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Asian Pacific Journal of Tropical Disease

journal homepage: www.elsevier.com/locate/apjtd

Malaria research doi: 10.1016/S2222-1808(15)61058-1

Plasmodium vivax malaria among pregnant women in Eastern Sudan

Duria Abdulwhab Rayis[1], Mohamed Awad Ahmed[2], Elsir Mirghani Omer[2], Ishag Adam[1*]

[1]*Faculty of Medicine, University of Khartoum, P. O. Box 102, Khartoum, Sudan*

[2]*Department of Obstetrics and Gynecology, New Halfa Hospital, New Halfa, Sudan*

ARTICLE INFO

Article history:
Received 4 Apr 2016
Received in revised form 18 Apr, 2nd revised form 22 Apr 2016
Accepted 18 May 2016
Available online 13 Jun 2016

Keywords:
Plasmodium vivax
Plasmodium falciparum
Malaria
Pregnancy
Sudan

ABSTRACT

Objective: To determine the epidemiology of malaria [especially *Plasmodium vivax* (*P. vivax*)] among pregnant women in Eastern Sudan.
Methods: A cross sectional study was conducted in the antenatal care of New Halfa hospital, Eastern Sudan to investigate the prevalence, manifestations and determinants of malaria (especially *P. vivax*) among pregnant women.
Results: Out of 2 378 pregnant women, there were 48 (2.0%) and 36 (1.5%) *Plasmodium falciparum* (*P. falciparum*) and *P. vivax* infection, respectively. There was no significant difference in the age, parity, gestational age between women with malaria and healthy controls. The mean ± SD of the temperature was significantly higher in patients with *P. vivax* than in patient with *P. falciparum* malaria [(38.6 ± 0.7) ℃ *vs.* (38.1 ± 0.6) ℃, $P = 0.001$]. Patients with *P. vivax* malaria had slightly (not reach statistical significance) lower hemoglobin level compared with *P. falciparum* malaria and healthy controls. The geometric parasite count showed no significant difference between patients with *P. vivax* and *P. falciparum* malaria infections (12 189.9 *vs.* 9 755.1 trophozoite/μL, $P = 0.356$).
Conclusions: *P. vivax* malaria is an existing health problem in Eastern Sudan. Further research is also needed.

1. Introduction

There are over 125 million pregnant women at risk of malaria. The majority (40 million) of these are at risk of *Plasmodium vivax* (*P. vivax*) and 32 million are at risk of *Plasmodium falciparum* (*P. falciparum*), and 53 million are at risk of co-infection of both *P. vivax* and *P. falciparum*[1]. Pregnant women are at increased risk, density and multiplicity of *P. vivax* infections than the non-pregnant ones[2-6].

In malaria endemic areas (especially areas of low malaria transmission), both *P. falciparum* and *P. vivax* infections have adverse effects on placental development and fetal outcomes[7-9]. It has been reported that compared to non-infected pregnant women, *P. vivax*-infected pregnant women were at higher risk of anemia and have lower birth weights in babies[2,10,11].

In sub-Saharan Africa (including Sudan), where the vast majority of malaria infections are due to *P. falciparum*, the placental infections and the adverse pregnancy outcomes have been extensively studied including epidemiology, anemia and low birth weight[12-15].

In sub-Saharan Africa, the paradigm of the Duffy antigen dependence for *P. vivax* and the benign character formerly attributed to *P. vivax* infection were challenged by the increasing number of reports of *P. vivax* in the blood of Duffy-negative individuals and severe disease associated with *P. vivax* infection[16-19]. There are few published data (especially in Africa) on *P. vivax* infection during pregnancy and no published data on *P. vivax* infection during pregnancy in Sudan[20,21]. This study was conducted to determine the epidemiology of malaria (especially *P. vivax*) among pregnant women in Eastern Sudan.

2. Materials and methods

A cross sectional study was conducted in the antenatal care of New Halfa hospital in the Eastern Sudan during the post-rainy season (August-December 2014). The area of the study is

*Corresponding author: Ishag Adam, Faculty of Medicine, University of Khartoum, P. O. Box 102, Khartoum, Sudan.
Tel: +249912168988
Fax: +249183771211
E-mail: ishagadam@hotmail.com

The study protocol was performed according to the Helsinki declaration and approved by Research Board at the Department of Obstetrics and Gynecology, Faculty of Medicine, University of Khartoum, Sudan. Informed written consent was obtained from Ministry of Health, Kassala, Sudan.

The journal implements double-blind peer review practiced by specially invited international editorial board members.

characterized by unstable malaria transmission. *P. falciparum* was the main species encountered in the area[22]. However, in the last few years, *P. vivax* infections were reported and even severe cases of *P. vivax* were observed[19]. After signing an informed consent from both the cases of malaria and healthy controls, obstetrics and medical (age, parity, gestational age) history were gathered using questionnaire. The women's weight and axillary temperature were recorded. The data of pregnant women who had malaria infection (*P. vivax*/*P. falciparum*) and healthy controls women were recorded.

The hemoglobin was measured. Women with malaria were treated with artesunate sulfadoxine-pyrimethamine which is the first line treatment for malaria in Sudan[23].

2.1. Blood smears for malaria and light microscopy

The blood smears were prepared as described in the previous work[13]. In summary, thick and thin blood films were prepared and stained with 10% Giemsa and examined under the 100 oil-immersion objective lens of a light microscope. The asexual parasites density was counted per 200 leukocytes assuming a leukocyte count of 8 000 leukocytes/μL (for thick films) or per 1 000 red blood cells (for thin films). Blood films were considered negative if no parasites were detected in 100 oil-immersion fields of a thick blood film.

2.2. Statistics

The data were entered into computer using SPSS for Windows. The mean ± SD of the medical and obstetrical variables (age, parity, gestational age, weight, hemoglobin) was compared between the women in the three groups (*P. vivax*, *P. falciparum* and healthy controls) using One-way ANOVA with *Post-hoc* Bonferroni analyses. The parasite count was compared between women with *P. vivax* and *P. falciparum* malaria by non-parametric test.

2.3. Ethics

The study protocol was performed according to the Helsinki declaration and approved by Research Board at the Department of Obstetrics and Gynecology, Faculty of Medicine, University of Khartoum, Sudan. Informed written consent was obtained from Ministry of Health, Kassala, Sudan.

3. Results

A total of 2 378 women attended the antenatal clinic during the study period. Out of these, there were 48 (2.0%) and 36 (1.5%) *P. falciparum* and *P. vivax* infection, respectively (ratio = 1.3:1.0). There was no *P. falciparum* and *P. vivax* co-infection. There was no significant difference in the age, parity, gestational age between women with malaria and healthy controls (Table 1).

Table 1

The pregnant women with *P. vivax* and *P. falciparum*, and healthy controls at Eastern Sudan.

Variables	*P. vivax* (n = 36)	*P. falciparum* (n = 48)	Healthy controls (n = 36)	*P*
Age (years)	29.4 ± 6.0	27.2 ± 6.3	29.2 ± 5.1	0.161
Parity	2.8 ± 2.2	2.3 ± 2.7	2.2 ± 2.2	0.570
Gestational age (weeks)	24.7 ± 5.7	23.2 ± 5.6	24.1 ± 5.2	0.532
Weight (kg)	59.1 ± 6.4	61.6 ± 6.5	60.1 ± 5.3	0.001
Temperature (°C)	38.6 ± 0.7	38.1 ± 0.6	37.2 ± 0.3	< 0.001
Hemoglobin	9.4 ± 1.1	9.9 ± 1.2	10.0 ± 1.1	0.084

All values were expressed as mean ± SD. -: Absent.

The mean ± SD of the temperature was significantly higher in patients with *P. vivax* compared with patients with *P. falciparum* malaria [(38.6 ± 0.7) °C *vs.* (38.1 ± 0.6) °C, P = 0.001].

Patients with *P. vivax* malaria had slightly (not reach statistical significance) lower hemoglobin level compared with *P. falciparum* malaria and healthy controls (Table 1).

There was no significant difference in the geometric parasite count between patients with *P. vivax* and *P. falciparum* malaria infections (12 189.9 *vs.* 9 755.1 trophozoite/μL, P = 0.356) (Figure1).

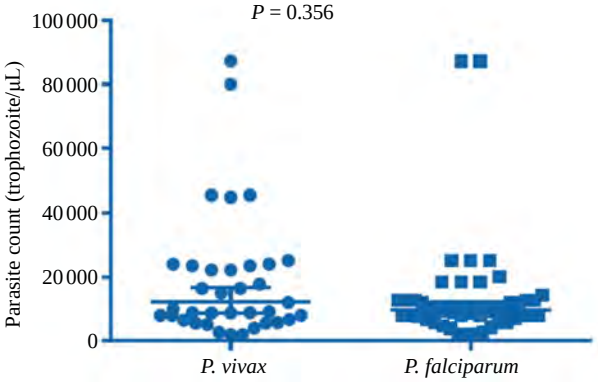

Figure 1. The geometric mean of the parasite count in *P. vivax* and *P. falciparum* malaria among pregnant women in Eastern Sudan.

4. Discussion

This is the first report of *P. vivax* malaria infections among pregnant women in Sudan. The previous reports have shown that *P. falciparum* was the sole species among pregnant women in the Eastern and Central Sudan[13,15,24]. It has recently been shown that *P. vivax* malaria is an existing health problem and even severe cases of *P. vivax* were observed among both children and adults in Eastern Sudan[18,19]. The influx of the Ethiopians through the border after signing the peace agreement was the explanation mentioned by some researchers[18]. There are generally few reports of *P. vivax* infections among pregnant women in Africa and *P. vivax* was considered rare before[20,21].

In the current study, there was no significant difference in the mean age and parity between pregnant women with *P. falciparum* and *P. vivax* infections, and healthy controls women. This goes with the previous reports where it has been shown that pregnant women in Eastern and Central Sudan were susceptible to *P. falciparum* infections regardless to their age and parity, and the low transmission of the malaria infections in the area was the main explanation. On the other hand, primigravidae were observed to have an increased risk of *P. falciparum* and *P. vivax* compared to multigravidae[25].

Interestingly, in this study, women with *P. vivax* malaria had significantly higher temperature than women with *P. falciparum* malaria. This goes with previous studies that showed that *P. vivax* had a lower pyrogenic threshold and cytokines released compared to *P. falciparum*[26-28]. Fever as well as the other clinical consequences of *Plasmodium* infection are manifest during the blood-stage of infection and are worsened by high densities of the parasitemia. The lower pyrogenic threshold and densities of the parasitemia could be explained by the ability of *P. falciparum* to invade all erythrocytes, whereas *P. vivax* selectively infests young erythrocytes (reticulocytes), and thus *P. vivax* could have a lower parasitemia than *P. falciparum*[29,30].

4.1. Limitations of the present study

The study was small size and might lack the power to estimate the difference between the *P. vivax* and *P. falciparum* malaria. Only

blood smears were performed to diagnose parasitaemia and PCR was not performed and women were not followed-up to further investigate the placentas and the pregnancy outcome.

Conflict of interest statement

We declare that we have no conflict of interest.

References

[1] Dellicour S, Tatem AJ, Guerra CA, Snow RW, ter Kuile FO. Quantifying the number of pregnancies at risk of malaria in 2007: a demographic study. *PLoS Med* 2010; **7**(1): e1000221.

[2] Krishna S, Bharti PK, Chandel HS, Ahmad A, Kumar R, Singh PP, et al. Detection of mixed infections with *Plasmodium* spp. by PCR, India, 2014. *Emerg Infect Dis* 2015; **21**(10): 1853-7.

[3] Singh N, Bharti PK, Singh MP, Singh R, Yeboah-Antwi K, Desai M, et al. What is the burden of submicroscopic malaria in pregnancy in central India? *Pathog Glob Health* 2015; **109**(1): 30-8.

[4] Singh N, Mehra RK, Srivastava N. Malaria during pregnancy and infancy, in an area of intense malaria transmission in central India. *Ann Trop Med Parasitol* 2001; **95**: 19-29.

[5] Campbell CC, Martinez JM, Collins WE. Seroepidemiological studies of malaria in pregnant women and newborns from coastal El Salvador. *Am J Trop Med Hyg* 1980; **29**: 151-7.

[6] Thanapongpichat S, McGready R, Luxemburger C, Day NP, White NJ, Nosten F, et al. Microsatellite genotyping of *Plasmodium vivax* infections and their relapses in pregnant and non-pregnant patients on the Thai-Myanmar border. *Malar J* 2013; **12**: 275.

[7] Rijken MJ, Papageorghiou AT, Thiptharakun S, Kiricharoen S, Dwell SLM, Wiladphaingern J, et al. Ultrasound evidence of early fetal growth restriction after maternal malaria infection. *PLoS One* 2012; **7**: e31411.

[8] McGready R, Lee SJ, Wiladphaingern J, Ashley EA, Rijken MJ, Boel M, et al. Adverse effects of falciparum and vivax malaria and the safety of antimalarial treatment in early pregnancy: a population-based study. *Lancet Infect Dis* 2012; **12**: 388-96.

[9] Machado Filho AC, da Costa EP, da Costa EP, Reis IS, Fernandes EA, Paim BV, et al. Effects of vivax malaria acquired before 20 weeks of pregnancy on subsequent changes in fetal growth. *Am J Trop Med Hyg* 2014; **90**: 371-6.

[10] Chaikitgosiyakul S, Rijken MJ, Muehlenbachs A, Lee SJ, Chaisri U, Viriyavejakul P, et al. A morphometric and histological study of placental malaria shows significant changes to villous architecture in both *Plasmodium falciparum* and *Plasmodium vivax* infection. *Malar J* 2014; **13**: 4.

[11] Brutus L, Santalla J, Schneider D, Avila JC, Deloron P. *Plasmodium vivax* malaria during pregnancy, Bolivia. *Emerg Infect Dis* 2013; **19**: 1605-11.

[12] Adam I, Khamis AH, Elbashir MI. Prevalence and risk factors for anaemia in pregnant women of eastern Sudan. *Trans R Soc Trop Med Hyg* 2005; **99**: 739-43.

[13] Adam I, Babiker S, Mohmmed AA, Salih MM, Prins MH, Zaki ZM. ABO blood group system and placental malaria in an area of unstable malaria transmission in eastern Sudan. *Malar J* 2007; **6**: 110.

[14] Silver KL, Zhong K, Leke RG, Taylor DW, Kain KC. Dysregulation of angiopoietins is associated with placental malaria and low birth weight. *PLoS One* 2010; **5**: e9481.

[15] Mohammed AH, Salih MM, Elhassan EM, Mohmmed AA, Elzaki SE, El-Sayed BB, et al. Submicroscopic *Plasmodium falciparum* malaria and low birth weight in an area of unstable malaria transmission in Central Sudan. *Malar J* 2013; **12**: 172.

[16] Ryan JR, Stoute JA, Amon J, Dunton RF, Mtalib R, Koros J, et al. Evidence for transmission of *Plasmodium vivax* among a duffy antigen negative population in Western Kenya. *Am J Trop Med Hyg* 2006; **75**: 575-81.

[17] Ménard D, Barnadas C, Bouchier C, Henry-Halldin C, Gray LR, Ratsimbasoa A, et al. *Plasmodium vivax* clinical malaria is commonly observed in Duffy-negative Malagasy people. *Proc Natl Acad Sci U S A* 2010; **107**: 5967-71.

[18] Abdallah TM, Abdeen MT, Ahmed IS, Hamdan HZ, Magzoub M, Adam I. Severe *Plasmodium falciparum* and *Plasmodium vivax* malaria among adults at Kassala Hospital, eastern Sudan. *Malar J* 2013; **12**: 148.

[19] Mahgoub H, Gasim GI, Musa IR, Adam I. Severe *Plasmodium vivax* malaria among Sudanese children at New Halfa Hospital, *Eastern Sudan. Parasit Vectors* 2012; **5**: 154.

[20] Dhorda M, Nyehangane D, Rénia L, Piola P, Guerin PJ, Snounou G. Transmission of *Plasmodium vivax* in south-western Uganda: report of three cases in pregnant women. *PLoS One* 2011; **6**(5): e19801.

[21] Nega D, Dana D, Tefera T, Eshetu T. Prevalence and predictors of asymptomatic malaria parasitemia among pregnant women in the rural surroundings of Arbaminch Town, South Ethiopia. *PLoS One* 2015; **10**(4): e0123630.

[22] Himeidan YE, Elbashir MI, El-Rayah el-A, Adam I. Epidemiology of malaria in New Halfa, an irrigated area in eastern Sudan. *East Mediterr Health J* 2005; **11**: 499-504.

[23] Adam I, Ali DM, Abdalla MA. Artesunate plus sulfadoxine-pyrimethamine in the treatment of uncomplicated *Plasmodium falciparum* malaria during pregnancy in eastern Sudan. *Trans R Soc Trop Med Hyg* 2006; **100**(7): 632-5.

[24] Alim A, Bilal NE, Abass AE, Elhassan EM, Mohmmed AA, Adam I. Complement activation, placental malaria infection, and birth weight in areas characterized by unstable malaria transmission in central Sudan. *Diagn Pathol* 2015; **10**: 49.

[25] McLean AR, Ataide R, Simpson JA, Beeson JG, Fowkes FJ. Malaria and immunity during pregnancy and postpartum: a tale of two species. *Parasitology* 2015; **142**(8): 999-1015.

[26] Luxemburger C, Thwai KL, White NJ, Webster HK, Kyle DE, Maelankirri L, et al. The epidemiology of malaria in a Karen population on the western border of Thailand. *Trans R Soc Trop Med Hyg* 1996; **90**(2): 105-11.

[27] Hemmer CJ, Holst FG, Kern P, Chiwakata CB, Dietrich M, Reisinger EC. Stronger host response per parasitized erythrocyte in *Plasmodium vivax* or ovale than in *Plasmodium falciparum* malaria. *Trop Med Int Health* 2006; **11**(6): 817-23.

[28] Yeo TW, Lampah DA, Tjitra E, Piera K, Gitawati R, Kenangalem E, et al. Greater endothelial activation, Weibel-Palade body release and host inflammatory response to *Plasmodium vivax*, compared with *Plasmodium falciparum*: a prospective study in Papua, Indonesia. *J Infect Dis* 2010; **202**(1): 109-12.

[29] Collins WE, Jeffery GM, Roberts JM. A retrospective examination of reinfection of humans with *Plasmodium vivax*. *Am J Trop Med Hyg* 2004; **70**(6): 642-4.

[30] Simpson JA, Silamut K, Chotivanich K, Pukrittayakamee S, White NJ. Red cell selectivity in malaria: a study of multiple-infected erythrocytes. *Trans R Soc Trop Med Hyg*1999; **93**(2): 165-8.