Published in final edited form as:

Am J Trop Med Hyg. 2007 September ; 77(3): 451–457.

Prevalence and Risk of *Plasmodium falciparum* and *P. vivax* Malaria among Pregnant Women Living in the Hypoendemic Communities of the Peruvian Amazon

Falgunee K. Parekh, Jean N. Hernandez, Donald J. Krogstad, W. Martin Casapia, and Oralee H. Branch*

Tulane University School of Public Health and Tropical Medicine, New Orleans, Louisiana; Division of Geographic Medicine, Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama; Ministerio de Salud, Direccion Regional de Salud Loreto, Iquitos, Peru

Abstract

The Amazon region of Iquitos, Peru is hypoendemic for *Plasmodium vivax* and *P. falciparum*. There is limited information regarding the epidemiology of malaria during pregnancy in this region. Passive surveillance for clinical malaria among pregnant women was conducted in eight health posts in 2004 and 2005. Community-based active surveillance was conducted to determine the incidence of malarial infection among pregnant women in the community of Zungarococha in 2004 and 2005. Passive surveillance demonstrated that pregnant women had a prevalence of clinical malaria of 7.5% in 2004 and 6.6% in 2005 compared with 20.6% and 22.4% of the total population. Active surveillance showed that pregnant women were 2.3 (95% confidence interval = 1.32–3.95, $P = 0.004$) times more likely to have a *P. falciparum* infection compared with non-pregnant women. This study demonstrated that because of detection bias, passive surveillance underestimates the burden of malarial infection during pregnancy, and that subclinical malarial infections may occur frequently among pregnant women in this region. Furthermore, pregnant women in this low-transmission and *P. vivax*-dominant setting, experience an increased risk for *P. falciparum* infection, but not *P. vivax* infection.

INTRODUCTION

Each year more than 24 million women become pregnant in malaria-endemic regions and are at increased risk of malaria infection and its severe maternal and fetal complications.^{1–6} Malaria infection during pregnancy can lead to several adverse pregnancy outcomes including low birth weight, intrauterine growth retardation, and maternal anemia. Pregnant women with relatively low levels of previously acquired immunity are particularly at high risk of the most severe complications of malaria during pregnancy, such as cerebral malaria, severe malaria anemia, abortions, stillbirths, and maternal and infant mortality.^{3,7} Underlying mechanisms of the increased susceptibility of pregnant women are still not well understood, but appear to be related to an assortment of epidemiologic, parasitologic, and

Copyright © 2007 by The American Society of Tropical Medicine and Hygiene

* Address correspondence to Oralee H. Branch, Division of Geographic Medicine, Department of Medicine, University of Alabama at Birmingham, 845 19th Street South, BBRB 554, Birmingham, AL 35294-2170. obranch@uab.edu.

Authors' addresses: Falgunee K. Parekh, 1620 East Jefferson Street, 206, Rockville, MD 20852, Telephone: 301-319-9920. Jean N. Hernandez and Oralee H. Branch, Division of Geographic Medicine, Department of Medicine, University of Alabama at Birmingham, 845 19th Street South, BBRB 554, Birmingham, AL 35294-2170, Telephone: 205-934-4721, Fax: 205-934-5600, obranch@uab.edu. Donald J. Krogstad, Tulane University School of Public Health and Tropical Medicine, 1440 Tulane Avenue, New Orleans, LA, Telephone: 504-988-3552. W. Martin Casapia, Asociacion Civil Selva Amazonica, Calle Fanning, Cdra. 4 Iquitos, Loreto, Peru, mcasapia@acsaperu.org.

immunologic factors.^{1,2} The level of endemicity of malaria transmission, the level of immunity acquired prior to pregnancy, and gravidity are some of the primary factors that contribute to the epidemiology of malaria during pregnancy in various regions.

Most previous studies investigating the epidemiology and impact of malaria during pregnancy have been conducted in regions with high endemicity for malaria where *Plasmodium falciparum* is the major infecting species. Those studies have shown that pregnant women are 4–12 times more likely to be parasitemic compared with other adults.⁸ Few studies have investigated *P. vivax* infection during pregnancy, but those that have also demonstrated an increased susceptibility to malaria and complications among pregnant women.^{9–13} However, the epidemiology of *P. falciparum* malaria during pregnancy in regions of low malaria endemicity, and malaria caused by *P. vivax* infections remains unclear and requires further description to develop effective preventive and control strategies for pregnant women. The Amazon region of Iquitos, Peru provides such an opportunity.

The Amazon region of Peru, known as the Department of Loreto, has experienced a re-emergence of malaria caused by *P. vivax* and *P. falciparum* during the last 15 years, reaching epidemic levels between 1995 and 1998.^{14–16} Malaria incidence has since remained low with *P. falciparum* and *P. vivax* annual infection incidence varying between 5 and 50 cases/1,000 persons.¹⁷ Most reported cases occurred in villages and communities surrounding the city of Iquitos. A recent active surveillance study in Zungarococha consisting of five villages showed a high prevalence of asymptomatic *P. vivax* and *P. falciparum* infections.¹⁷ In Zungarococha in 2003 and 2004, the annual active case detection point prevalence was 31% for *P. vivax* and 11% for *P. falciparum*.¹⁷

Little information is currently available on the epidemiology and impact of malaria during pregnancy in this region, which makes it difficult to develop effective preventive and control strategies specific for pregnant women. Therefore, a retrospective analysis of 2004 and 2005 health post data from the Peruvian Ministry of Health was conducted to provide a preliminary description of the prevalence of clinical malaria in pregnant women and the risk factors associated with clinical malaria. Additionally, active follow-up data from a cohort study conducted in the community of Zungarococha was analyzed to assess the incidence of infection in pregnant women compared with their non-pregnant counterparts. The goals of the current study were 1) to determine the prevalence of clinical malaria in pregnant women compared with that in the total population detected at eight health posts that serve malaria-endemic areas; 2) to determine the incidence of malaria infection in pregnant women compared with that in non-pregnant women and men 14–45 years of age who were enrolled in a community-based active follow-up study in Zungarococha; and 3) to assess the risk factors associated with malarial infection in pregnant women who were identified in Zungarococha.

MATERIALS AND METHODS

Prevalence of clinical malaria at eight health posts

The Peruvian Ministry of Health has numerous health posts and centers of health that serve the populations living in small villages and communities throughout Loreto. A retrospective analysis of passive case detection data from health posts was conducted to assess the prevalence of malaria in pregnant women and the total population. This study was limited to data from 8 health posts that serve at least 12 communities located near the city of Iquitos in regions known to be endemic for malaria. Patients entering the health posts with symptoms of malaria, including fever, headache, and malaise are routinely tested by microscopic examination for malarial parasites. Therefore, this analysis considered cases of symptomatic

clinical malaria because they were patients who were tested and diagnosed for malaria based on the presence of symptoms. Microscopy is conducted on blood smears stained with Giemsa using a standard procedure using 1,000× magnification to read the thick smear. All microscopists in the health centers are employed and trained by Ministry of Health and at least 20% of all blood slides undergo a second quality control reading by the Ministry of Health reference laboratory.

In accordance to Peruvian National Drug Policy, a diagnosis of *P. vivax* malaria in pregnant women resulted in treatment with chloroquine (and primaquine after delivery). A diagnosis of uncomplicated *P. falciparum* malaria in pregnant women resulted in treatment with oral quinine and clindamycin, and a diagnosis for complicated malaria resulted in an initial dose of intravenous quinine (10 mg/kg over a four-hour period and diluted in 500 mL of 10% glucose) followed by oral quinine and clindamycin. There is currently no national policy on chemoprophylaxis for pregnant women because malaria during pregnancy has not yet been extensively investigated in this region.

Malaria cases diagnosed between January and December 2004 and between January and August 2005 were included in this retrospective analysis. The prevalence of clinical malaria in the total population was calculated as the number of malaria cases diagnosed in the health post during this time period divided by the total population of the communities that the individual health post serves. The prevalence of clinical malaria in pregnant women was calculated as the number of pregnant women diagnosed with malaria in the health post divided by the total number of pregnant women in the communities during this time period. Pregnancy was determined based on self-report as well as the records of women going to health post for prenatal visits. Prevalence ratios and 95% confidence intervals (CIs) were calculated to compare the prevalence of clinical malaria in pregnant women to that in the total population as detected by passive case surveillance.

Cumulative incidence of malaria infection in the Zungaro-cocha-based study

A subsequent analysis was conducted in Zungarococha using data from a prospective communitybased active follow-up study to compare the incidence of malarial infection (asymptomatic and symptomatic) in pregnant women and their non-pregnant counterparts of the same age group. In this prospective study, households were enrolled in Zungarococha and followed for at least a four-week period during the peak transmission season of January to August in 2004 and 2005.¹⁷ Each week a blood smear was taken and examined, and patients were asked if they experienced any symptoms in the previous week. Microscopic examination of blood smears was also conducted as described above. Women of fertile age (14–45 years) were asked if they were pregnant upon enrollment. However, no effort was made to particularly enroll pregnant women or households with pregnant women. For this analysis, a case was defined as someone who experienced a symptomatic or asymptomatic infection at any time during the four-week follow-up period. Those with a positive smear more than once during this period were counted as only one case because of issues of recrudescence and relapse. This analysis was limited to non-pregnant women and men 14–45 years of age and pregnant women to ensure the comparability of the groups. The incidence of infection in pregnant women was calculated as total number of cases in pregnant women divided by total number of pregnant women enrolled in the study. The incidence of infection was similarly computed in non-pregnant women and men 14–45 years of age. Risk ratios (RRs) and 95% CIs were computed to estimate the risk of malaria infection in pregnant women compared with that in non-pregnant women of fertile age as detected by active surveillance.

Risk factors associated with malaria infection in pregnant women at the Zungarococha health post

A risk factor analysis was conducted on pregnant women detected by both the passive surveillance data from the Zungarococha health post and the active community follow-up study. Information on age, gravidity, reported number of previous malarial infections, and gestational age at time of entrance into the health post or enrollment in the community-based study was available for 75 (86.2%) of 87 pregnant women identified in 2004 and all 48 (100%) pregnant women in 2005 for a total of 123 pregnant women. The above mentioned risk factors were compared between *Plasmodium*-infected and -uninfected pregnant women.

Statistical methods

Prevalence, incidence, prevalence ratio, and RR were calculated as described above. Univariate analysis was conducted to calculate the median age, gravidity, and number of previous malarial infections among pregnant women at the Zungarococha health post. A Wilcoxon rank sum test was conducted to determine if there was an association between the risk factors and diagnosis of malaria during pregnancy. Analysis was conducted in SAS version 9.1 (SAS Inc., Cary, NC).

RESULTS

Prevalence of clinical malaria at eight health posts

The eight health posts included in the study were those located in the following communities: Manacamire, Padrecocha, Paujil, Quistococha, Santa Clara, Santo Tomas, Varillal, and Zungarococha. The total population served by these health posts in 2004 was 27,571, of which 6,407 (23.2%) were women of fertile age (14–45 years), and 1,463 (5.3%) were pregnant (Table 1). Between January and August 2005, the total population served by these health posts was 29,661, of which 4,829 (16.3%) were women 14–45 years of age and 1,648 (5.6%) were pregnant women. Although it is difficult to determine whether the cases diagnosed in the health posts are caused by new infections, the computed prevalence is assumed to be a valid estimate of symptomatic infections because this is a region of low transmission of malaria and the population was aware of and used the free diagnosis and treatment available at the Ministry of Health community health posts.

During 2004, 5,005 cases of malaria caused by *P. vivax* and *P. falciparum* infection were diagnosed in the eight health posts, giving an overall prevalence of approximately 18.2%. Approximately 93% of the malaria cases were caused by *P. vivax*, which is consistent with the fact that *P. vivax* is the dominant infecting species in this region.¹⁷ The health post records for malaria detection could only be evaluated by comparing the malaria cases in pregnant women versus the malaria cases in the total population; i.e., malaria cases in the total population were not further classified by sex or age group. Among the 1,463 pregnant women, 118 (8.1%) were diagnosed with malaria in 2004. Similarly, the prevalence of clinical malaria between January and August 2005 was 22.4% in the total population and 6.6% in pregnant women.

Tables 2 and 3 show the number and prevalence with 95% CIs of malaria in each community for the total population and for pregnant women. The prevalence was computed using cases caused by both species because the number caused by *P. falciparum* was low. The prevalence of clinical malaria in the total population was highly variable by community for both 2004 (range = 12.7–44.9%) and 2005 (range = 9.9–35.6%) (Tables 2 and 3). The clinical malaria prevalence in pregnant women was similarly highly variable among the eight communities in 2004 (range = 2.6–24.1%) and 2005 (range = 2.3–31.8%). Prevalence ratios were computed as the prevalence of clinical malaria in pregnant women divided by

the prevalence of clinical malaria in the total population. The prevalence ratio of all eight communities combined was 0.44 (95% CI = 0.37–0.53) in 2004 and 0.29 (95% CI = 0.24–0.35) in 2005. Additionally, the prevalence ratios for both years for all communities were less than 1.0, which demonstrated that on the basis of passive surveillance of health post data pregnant women were significantly less likely to have a clinical malaria diagnosis in the health posts compared with the total population.

Cumulative incidence of malarial infection in Zungaroco-cha-based active follow-up study

In Zungarococha, we are conducting an ongoing malaria study that enabled us to determine the number of malaria infections occurring in pregnant women and non-pregnant women and men of the same age group (14–45 years) in individuals followed-up by both passive case detection and active case detection. Either between January and August 2004 or between January and August 2005 (the malaria seasons of 2004 and 2005), 51 pregnant women, 601 non-pregnant women, and 659 men 14–45 years of age were enrolled and actively followed-up, regardless of symptoms, once a week for one month. In addition to this month of active case detection either in 2004 or 2005, the individuals could go to the health post for the usual Ministry of Health passive case detection during the given year. Table 4 shows the number of those infected with *P. vivax* or *P. falciparum* during the study period. The incidence of any malarial infection in pregnant women was 43.1% (22 of 51) compared with 31.6% (190 of 601) in non-pregnant women, and 38.2% (252 of 659) in men 14–45 years of age. Table 4 shows the RRs for any infection, *P. vivax* infection, and *P. falciparum* infection. Pregnant women were not more likely to have a *P. vivax* infection compared with non-pregnant women and men. In contrast, pregnant women were significantly more likely to have a *P. falciparum* infection compared with non-pregnant women (RR = 2.3, 95% CI = 1.32–3.95) and men of the same age group (RR = 1.7, 95% CI = 1.00–2.90) (Table 4).

Risk factors associated with malaria in pregnant women in Zungarococha

In addition to the 51 pregnant women enrolled in the community-based active follow-up study, there were 84 women who were pregnant at sometime during 2004 and 2005 who were not enrolled in active case detection during their pregnancy. Of these 84 additional pregnant women, only 61 had risk factor data available. The occurrence of malaria infection in these mothers was considered whether the infections were detected by passive case detection at the health post or by active case detection in the community. Among the 123 pregnant women with risk factor data available, there were 38 malarial infections (30.8%) in 34 women: 20 *P. vivax* infections and 18 *P. falciparum* infections. Each infection was counted individually in the analysis because they occurred at different times during pregnancy. Most infections were detected in women by active case detection: 22 infections in the 51 women with one month of active case detection during their pregnancy versus 16 passive case detections in 61 pregnant women without active case detection.

Infected pregnant women in Zungarococha were older, with a median age 24 years compared with uninfected who had a median age of 21 years ($P = 0.089$). This unexpected trend of older women having malaria was mostly attributable to *P. vivax*-infected women ($P = 0.067$) (Table 5). Although gravidity was not significantly associated with either *P. vivax* or *P. falciparum* infection, most of those infected were primigravid, and lack of significance may have been due to inadequate power (Table 5). Approximately 90% of both infected and non-infected women reported at least one previous *P. vivax* infection. In contrast, infected cases were 2.5 times (95% CI = 1.1–5.7, $P = 0.03$) more likely to have reported a previous *P. falciparum* infection compared with uninfected cases. A high proportion of all pregnant women reporting at least one previous *P. vivax* infection was expected because of the higher prevalence and increased geographic range of *P. vivax* in Iquitos. In contrast, *P. falciparum*

prevalence is more focused in regions of higher overall malaria transmission. Therefore, increased history of *P. falciparum* infection in the malaria-infected pregnant women might be reflecting these mothers living or traveling to regions with greater malaria transmission. The median gestational age at time of diagnosis of malarial infection was 23.5 weeks (Table 5).

DISCUSSION

The epidemiology of malaria during pregnancy has been well described in many regions with high endemicity, particularly in sub-Saharan Africa where *P. falciparum* is the primary infecting species.^{1–5,8} However, little is known about the epidemiology and impact of malaria during pregnancy in regions of low endemicity and regions where malaria is caused by both *P. vivax* and *P. falciparum*. The results of this study provide a preliminary description of the epidemiology of malaria in pregnant women living in the Amazon region of Iquitos, Peru. Analysis of the Ministry of Health passive surveillance data from the eight health posts demonstrated that pregnant women had a lower prevalence of clinical malaria compared with the rest of the population. This is in contrast to the results of most previous studies conducted in a variety of transmission settings, which have all shown an increased susceptibility of pregnant women to malaria infection and disease complications.^{1,18,19} This apparent decreased prevalence or risk of clinical malaria in pregnant women versus the total population observed in the health post passive case detection data may have arisen owing to several reasons including 1) surveillance/detection bias, 2) placental sequestration, and 3) occurrence of asymptomatic infections during pregnancy.

First, a surveillance and detection bias may be occurring at the health posts. The usual policy is that all individuals entering the health post with a fever are tested by microscopy for malaria. However, the health care worker may attribute a fever in pregnant women to urinary and genital infections common in pregnancy²⁰ and, therefore, check first for these infections and then, if the results are positive, not check for malaria.

Second, pregnant women may have symptoms, but a peripheral blood smear is negative by microscopic examination because parasites are sequestering/accumulating in the placenta. Several studies have shown that a placental infection is common in the absence of a peripheral infection that is detectable by microscopy.^{7,21–25} If placental sequestration was occurring more frequently in infected pregnant women in comparison to general sequestration in non-pregnant women, the lower prevalence of malaria in pregnant women versus the total population would be expected.

Third, the decreased prevalence of clinical malaria among pregnant women may have been observed because pregnant may have asymptomatic infections. Asymptomatic malaria in Zungarococha has been detected in a previous study.¹⁷ Although the previous study did not investigate pregnant women specifically, it is possible that pregnant women as well as the total population in general experience asymptomatic malarial infections that would not be identified by passive case detection. Furthermore, the passive case detection data for the eight health posts only distinguishes between nonpregnant and pregnant women; therefore, the comparison group or total population consists of a mixed population of men, women, and children of all ages with various risks for clinical malaria. In particular, the total population group included those at the highest risk for clinical malaria, such as men with outdoor occupations and children. If most clinical malaria cases in the total population group occurred in those in the highest risk groups, as would be expected, the prevalence of the total population may be inflated, which would bias the results. A more accurate comparison group for pregnant women would be non-pregnant women and men of the same age group (14–45 years). For these reasons, analysis of the community-based data from Zungarococha

was undertaken to identify both symptomatic and asymptomatic malarial infections and directly assess and compare the number of infections between pregnant women and non-pregnant women or men of the same age group.

Analysis of the community-based data from Zungarococha found that pregnant women were significantly more likely to be infected with *P. falciparum* compared with nonpregnant women of the same age group (Table 4). Although pregnant women did not demonstrate an increased risk to *P. vivax* infection compared with non-pregnant women, the measured incidence was approximately 20%, which is significantly higher than the prevalence measured in the passive surveillance health post data (6.0–7.5%). This is in concordance with a study conducted in the Brazilian Amazon, which found an increased *P. falciparum* to *P. vivax* infection ratio among pregnant women compared with non-pregnant women (1:2.3 versus 1:5.6).²⁶ Thus, it is possible that the increased susceptibility of malaria during pregnancy may be due to *P. falciparum* infection.

The risk factor analysis of the pregnant women living in Zungarococha demonstrated that pregnant women with malarial infection tend to be older and of increased gravidity compared with uninfected pregnant women. This contradicts previous studies from malaria-endemic regions that have shown that development of resistance to clinical malaria in pregnant women is dependent on age and gravidity. This may be attributable to the fact that older women, and thus women of higher gravidity, are more likely to participate in outdoor activities such as fishing and agricultural activities that place them at increased risk for infection. Infected pregnant women, particularly *P. falciparum*-infected women, were significantly more likely to have reported a previous *P. falciparum* infection compared with non-infected women, which suggests that a sub-group of pregnant women were more involved in activities that put them at increased risk of *P. falciparum* infection.

Finding asymptomatic malaria infections in pregnant women is a particular public health concern. The community-based study showed that pregnant women in this region have an increased frequency of both *P. vivax* and *P. falciparum* infection compared with that measured and diagnosed in health posts, which indicated that subclinical asymptomatic infections may occur frequently in pregnant women. The increased risk to *P. falciparum* infection, even if asymptomatic, has important implications for the health of pregnant women and her fetus. A *P. falciparum* infection is known to often cause more severe disease manifestations than *P. vivax*, including cerebral malaria, severe malaria anemia, and hypoglycemia. Additionally, *P. falciparum*-infected red blood cells are known to accumulate in the placenta and bind to chondroitin sulfate A and hyaluronic acid expressed on the surface of placental cells, which can result in decreased efficiency of materno-fetal transfer of oxygen and nutrients affecting the growth and development of the fetus.^{27–29} An asymptomatic infection in pregnant women can have more severe consequences than in non-pregnant women because it may go undetected and continue to have serious impact on both maternal and infant health that include severe anemia, intrauterine growth retardation, and low birth weight.

This study provides the first description of the epidemiology of malaria in pregnant women living in the Amazon region of Iquitos, Peru. The retrospective analysis of data from eight health posts showed that pregnant women had a lower prevalence of clinical malaria compared with the total population. However, this surprising finding is most likely a result of detection and surveillance bias. Results from the community-based study in Zungarococha showed that pregnant women may have a high frequency of subclinical malarial infections, and are more likely to be infected with *P. falciparum* compared with her non-pregnant male and female counterparts.

This study showed that malaria during pregnancy is a serious public health problem in and around Iquitos. Public health workers should be encouraged to test pregnant women coming to the health post for malaria, even if they are first diagnosed with other pregnancy-associated illnesses. The results of this study justify a detailed investigation of pregnant women at the time of delivery to assess adverse pregnancy outcomes such as maternal anemia and infant low birth weight associated with symptomatic and asymptomatic malarial infection.

Acknowledgments

Financial support: This study was supported by the Gorgas Memorial Institute, the Centers for Disease Control and Prevention (grant UR3/CCU 418652 to for Falgunee K. Parekh), and the American Society of Tropical Medicine and Hygiene.

REFERENCES

1. Menendez C. Malaria during pregnancy: a priority area of malaria research and control. *Parasitol Today*. 1995; 11:178–183. [PubMed: 15275350]
2. Okoko BJ, Enwere G, Ota MO. The epidemiology and consequences of maternal malaria: a review of immunological basis. *Acta Trop*. 2003; 87:193–205. [PubMed: 12826295]
3. Steketee RW, Nahlen BL, Parise ME, Menendez C. The burden of malaria in pregnancy in malaria-endemic areas. *Am J Trop Med Hyg*. 2001; 64:28–35. [PubMed: 11425175]
4. McGregor IA. Epidemiology, malaria and pregnancy. *Am J Trop Med Hyg*. 1984; 33:517–525. [PubMed: 6383091]
5. McGregor IA, Wilson ME, Billewicz WZ. Malaria infection of the placenta in The Gambia, west Africa; its incidence and relationship to stillbirth, birthweight and placental weight. *Trans R Soc Trop Med Hyg*. 1983; 77:232–244. [PubMed: 6346592]
6. Steketee RW, Wirima JJ, Slutsker L, Heymann DL, Breman JG. The problem of malaria and malaria control in pregnancy in sub-Saharan Africa. *Am J Trop Med Hyg*. 1996; 55:2–7. [PubMed: 8702033]
7. Cot M, Deloron P. Malaria prevention strategies. *Br Med Bull*. 2003; 67:137–148. [PubMed: 14711760]
8. Brabin B. An assessment of low birthweight risk in primiparae as an indicator of malaria control in pregnancy. *Int J Epidemiol*. 1991; 20:276–283. [PubMed: 2066235]
9. Nosten F, McGready R, Simpson JA, Thwai KL, Balkan S, Cho T, Hkirijsaroen L, Looareesuwan S, White NJ. Effects of *Plasmodium vivax* malaria in pregnancy. *Lancet*. 1999; 354:546–549. [PubMed: 10470698]
10. Nosten F, ter Kuile F, Maelankirri L, Decludt B, White NJ. Malaria during pregnancy in an area of unstable endemicity. *Trans R Soc Trop Med Hyg*. 1991; 85:424–429. [PubMed: 1836685]
11. Luxemburger C, McGready R, Kham A, Morison L, Cho T, Chongsuphajaisiddhi T, White NJ, Nosten F. Effects of malaria during pregnancy on infant mortality in an area of low malaria transmission. *Am J Epidemiol*. 2001; 154:459–465. [PubMed: 11532788]
12. 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. [PubMed: 11235550]
13. Singh N, Saxena A, Shrivastava R. Placental *Plasmodium vivax* infection and congenital malaria in central India. *Ann Trop Med Parasitol*. 2003; 97:875–878. [PubMed: 14754501]
14. Aramburu GJ, Ramal AC, Witzig R. Malaria reemergence in the Peruvian Amazon region. *Emerg Infect Dis*. 1999; 5:209–215. [PubMed: 10221872]
15. Roshanravan B, Kari E, Gilman RH, Cabrera L, Lee E, Metcalfe J, Calderon M, Lescano AG, Montenegro SH, Calampa C, Vinetz JM. Endemic malaria in the Peruvian Amazon region of Iquitos. *Am J Trop Med Hyg*. 2003; 69:45–52. [PubMed: 12932096]

16. Roper MH, Torres RS, Goicochea CG, Andersen EM, Guarda JS, Calampa C, Hightower AW, Magill AJ. The epidemiology of malaria in an epidemic area of the Peruvian Amazon. *Am J Trop Med Hyg.* 2000; 62:247–256. [PubMed: 10813480]
17. Branch O, Casapia WM, Gamboa DV, Hernandez JN, Alava FF, Roncal N, Alvarez E, Perez EJ, Gotuzzo E. Clustered local transmission and asymptomatic *Plasmodium falciparum* and *Plasmodium vivax* malaria infections in a recently emerged, hypoendemic Peruvian Amazon community. *Malar J.* 2005; 4:27. [PubMed: 15975146]
18. Shulman CE, Marshall T, Dorman EK, Bulmer JN, Cutts F, Peshu N, Marsh K. Malaria in pregnancy: adverse effects on haemoglobin levels and birthweight in primigravidae and multigravidae. *Trop Med Int Health.* 2001; 6:770–778. [PubMed: 11679125]
19. van Geertruyden JP, Thomas F, Erhart A, D'Alessandro U. The contribution of malaria in pregnancy to perinatal mortality. *Am J Trop Med Hyg.* 2004; 71:35–40. [PubMed: 15331817]
20. Bouyou-Akotet MK, Ionete-Collard DE, Mabika-Manfoumbi M, Kendjo E, Matsiegui PB, Mavoungou E, Kombila M. Prevalence of *Plasmodium falciparum* infection in pregnant women in Gabon. *Malar J.* 2003; 2:18. [PubMed: 12919637]
21. Watkinson M, Rushton DI. Plasmodial pigmentation of placenta and outcome of pregnancy in West African mothers. *Br Med J (Clin Res Ed).* 1983; 287:251–254.
22. Matteelli A, Donato F, Shein A, Muchi JA, Leopardi O, Astori L, Carosi G. Malaria and anaemia in pregnant women in urban Zanzibar, Tanzania. *Ann Trop Med Parasitol.* 1994; 88:475–483. [PubMed: 7979637]
23. Matteelli A, Caligaris S, Castelli F, Carosi G. The placenta and malaria. *Ann Trop Med Parasitol.* 1997; 91:803–810. [PubMed: 9625937]
24. Walter PR, Garin Y, Blot P. Placental pathologic changes in malaria. A histologic and ultrastructural study. *Am J Pathol.* 1982; 109:330–342. [PubMed: 6758604]
25. Rogerson SJ, Mkundika P, Kanjala MK. Diagnosis of *Plasmodium falciparum* malaria at delivery: comparison of blood film preparation methods and of blood films with histology. *J Clin Microbiol.* 2003; 41:1370–1374. [PubMed: 12682116]
26. Fried M, Duffy PE. Adherence of *Plasmodium falciparum* to chondroitin sulfate A in the human placenta. *Science.* 1996; 272:1502–1504. [PubMed: 8633247]
27. Duffy PE, Fried M. Malaria during pregnancy: parasites, antibodies and chondroitin sulphate A. *Biochem Soc Trans.* 1999; 27:478–482. [PubMed: 10917625]
28. Rogerson SJ, Chaiyaroj SC, Ng K, Reeder JC, Brown GV. Chondroitin sulfate A is a cell surface receptor for *Plasmodium falciparum*-infected erythrocytes. *J Exp Med.* 1995; 182:15–20. [PubMed: 7790815]
29. Martinez-Espinosa F, Daniel-Ribeiro CT, Alecrim WD. Malaria during pregnancy in a reference centre from the Brazilian Amazon: unexpected increase in the frequency of *Plasmodium falciparum* infections. *Mem Inst Oswaldo Cruz.* 2004; 99:19–21. [PubMed: 15057341]

Table 1
Population distribution of the eight health post communities in Iquitos, Peru, 2004 and 2005

Community	Total population 2004	Population of fertile women (14-45 years of age) (% of total) 2004	Population of pregnant women (% of total) 2004	Total population 2005	Population of fertile women (14-45 years of age) (% of total) 2005	Population of pregnant women (% of total) 2005
Manacamire	868	200 (23.0)	39 (4.5)	880	204 (23.2)	34 (3.9)
Padrecocha	2,467	568 (23.0)	158 (4.0)	2,463	540 (21.9)	158 (6.4)
Paujil	5,279	1,271 (24.1)	504 (9.5)	5,912	1,371 (23.2)	181 (3.1)
Quistococha	2,478	571 (23.0)	100 (4.0)	1,960	137 (7.0)	352 (17.9)
Santa Clara	4,671	1,076 (23.0)	188 (4.0)	7,089	1,643 (23.2)	363 (5.1)
Santo Tomas	6,649	1,532 (23.0)	267 (4.0)	5,781	355 (6.1)	385 (6.7)
Varillal	2,981	687 (23.0)	120 (4.0)	2,875	280 (9.7)	131 (4.6)
Zungarococha	2,178	502 (23.0)	87 (4.0)	2,701	299 (11.1)	48 (1.8)
Total	27,571	6,407 (23.2)	1,463 (5.3)	29,661	4,829 (16.3)	1,652 (5.6)

Table 2

Number and prevalence of malaria cases diagnosed in eight health posts in Iquitos, Peru, 2004*

Community	Malaria cases in total population		Malaria cases in pregnant women		Prevalence of malaria in total population (95% CI)	Prevalence of malaria in pregnant women (95% CI)	Prevalence ratio (95% CI)
	<i>Plasmodium falciparum</i>	<i>P. vivax</i>	<i>P. falciparum</i>	<i>P. vivax</i>			
Manacmire	6	384	0	7	44.9 (41.6–48.3)	17.9 (5.9–30.0)	0.39 (0.20–0.78)
Padrecocha	16	639	0	7	26.6 (24.8–28.3)	4.4 (1.2–7.6)	0.17 (0.08–0.35)
Paujil	12	658	1	12	12.7 (11.8–13.6)	2.6 (1.2–4.0)	0.20 (0.12–0.35)
Quistococha	5	425	0	8	17.4 (15.9–18.8)	8.0 (2.7–13.3)	0.43 (0.22–0.84)
Santa Clara	78	970	0	18	22.4 (21.2–23.6)	9.6 (5.4–13.8)	0.43 (0.27–0.66)
Santo Tomas	50	1,116	0	27	17.5 (16.6–18.5)	10.1 (6.5–13.7)	0.58 (0.41–0.83)
Varillal	19	430	3	6	15.1 (13.8–16.3)	7.5 (2.8–12.2)	0.50 (0.26–0.94)
Zungarococha	200	674	8	13	40.1 (38.1–42.2)	24.1 (15.1–33.1)	0.60 (0.41–0.88)
Total	351	4,654	19	99	18.2 (17.7–18.6)	8.1 (6.7–9.5)	0.44 (0.37–0.53)

* CI = confidence interval.

Table 3

Number and prevalence of malaria cases diagnosed in eight health posts in Iquitos, Peru, 2005 *

Community	Malaria cases in total population		Malaria cases in pregnant women		Prevalence of malaria in total population (95% CI)	Prevalence of malaria in pregnant women (95% CI)	Prevalence ratio (95% CI)
	<i>Plasmodium falciparum</i>	<i>P. vivax</i>	<i>P. falciparum</i>	<i>P. vivax</i>			
Manacamire	22	291	0	4	35.6 (32.4–38.7)	11.8 (3.3–27.5)	0.33 (0.13–0.83)
Padrecocha	28	649	0	16	27.5 (25.7–29.2)	10.1 (5.4–14.8)	0.37 (0.23–0.59)
Paujil	36	551	0	9	9.9 (9.2–10.7)	5.0 (1.8–8.1)	0.50 (0.26–0.95)
Quistococha	34	455	1	19	24.9 (23.0–26.9)	5.7 (3.3–8.1)	0.23 (0.15–0.35)
Santa Clara	279	1,721	7	26	28.2 (27.2–29.3)	9.1 (6.1–12.0)	0.32 (0.23–0.45)
Santo Tomas	108	1,124	1	8	21.3 (20.3–22.4)	2.3 (0.83–3.8)	0.11 (0.06–0.21)
Varillal	20	355	0	3	13.0 (11.8–14.3)	2.3 (0.47–6.5)	0.18 (0.06–0.54)
Zungarococha	296	664	12	11	35.5 (33.7–37.3)	47.9 (33.7–62.0)	1.35 (0.99–1.82)
Total	823	5,810	11	97	22.4 (21.9–22.8)	6.6 (5.4–7.7)	0.29 (0.24–0.35)

* CI = confidence interval.

Cumulative incidence* and incidence ratios of Zungarococha community-based study of pregnant women, non-pregnant women, and men 14–45 years of age, January–August 2004 and January–August 2005†

Table 4

Infection type	Cumulative incidence in pregnant women (n = 51)	Cumulative incidence in non-pregnant women 14–45 years of age (n = 601)	Incidence ratio (95% CI), P value inc. in pregnant/ inc. in non-pregnant	Cumulative incidence in men 14–45 years of age (n = 659)	Incidence ratio (95% CI), P value inc. in pregnant/ inc. in males
Any	43.1%	31.6%	1.36 (0.97–1.91) 0.092	38.2%	1.13 (0.81–1.57) 0.49
<i>Plasmodium vivax</i>	19.6%	21.3%	0.92 (0.52–1.64) 0.78	24.4%	0.80 (0.45–1.42) 0.44
<i>P. falciparum</i>	23.5%	10.3%	2.28 (1.32–3.95) 0.004	13.8%	1.7 (1.00–2.90) 0.058

* Cumulative Incidence calculated for cumulative period of January–August 2004 and January–August 2005.

† CI = confidence interval; Inc. = increase.

Table 5

Risk factors associated with malaria infection in pregnant women from Zungarococha

Risk factors	Malaria negative (n = 88)*	Malaria positive (n = 38) (P value)	<i>P. vivax</i> positive (n = 20) (P value)	<i>P. falciparum</i> positive (n = 18) P value)
Median age in years	21 (n = 87)	24 (0.089)	24.5 (0.067)	23 (0.46)
Median gravidity	2	3 (0.35)	3 (0.10)	2 (0.49)
Number primigravid (%)	63 (71.6%)	29 (76.3%) (0.58)	18 (90%) (0.15)	11 (64.7%) (0.38)
Number reported previous <i>Plasmodium vivax</i>	72 (n = 80, 90.0%)	34 (89.5%) (0.93)	17 (85%) (0.69)	17 (94%) (1.0)
Number reported previous <i>P. falciparum</i>	18 (n = 80, 22.5%)	16 (42.1%) (0.028)	7 (35%) (0.26)	9 (50%) (0.037)
Median gestational age at time of diagnosis in weeks		23.5 (n = 26)	26 (n = 15)	23 (n = 11)

* Reference group.