1985; 79: 349-355.
14. Hira PR, Al-Ali F, Soriano EB, Behbehani K. Aspects of imported malaria at a District General Hospital in Non-Endemic Kuwait, Arabian Gulf. Eur J Epidemiol 1988; 4: 200-205.
15. Kain KC, Keystone JS. Malaria in travelers: Epidemiology, disease and prevention. Infect Dis Clin North Am 1998; 12: 267-283.
16. Facer CA. Hematological aspects of malaria. In: Infection and Hematology. Oxford: Butterworth Heinemann Ltd; 1994. p. 259-294.
17. Essien EM. Medical Hypothesis. The circulating platelet in acute malaria infection. Br J Haematol 1989; 72: 589-590.
18. Al-Rajhi A, Frayha HH. Chloroquine-resistant Plasmodium falciparum: Is it our turn? Annals of Saudi Medicine 1997; 17: 151-153.
19. Manohar S, Baker A, Pawar AR, Oridota T. Chloroquine-resistant Plasmodium falciparum malaria in a pregnant women. Annals of Saudi Medicine 1997; 17: 247-249.
20. Malik GM, Khan AM, Abdalla SEA. No response to chloroquine therapy in a case of a Saudi falciparum malaria. Saudi Med J 1997; 18: 99-100.