ORIGINAL RESEARCH

MALARIA ASSOCIATED FACTORS IN THAR DESERT OF RAJASTHAN, INDIA: A CASE-CONTROL STUDY

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ABSTRACT

Objective: In 2007 the Rajasthan state of India reported 55,000 malaria cases and 46 deaths caused by malaria. District Jodhpur is the gateway to the Thar Desert in Western Rajasthan. Here malaria is endemic. Between 2002 and 2006 the slide positivity rate ranged between 0.56% and 2.29 % in Jodhpur. The present study aimed to identify factors associated with malaria in Jodhpur. Methods: An age and gender matched 1:2 case-control study was conducted at three primary health centres in the block Banar of Jodhpur. We recruited prospectively 42 microscopically confirmed cases of malaria and 84 non-fever patients as controls. Information was collected by means of a pre-tested questionnaire after consent was given by the participant. Univariate and multivariate analyses were performed. Results were presented as odds-ratios (OR) and 95% confidence intervals (95% CI). Results: Multivariate conditional logistic regression analysis revealed that cases were 4.9 times more likely compared to controls to report a history of travel within previous month (95% CI 1.3, 17.9; p=0.017), were 11.8 times more likely than controls to report a history of malaria in a family member during the previous month (95% CI 1.1, 124.4; p= 0.041) and were 4.9 times more likely to report the plant *Prosopis juliflora* within 1 km radius of home (95% CI 1.0, 24.0; p=0.0496). Conclusions: Households with a history of frequent travelling and malaria in family, and monitoring *Prosopis juliflora* should be given priority during routine screening and treatment under the National Malaria Programme.

KEY WORDS: Desert; Family history of malaria; Jodhpur; Travel history; *Prosopis juliflora*; India.

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INTRODUCTION

World Malaria Report 2008 estimated about 247 million cases of malaria and one million deaths due to malaria world wide for 2006 (World Malaria Report, 2008). This report indicated the persistence of malaria in 109 countries of the world. Estimated figures for cases and deaths due to malaria were 21 million and 35,000, respectively, for South East Asia in 2006 (World Malaria Report, 2008). Malaria is endemic in various states of India. The National Vector Borne Disease Control Programme of India reported 1.47 million cases and 1,173 deaths in the country for the year 2007 (NVBDCP India, 2008). In 2007 in the state of Rajasthan the reported number of malaria cases was 55,000 with 46 deaths (NVBDCP India, 2008). District Jodhpur is the gateway to the Thar Desert of India. Malaria is persisting here. Between 2002 and 2006 the slide positivity rate ranged between 0.56% and 2.29% in Jodhpur (pers. comm. Chief Medical and Health Office, Jodhpur).

Malaria is known to be an exclusively local phenomenon. Transmission, prevalence and distribution of parasite species are determined by local conditions (Sharma, 1986). Transmission of malaria may differ even from one village to the next (Yazoumé, 2007). Previous studies identified the following "local" risk factors for malaria transmission: introduction of cases from other areas (Joshi, 2006), travel history (Osorio, 2004; Moore, 2004; CDC, 2003), poor knowledge, sleeping on the floor, history of malaria in family (Rogelio, 2007), male forest workers, children in forest fringe villages, distance to nearest health facility (Sandra, 2007), forest activities (Ngo, 2008), vegetation index, number of cases during previous month (Alberto, 2007), rainfall (Olivier, 2008; David, 2005), agriculture land (Shilpa, 2004), proximity to river distributaries (MJAM, 2006), live stock (Matthew, 2008), type of house (Yazoume, 2006) and socio-economic conditions (Srivastava, 2007).

Prosopis juliflora (*P. juliflora*), which is known as "Mesquite" in English and "Vilaythi Babul" in the Hindi language, is a thorny, large crowned, evergreen to semi-evergreen tree. It is native to South-Western America. The ruler of the state of "Marwar" (ancient name of Jodhpur) introduced *P. juliflora* to Jodhpur in 1913 to green the vegetation scarce area. Later on, it proved to be the most versatile plant for forestation of the shifting sand dunes and wastelands, where rainfall is scanty and erratic. The plant grows well in regions of 150 to 600 mm rainfall and is draught resistant. Flowering is generally from August to October. Flowers produce nectar for good quality honey (Muthana, 1983). Incidence of malaria with the *P. juliflora* plant thickets was found to be the most frequently mentioned problem, in an observational case study in Kenya (Esther, 2005).

The state of Rajasthan has witnessed a manifold increase in growth of forest plantations, from 50,000 hectares

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during the 1960s to more than 450,000 hectares in the 1990s. Monoculture of certain species, *P. juliflora* is one among them, has dominated the plantation programme. Such monocultures are expected to put ecological stress on deserts like the Thar (State of environment report, Rajasthan, 2007).

The present study was planned to identify personal, family, household and environmental risk factors, including *P. juliflora,* for malaria in the desert environment of Jodhpur, Rajasthan, India. The identification of specific local risk factors can play an important role in improving the control of malaria in this particular setting.

METHODS

Study site

District Jodhpur stretches between $26^0 0'$ and $27^0 37'$ north latitude and between $72^0 55'$ and $73^0 52'$ east longitude. It is situated between 250 to 300 meters above sea level. The district is an arid zone of the Rajasthan state of India. Its ambient temperature varies from 1^0 C in winter to 49^0 C in summer. Average annual rainfall is 302 mm. There is no perennial river in the district (Administrative setup Jodhpur, 2010).

The present study was conducted in the sub district (block) Banar, which was selected by simple random sampling from nine sub districts which make up Jodhpur (Figure 1). We randomly chose three Primary Health Centres (PHCs) namely Banar, Bisalpur and Fidusar as data collection sites out of six PHCs in the block to adequately represent the study area. Our target population was the general population residing in Banar, Jodhpur, Rajasthan, India.

Study design

A matched case-control study was conducted in collaboration with the state department for health between May and October 2008. We recruited malaria cases, confirmed through microscopic examination of peripheral blood smear for malaria parasite. Controls were non-fever cases attending the same PHC from where the cases were recruited. In India, each PHC caters for a cluster of villages, providing curative and preventive services. Hence, essentially the cases and controls were recruited from the same neighbourhood – either the same village or the neighbouring village.

Sample size

Sample size was estimated in Statcalc of the Epiinfo software (version 3.3.2) assuming values for the level of significance of 5%, statistical power 80%, a control to case ratio of 3:1, and an expected exposure amongst controls of 50%, and OR to be 3 or higher, and 10% non-responders. The final estimated sample size was 48 cases and 145 controls. However due to less availability of matched controls and time constraints, we could only recruit 42 cases and 84 matched controls.

Sampling procedure

Consecutive cases attending the PHCs were enrolled into the study. Matched controls were selected for each case based on their similarity with respect to gender and age (± 5 years of age of case).

Data collection procedure

Trained public health workers interviewed the cases and controls and collected the data by administering a pretested questionnaire written in the local language "Marwari". Data collection took approximately ten minutes each. The local calendar of events was used in ensuring the referent time of exposure. Local landmarks were used to ensure a reference of distance to potential exposures such as a pond or to *P. juliflora* plants.

Ethical clearance

The study protocol was approved by the institutional Ethics Committee of the National Institute of Epidemiology, Chennai. Informed and written consent was granted by all participants. Cases were given treatment as per guidelines of the National Anti Malaria Programme. Controls were treated for their illnesses as per advice of their physicians.

Data analysis

Two controls were matched with respect to gender and age for each case. Therefore analysis was done on 42 sets of two controls and one case. Univariate and multivariate conditional logistic regression analysis were performed using Epiinfo software (version 3.3.2). Odds ratios (OR) adjusted using the Mantel Haenszel procedure were estimated and used as a measure of association between potential risk factors and malaria. Factors with p-values less than 0.2 in univariate analysis, were considered in the multivariate analysis. Conditional logistic regression modelling by step down technique was utilised (Ngo, 2008). The multivariate analysis showed the individual strength of association of factors with malaria, by simultaneously controlling for other fitted variables. Two tailed probability values less then 0.05 were considered as statistically significant.

RESULTS

Malaria cases and controls were recruited from the month of May to October 2008. Out of the 6 months period, 27 cases were recruited in August and September, usually months of the rainy season (Figure 2). The response rate was 100%. Fidusar PHC recruited 27 cases, whereas these figures for Banar and Bisalpur PHCs were 5 and 10 respectively (Figure 1).

All cases of malaria were due to *Plasmodium vivax* species. A majority of cases was male (71.4%) and another 71.4% of cases occurred in the 15 to 44 years age category (Table 1). There were only marginal demographic and socio-economic differences between cases and controls (Table 1).

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Figure 1: Selection of study area and malaria cases in selected primary health centres of sub district Banar, district Jodhpur, Rajasthan, India, 2008.

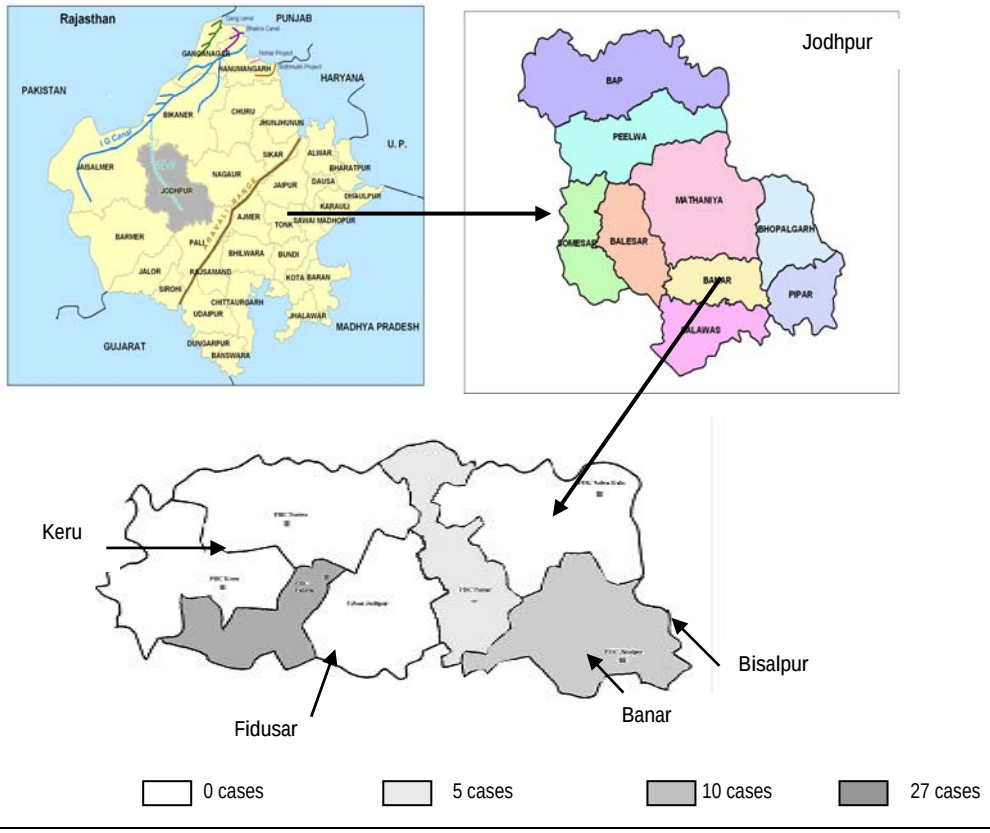

Figure 2: Monthly distribution of malaria cases in sub district Banar district Jodhpur, Rajasthan during study period May to October 2008.

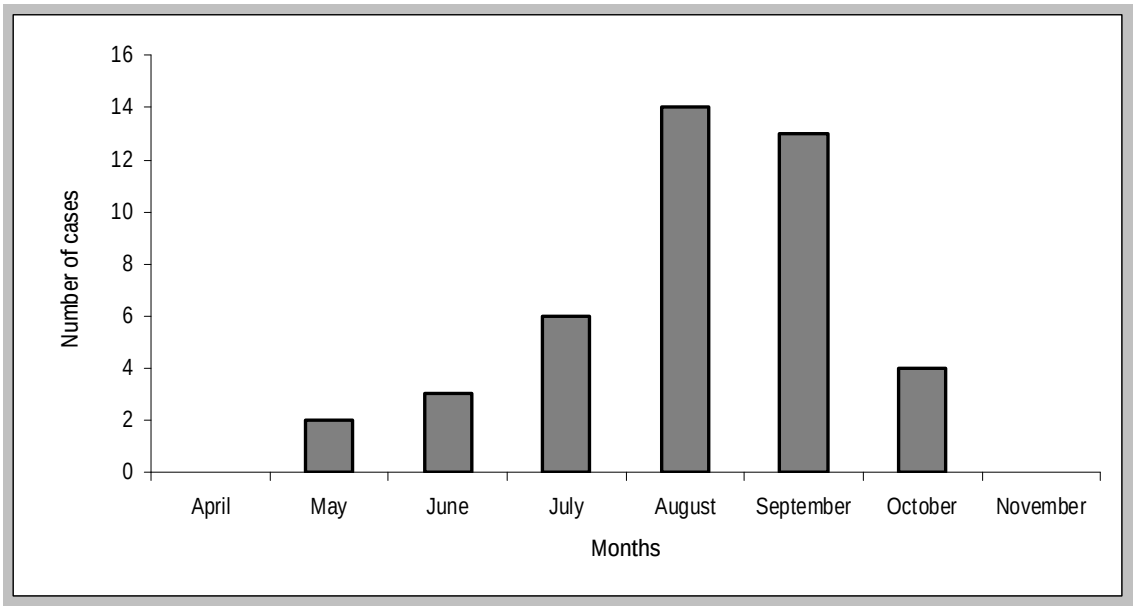

Table 1: General characteristic of malaria cases in block Banar, district Jodhpur, Rajasthan, India, 2008.

Characteristics		Cases (n=42)		Controls (n=84)	
		Number	Percentage	Number	Percentage
Age	< 5 years	2	4.8	3	3.5
	5-14 years	7	16.7	14	16.6
	15-44 years	30	71.4	61	72.6
	45 years and older	3	7.1	6	7.1
Gender	Male	30	71.4	60	71.4
	Female	12	28.6	24	28.5
Residence	Urban	19	45.2	33	39.3
	Rural	23	54.8	51	60.7
Occupation	Non earning	13	31.0	26	30.9
	Manual labour	21	50.0	43	51.1
	Sedentary occupation	8	19.0	15	17.8
Education	Illiterate	15	35.7	27	32.14
	Primary educated	18	42.9	36	42.85
	Secondary and above	9	21.4	21	25.0
Monthly financial income	Up to 1000 INR	18	42.9	44	52.4
	> 1000 INR	24	57.1	40	47.6
Religion	Hindu	36	85.7	82	97.6
	Muslim	6	14.3	2	2.4

Table 2: Association of selected exposures with malaria in univariate analysis in block Banar, district Jodhpur, Rajasthan, India, 2008.

Exposure factor	Discordant pairs Case exposed	Discordant pairs Case unexposed	OR*	95% CI**	p-value***
Illiteracy	15	12	1.25	0.49-3.1	0.81
Rural residence	8	13	0.61	0.20-1.8	0.26
Income less than 1000 INR	6	14	0.42	0.13-1.3	0.08
Labour occupation	14	15	0.93	0.38-2.2	0.70
Do not read newspaper	24	13	1.84	0.80-4.2	0.19
Do not view television	28	17	1.64	0.79-3.4	0.23
Unaware about malaria transmission	4	9	0.44	0.09-1.9	0.12
Unaware about malaria prevention	10	8	1.25	0.40-3.8	0.92
Do not use mosquito spray	17	12	1.41	0.57-3.4	0.60
History of recent travel	18	5	3.6	1.17-11	0.04
History of malaria in family	9	1	9	0.98-82	0.06
Mine work	6	6	1	0.25-3.9	0.74
Mud room house	28	18	1.55	0.76-3.1	0.30
Pets at home	20	14	1.42	0.62-3.2	0.53
Pond near home	21	10	2.1	0.84-5.2	0.17
Prosopis juliflora plant near home	13	3	4.33	0.83-22	0.12

*OR = odds-ratio adjusted according to Mantel-Haenszel; **95%CI = 95% confidence interval; ***Corrected chi-square p-value.

More than half of the cases resided in the rural area (54.8%) of the sub district. The majority (85.7%) of cases were of Hindu religion (Table 1). Univariate analysis showed that cases were 3.6 times more likely than controls to report a history of travel within previous month (p=0.04)(Table 2). Cases were 9 times more likely than controls to have a history of malaria in the family during the previous month (p= 0.06) and were 4.3 more likely to report the plant *P. juliflora* within 1 km radius of home (p=0.12) (Table 2), however those results were univariately not significant.

Multivariate conditional logistic regression analysis revealed that cases were 4.9 times more likely compared to controls to report a history of travel within previous month (95% CI 1.3, 17.9; p=0.017), were 11.8 times more likely than controls to have a recent history of malaria in the family (95% CI 1.1, 124.4; p= 0.041) and were 4.9 times more likely to report the plant *P. juliflora* within 1 km radius of home (95% CI 1.0, 24.0; p=0.0496). No other factors reached significance within the multivariate analysis.

DISCUSSION

In Banar, district Jodhpur, Rajasthan, India, malaria is a disease of the rainy season (July to September) and additionally also of the summer months (May and June). Almost half of participating cases were recruited during the rainy season. The association between rain and malaria was previously reported (Alberto, 2007; Olivier, 2008; David, 2005).

In Banar, malaria affects almost all age groups. The large proportion of cases amongst the young and middle aged persons was consistent with the distribution of malaria in a low risk area (Ngo, 2008). Herd immunity might be relatively low in the area making all age groups susceptible to malaria. Malaria is the disease of the productive age group in Jodhpur. Cases came in almost equal parts from urban and rural areas.

The study found that cases were almost five times more likely to have travelled recently in comparison to controls. Hence infection might have occurred while away from home. History of travel was found previously to be associated with malaria (Osorio, 2004; Moore, 2004;

CDC, 2003; Rogelio, 2007). Rogelio and co-workers showed this association important in settings of low transmission (Rogelio, 2007). Desert residents returning from malaria endemic areas might introduce the infection into their harsh home environment. Joshi et al reported the introduction of malaria cases as the major cause for the seasonal occurrence of malaria in desert settings (Joshi et al., 2006). These findings were supported by our study.

The importance of recent family history of malaria is consistent with a study conducted by Rogelio and co-workers focussing on residual transmission in Oaxaca, Mexico (Rogelio, 2007). Rogelio et al. reported a six times higher risk of infection in those households, which had malaria cases in the previous year. In comparison, our study found an almost 12 times increased risk of malaria amongst those persons who reported a family history within the previous month. Family history indicates the circulation of malaria parasites at the household level. This focalised transmission of malaria at household level can explain the maintenance of malaria parasites at micro foci. These micro foci may act as a source of further spread of malaria in the wider community whenever favourable environmental conditions are met. This mechanism could explain the low transmission of malaria during the dry season in Jodhpur and its outbreak when other favourable factors are met, such as heavy rain, high mosquito density, or immigration of cases from other places.

Although Esther and Swallow had reported a link between *P. juliflora* thickets and malaria in their case study (Esther, 2005), this was based only on the perception of residents of their own study area. Our study estimated the risk of occurrence of malaria among those exposed to *P. juliflora* thickets in an analytical way. This association, which was only marginally significant, is important for the desert environment, which is in general deficient of shrubs. Although the odds of exposure to the plant within 1 kilometre radius from home was almost five times higher in cases compared to controls, the 95% confidence interval was very wide, due to the small sample size. It is plausible that this plant might be prolonging the survival of the malaria vector by raising the relative humidity in the vicinity of households in a desert setting which would be otherwise not favourable for malaria. Simultaneously flower nectar of the plants can provide an energy source for male and female anopheles mosquitoes (CDC-Anopheles, 2010); this can lead to increased chances of vector reproduction and increased risk of malaria in turn. However it is currently difficult to comment on the causality of malaria due to presence of *P. juliflora*. Our results may, however, provide a different line of thinking while conducting aetiologic studies in vegetation scarce and erratic rainfall areas with low intensity of disease transmission.

Although the present study identified risk factors associated with malaria in a desert setting of Jodhpur, Rajasthan, its results should be interpreted with caution. We anticipated information bias in our study at the planning stage. Therefore we used the WHO defined case definition for confirmed malaria (WHO, 1999) and operational definitions for controls to recruit malaria cases and non-malaria patients as controls. Since the study intended to collect information on exposure during the previous month, recall bias was anticipated as cases might have recalled events more precise than controls. Use of proper case definitions, recruitment of cases and controls at PHCs, and training of interviewer to collect retrospective information using the local calendar of events, should have minimized information and recall bias.

Travelling to the villages of the cases and recruiting healthy controls in a desert environment proofed to be a time intensive process. Hence, controls were selected from the PHCs and not from the general population. This is a limitation of the study as selection bias might have occurred. Age and gender, two well known confounders, were considered through the matching process at the planning stage of this study. Multivariate conditional logistic regression analysis was applied to control for confounding of characteristics while estimating the association of one factor with malaria. However, the small sample size restricted the usefulness of the multivariate analysis. The study did not reach the planned power of 80% due to less than expected availability of controls. Therefore some risk factors might have remained undetected.

Further, blood from control participants was not routinely examined to ensure the absence of the malaria parasite. Public health physicians do not advise for malaria microscopy, if a patient neither has fever nor reports a history of fever in the previous 15 days. This practice is as per national programme guidelines. Hence, there was the possibility for parasite carriers to be recruited as controls into the study. However, the proportion of asymptomatic parasitemia might have only minimally affected results because of the low transmission of malaria and the low herd immunity against it in Jodhpur.

Lastly, we did not ask the participants to report the presence of vegetation other than *P. juliflora* around households. Lack of this information might have affected the association between *P. juliflora* and malaria. However in the study setting *P. juliflora* dominated and other vegetation was scarce.

In conclusion, people who travel frequently, report a history of malaria in the family and who live close to the presence of *P. juliflora* showed an increased risk for malaria in the desert environment of Jodhpur, India. Routine screening as well as treatment under the National Malaria Programme should focus on frequent travellers and families with a history of malaria to reduce the burden. Further multidisciplinary research of malaria in this desert part of Rajasthan, India, is warranted including entomological, environmental, and epidemiological studies.

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