Effect of agricultural activities on prevalence rates, and clinical and presumptive malaria episodes in central Côte d'Ivoire

Benjamin G. Koudou, Yao Tano, Jennifer Keiser, Penelope Vounatsou, Olivier Girardin, Kouassi Kléré, Mamadou Koné, Eliézer K. N’Goran, Guéadio Cissé, Marcel Tanner, Jürg Utzinger

Centre Suisse de Recherches Scientifiques, 01 BP 1303, Abidjan 01, Cote d’Ivoire
UFR Sciences de Nature, Université d’Abobo-Adjamé, 02 BP 801, Abidjan 02, Cote d’Ivoire
UFR Biosciences, Université de Cocody-Abidjan, 22 BP 522, Abidjan 22, Cote d’Ivoire
Department of Medical Parasitology and Infection Biology, Swiss Tropical Institute, P.O. Box, CH-4002 Basel, Switzerland
Department of Public Health and Epidemiology, Swiss Tropical Institute, P.O. Box, CH-4002 Basel, Switzerland
Fondation Rural Inter Jurassienne, CH-2852 Courtételle, Switzerland
Centre de Santé Urbain de Tiémélékro, Bongouanou, Cote d’Ivoire
Centre de Santé Rural de Zatta, Yamoussoukro, Cote d’Ivoire

Abstract

Agricultural activities, among other factors, can influence the transmission of malaria. In two villages of central Côte d’Ivoire (Tiémélékro and Zatta) with distinctively different agro-ecological characteristics, we assessed Plasmodium prevalence rates, fever and clinically confirmed malaria episodes among children aged 15 years and below by means of repeated cross-sectional surveys. Additionally, presumptive malaria cases were monitored in dispensaries for a 4-year period. In Tiémélékro, we observed a decrease in malaria prevalence rates from 2002 to 2005, which might be partially explained by changes in agricultural activities from subsistence farming to cash crop production. In Zatta, where an irrigated rice perimeter is located in close proximity to human habitations, malaria prevalence rates in 2003 were significantly lower than in 2002 and 2005, which coincided with the interruption of irrigated rice farming in 2003/2004. Although malaria transmission differed by an order of magnitude in the two villages in 2003, there was no statistically significant difference between the proportions of severe malaria episodes (i.e. axillary temperature > 37.5°C plus parasitaemia > 5000 parasites/µl blood). Our study underscores the complex relationship between malaria transmission, prevalence rate and the dynamics of malaria episodes. A better understanding of local contextual determinants, including the effect of agricultural activities, will help to improve the local epidemiology and control of malaria.

© 2009 Elsevier B.V. All rights reserved.

1. Introduction

Recent estimates suggest that the global number of clinical malaria episodes due to Plasmodium falciparum exceeds 500 million (Snow et al., 2005). Most of these episodes and malaria-related mortality are concentrated in sub-Saharan Africa (WHO, 2004; Snow et al., 2005; Lopez et al., 2006). Development and spread of resistance to common antimalarial drugs and insecticides, in the face of fragile and often deteriorating health systems, are among the chief reasons why the global burden of malaria has doubled over the past 20 years (Brennan et al., 2004). In Côte d’Ivoire, malaria remains the first cause of health-seeking in dispensaries, particularly during and shortly after the rainy season, accounting for 42% of all visits. Moreover, malaria is the leading cause of hospitalization (70%) and mortality (15%), as recorded at paediatric units of hospitals (Anonymous, 2001).

Malaria prevalence, morbidity and mortality are influenced by the intensity of transmission, but the relationships are complex (Smith et al., 2001, 2005; Snow et al., 2004; Bodker et al., 2006). In areas characterized by seasonal malaria transmission, for example, a positive association has been found between the number of clinical episodes in children and transmission intensity (Trape et al., 1994; Carme, 1996; Sylla et al., 2001). In low transmission areas (e.g. urban settings) no clear relationship has been found between malaria-specific morbidity and mortality on one hand and transmission intensity on the other hand (Trape et al., 1987; Bonnet et al., 2002). Moreover, the incidence of acute malaria attacks among older children and adults is relatively more important than their...
young people compared to high transmission areas (Smith et al., 2006). Hence, the association between transmission dynamics and malaria burden is influenced by local determinants, including agro-ecological, behavioural, demographic and socioeconomic factors.

Recent studies have investigated the relationship between agricultural activities, and entomological and clinical parameters of malaria in several African countries. A study carried out in the Savannah region of northern Côte d'Ivoire found no association between the incidence of malaria and different rice farming systems (Henry et al., 2003). In central Côte d'Ivoire, changes in irrigated rice farming significantly impacted on malaria transmission dynamics (Koudou et al., 2005, 2007). In Mali, close proximity of villages to rice irrigation perimeters and the numbers of Anopheles gambiae showed a positive association (Diuk-Wasser et al., 2007). Irrigated rice farming resulted in a significant increase of Plasmodium prevalence rates in Kenya and Madagascar (Githiko et al., 1993; Marrama et al., 1995). Other studies found that malaria transmission, prevalence rates and the number of presumptive and clinical malaria episodes were not related to agricultural activities, but instead to the season (Dossou-Yovo et al., 1995, 1998; Sissoko et al., 2004).

In the study presented here, we investigated whether changes in agricultural activities have an effect on Plasmodium prevalence rates and the dynamics of presumptive and clinically confirmed malaria episodes. Our study was carried out in two villages of central Côte d'Ivoire that are characterized by different agricultural activities. Emphasis was placed on clinical illness, as reported at dispensaries, and parasite rates in children aged ≤15 years, determined by repeated cross-sectional surveys. Malaria transmission was investigated through entomological surveys with details presented elsewhere (Koudou et al., 2005, 2007).

2. Materials and methods

2.1. Study area

Details of the study area have been reported previously (Girardin et al., 2004; Koudou et al., 2005, 2007; Essé et al., 2008). In brief, the study was carried out in the villages of Tiémélékro (geographical coordinates: 6° 50' N latitude, 4° 17' E longitude) and Zatta (6° 88' N, 5° 39' E), both located in central Côte d'Ivoire (for a map of Côte d'Ivoire and the two study villages see: Koudou et al. (2007) and Essé et al. (2008)). The mean annual precipitation in the area is slightly above 1000 mm, and the mean annual temperature is 26°C. There are two seasons; a rainy season between May and October and a dry season between November and March.

The main agricultural activity in Zatta is irrigated rice farming, facilitated by an irrigation system with a size of 36 ha that has been established in 1997. This rice perimeter is located in close proximity to residential houses. Irrigation was interrupted in 2003 and 2004 because of a farmers’ conflict over land. In 2005, irrigated rice farming was again practiced. The entomological inoculation rate (EIR) for the years 2002, 2003 and 2005 has been estimated at 789, 38 and 295, respectively (Koudou et al., 2005, 2007). In Tiémélékro, subsistence farming is the primary agricultural activity, but there is growing cash crop production (e.g. intensive vegetable farming with cabbage, okra and tomato). The EIR in 2002, 2003 and 2005 was 233, 342 and 572, respectively (Koudou et al., 2005; 2007).

2.2. Ethical approval and informed consent

Our study was cleared by the institutional research commission of the Centre Suisse de Recherches Scientifiques (Abidjan, Côte d'Ivoire). Ethical approval was granted by the Ministry of Public Health in Côte d'Ivoire and the study was an integral part of the research component of the national malaria control programme. The heads of household in Tiémélékro and Zatta were informed and the parents or legal guardians of participating children signed a written informed consent sheet. Patients with malaria-related symptoms who presented at the dispensaries were treated free of charge according to the national malaria policy (i.e. artesunate plus amodiaquine combination therapy used as first-line antimalarials at the time of the study).

2.3. Cross-sectional parasitological surveys

Repeated cross-sectional surveys were carried out in the study villages to assess malaria parasitaemia and clinical malaria in children aged ≤15 years. The first survey was done in June 2002. In 2003, two surveys were carried out in Zatta and three in Tiémélékro. The planned June 2003 survey in Zatta had to be abandoned because of tightened security issues in parts of Côte d'Ivoire at the time. Whilst no surveys were carried in 2004, in the following year, three surveys were conducted in each village.

The research team first worked in the primary schools and all children aged between 7 and 15 years from randomly selected classes were invited for a finger prick blood sample. Next, mothers and caregivers of under 7-year-old children were invited to accompany their children to a designated community location where a blood sample was taken from each child.

Thick and thin blood films were prepared on microscope slides. The slides were air-dried prior to transfer to a nearby laboratory where they were stained with Giemsa for 45 min. The slides were examined by the same experienced laboratory technician throughout the study under a microscope at high magnification. Plasmodium species and gametocytes were identified and counted against 200 leucocytes. When less than 10 parasites were found, reading was continued for a total of 500 leucocytes. Parasitaemia was expressed by the number of parasites per µl of blood, assuming for a standard count of 8000 leucocytes/µl blood. For quality control, 10% of the slides were randomly selected and re-examined by a second senior technician.

In our study, fever was defined when an individual had an axillary temperature >37.5°C. Clinical malaria was defined as fever plus parasitaemia (Smith et al., 1994). Particular emphasis was placed on clinical cases with a parasitaemia >5000 parasites/µl blood. The latter threshold has been chosen after comparing the proportions of fever cases and asymptomatic carriers for different classes of parasite density (Gaye et al., 1989). Subjects with malaria-related symptoms (e.g. headache) plus axillary temperature >37.5°C were given artesunate plus amodiaquine (the respective first-line antimalarial treatment at the time of the study) and paracetamol.

2.4. Monitoring of presumptive malaria cases at dispensaries

The public health nurses at the dispensaries in each of the two study villages recorded all presumptive malaria cases from January 2002 to December 2005. Blood samples were taken from these individuals, and examined by the same experienced laboratory technician who read the slides from the cross-sectional surveys. The proportion of cases with parasitaemia was determined.

2.5. Statistical analysis

Data were analysed in STATA version 9.0 (STATA Corporation, College Station, USA). A chi square (χ²) test was used to compare malaria prevalence rates in different age groups, villages and subsequent surveys. Prevalence rates were averaged for the years 2003 and 2005 and then compared. Comparison was also
made between the number of presumptive and clinically confirmed malaria episodes, stratified by village and year of survey. A Poisson regression model was employed to assess the incidence risk ratio (IRR) of malaria transmission on the annual number of presumptive malaria cases, and to investigate whether the annual number differed significantly between the two villages and over time. A 5% significance level was used.

3. Results

3.1. Malaria parasite infection rates

Fig. 1 shows the timing of the cross-sectional surveys and the number of children examined in each survey. The predominant malaria parasite was *P. falciparum*. Its frequency among positive blood films obtained during the cross-sectional surveys was above 90% and in one survey it reached a level of 97.9%. Single infections with *P. ovale* were found in 2.6–4.3% of the positive slides. Mixed species infections with *P. falciparum* and *P. malariae* ranged between 0.8 and 4.2%. Neither *P. ovale* nor *P. vivax* single infections were diagnosed throughout the study.

The annual gametocyte rates in Tiémélékro, in 2003 and 2005, were 3.8 and 4.6%, respectively. The respective rates in Zatta were 6.1 and 5.8%.

3.2. *P. falciparum* prevalence rates

Table 1 summarises the results of the *P. falciparum* prevalence rates obtained during the cross-sectional surveys, stratified by age (≤2, 3–6 and 7–15 years). In both villages, the peak prevalence of *P. falciparum* was generally observed in children aged 3–6 years. There were four exceptions: in Tiémélékro, the peak prevalence of *P. falciparum* during the May 2005 survey was found in the youngest age group (≤2 years) and in the June 2003 survey in the age group 7–15 years, whereas in Zatta, the highest prevalence in the baseline survey (June 2002) and the second last survey (May 2005) was observed in children aged 7–15 years.

In June 2002, similarly high *P. falciparum* prevalence rates were observed in Zatta (85.4%) and Tiémélékro (86.1%). In Zatta, a significant decrease in the mean *P. falciparum* prevalence rate occurred from 2002 to 2003 (58.4%; χ² = 42.33, degree of freedom (df) = 1; P < 0.001). There was a significant increase from 2003 to 2005 (66.0%; χ² = 14.78, df = 1, P = 0.002). In Tiémélékro, the *P. falciparum* prevalence rate in June 2003 (78.2%) was significantly lower than during the June 2002 survey (χ² = 4.92, df = 1; P = 0.027). The annual *P. falciparum* prevalence rate decreased significantly from 2003 (70.7%) to 2005 (60.4%; χ² = 17.27, df = 1; P < 0.001).

3.3. Fever cases and asymptomatic carriers, stratified by parasite density

Table 2 shows how many of the children examined with parasitaemia in the 2003 surveys were either asymptomatic carriers or presented with a fever. The data are stratified into three parasitaemia levels (<1000, 1000–5000 and ≥5000 parasites/μl blood). There was a strong seasonal variation in the proportion of fever cases among individuals with parasitaemia. In Zatta, for example, the proportion of fever cases among *Plasmodium*-positive individuals was significantly higher towards the end of the rainy season (August) when compared to the dry season (March) (22.1% versus 9.9%; χ² = 9.90, df = 1; P = 0.002). In Tiémélékro, considerably higher frequencies of fever cases among *Plasmodium*-positive individuals were recorded during the peak rainy season in June (27.3%) and towards the end of the rainy season in August (25.5%) when compared to the dry season in March (15.9%; P < 0.05 for both comparisons).

In Zatta, all individuals with a high level of parasitaemia (≥5000 parasites/μl blood) presented with a fever, accounting for a highly significant difference between the proportion of asymptomatic carriers and fever cases in this parasitaemia class (P < 0.001). Similarly,
there was a significant association between the fever cases and high parasitaemia in the three surveys carried out in 2003 in the village of Tiémélékro (P < 0.05). No statistically significant difference was found in children with lower parasitaemias (1000–5000 parasites/μl of blood), neither in Zatta (March: χ² = 1.53; df = 1; P = 0.216) nor in Tiémélékro (March: χ² = 0.18; df = 1; P = 0.671, June: χ² = 2.23; df = 1; P = 0.135 and August: χ² = 0.001; df = 1; P = 0.973).

The majority of fever cases examined positive for Plasmodium after blood examination were observed among children below the age of 6 years during or at the end of the rainy season.

3.5. Annual variation of presumptive cases and malaria transmission

Figs. 2 and 3 present the monthly number of presumptive malaria cases per 1000 inhabitants recorded by the local nurses in the two study villages from January 2002 to December 2005. In Zatta, 966, 812, 693 and 884 presumptive cases were recorded in 2002, 2003, 2004 and 2005, respectively. The annual number of presumptive malaria cases decreased significantly by 15.1% and 14.7%, respectively, from 2002 to 2003 (IRR = 0.841, P < 0.001) and from 2003 to 2004 (IRR = 0.853, P = 0.002). An opposite trend was observed from 2004 to 2005: the number of presumptive malaria cases increased significantly by 27.5% (IRR = 1.276, P = 0.001). The monthly number of presumptive cases was not related to the monthly number of infective bites per person (IRR = 0.994, P = 0.827).

In Tiémélékro, the yearly numbers of presumptive malaria cases were 2089, 1858, 1655 and 1541. Thus, we observed significant decreases in the yearly number of presumptive cases by 11.1% from 2002 to 2003 (IRR = 0.889, P < 0.001), 9.0% from 2003 to 2004 and 3.4% from 2004 to 2005. No statistically significant difference was observed between the proportions of clinical malaria cases among children aged below 6 years during or at the end of the rainy season.
Fig. 2. Monthly number of presumptive malaria cases per 1000 inhabitants (●) and monthly number of infective bites per person (□) from 2002 to 2005 in Tiémélékro, central Côte d’Ivoire.

IRD = 0.910, \( P = 0.005 \) and 8.9\% from 2004 to 2005 (IRD = 0.911, \( P = 0.008 \)). As in the case of Zatta, the monthly number of presumptive cases was not related to the monthly number of infective bites per person (IRD = 1.007; \( P = 0.776 \)).

4. Discussion

An important finding of our study is that in Zatta, where irrigated rice farming was interrupted in 2003/2004, \textit{Plasmodium} prevalence rates and the number of presumptive malaria cases decreased. This observation is corroborated by a significant decrease in the EIR from 2002 to 2003 (Koudou et al., 2005) and a significant increase from 2003 to 2005 (Koudou et al., 2007). However, our study has a couple of shortcomings that are worth mentioning. First, prevalence rates were assessed in children below the age of 15 years, hence covering a large age range, whereas previous studies in highly endemic areas of Africa have often focussed on children aged below 5 years (Smith et al., 2001). Second, not all of the planned entomological surveys could be carried out, which is partially explained by political unrest during part of the study (Koudou et al., 2005, 2007). Third, the number of presumptive malaria cases was assessed passively by nurses working at the local dispensaries. It is conceivable that a considerable number of additional malaria cases would have been discovered using a more active surveillance system.

Notwithstanding these shortcomings, it was found before that irrigated rice cultivation is associated with elevated malaria prevalence rates, as well as high numbers of presumptive malaria cases, as seen in Burundi (Coosemans, 1985), Kenya (Githeko et al., 1993) and Madagascar (Marrama et al., 1995). However, research carried out in Tanzania showed that irrigated rice farming was not associated with a higher risk of malaria. One important reason for this observation is that farmers engaged in irrigated rice farming have the opportunity to gain some extra money, part of which is spent for protective measures against malaria. A reduced risk of malaria despite enhanced rice production has been termed ‘paddies paradox’ (Ijumba and Lindsay, 2001). A recent literature review concluded that there was indeed no clear association between irrigated rice agriculture and malaria (Keiser et al., 2005).

Socioeconomic data at the household level and detailed information on knowledge, attitude, practices and beliefs of malaria and its control are available for the two study villages, and have

Fig. 3. Monthly number of presumptive malaria cases per 1000 inhabitants (●) and monthly number of infective bites per person (□) from 2002 to 2005 in Zatta, central Côte d’Ivoire.
been published elsewhere (Girardin et al., 2004; Essé et al., 2008). Malaria prevention was strongly influenced by socioeconomic status, and the methods used for prevention depended on their perceived cost. For example, the wealthiest families reported the use of bed nets, perceived as expensive in this setting, more often than their poorer counterparts (Essé et al., 2008).

In Tiémélékro, where subsistence farming is the main agricultural activity, we observed a decrease in malaria prevalence rates, despite a significant increase in EIR from 2002 to 2003, and from 2003 to 2005 (Koudou et al., 2005, 2007). Our previous entomological investigations in this village revealed that *Anopheles funestus* is the main malaria vector. In the Savannah part of Senegal, this vector was responsible for *P. malariae* transmission during the rainy season (Trape et al., 1994). The observed reduction in the transmission of *Plasmodium* by *An. gambiae* might be explained by changes in agricultural activities. In fact, after 2003, most of the farmers were engaged in the traditional production of rice and some intensive vegetable farming. In addition, they started to cultivate cash crops such as cocoa, coffee and rubber because the price of these crops was high and stable. As showed recently, agricultural trenches, irrigation wells and rice paddies are the main *Anopheles* breeding sites in urban settings of West and East Africa (Sattler et al., 2005; Mattheys et al., 2006). A shift towards cash crops might have contributed to a reduction in the number of *An. gambiae* breeding sites in Tiémélékro, which might explain the lower prevalence rate of *Plasmodium* in 2005.

In 2003, though the annual EIR of Tiémélékro was 11-fold higher than that observed in Zatta (Koudou et al., 2005), the differences between the proportions of diagnosed and confirmed malaria cases recorded in both villages were not significant. Similar observations were made in a rural area of Cameroon, where, despite a 10-fold difference in the annual EIR recorded between two study areas, there was no significant difference in the malaria prevalence rates and the annual number of clinical malaria cases (Bonnet et al., 2002). It has been suggested that there is no marked variation in malaria morbidity according to transmission when the EIR exceeds 1 (Trape and Rogier, 1996). Thus, to significantly reduce the number of clinical malaria cases in the study villages, it seems that the number of infective bites per person per year would need to be reduced drastically. It is conceivable that in high transmission areas such as Zatta and Tiémélékro in central Côte d’Ivoire, rigorous use of personal protection against mosquito bites could have a beneficial effect on morbidity rates in children below the age of 5 years. At present, however, the use of protective measures against mosquito bites, particularly sleeping under a bed net, is very low (Essé et al., 2008).

The malaria prevalence rates observed in Zatta between three different age groups of children ≤ 15 years in the surveys conducted in 2003 and 2005 were similar. In Tiémélékro, however, there were significant differences between prevalence rates according to age. The highest prevalence rates were usually observed among children below the age of 7 years. As mentioned before, the results observed in Zatta are consistent with previous studies carried out in epidemic areas, where all age groups are at similar risk of malaria (Gazin, 1991). In contrast, in endemic areas, malaria prevalence rates usually decrease with age (Chippaux et al., 1991). Our findings are in agreement with previous studies carried out in Savannah areas of northern Côte d’Ivoire, which showed that the proportions of high parasite densities decreased with age (Dossou-Yovo et al., 1998; Henry et al., 2003).

In central Côte d’Ivoire, *P. falciparum* is the predominant malaria species, and the proportion of *P. malariae* infection rates and that of mixed species infections are low. The predominance of *P. falciparum* and low levels of mixed *P. falciparum* and *P. malariae* infections have also been observed elsewhere in Côte d’Ivoire (Dossou-Yovo et al., 1998; Anonymous, 2001; Henry et al., 2003; Silué et al., 2008) and in neighbouring countries of Burkina Faso (Gazin et al., 1988) and Mali (Sissocko et al., 2004).

We conclude that in Zatta, from 2002 to 2003, the highly significant reduction in the annual EIR was paralleled by a significant reduction in the *Plasmodium* prevalence rate, and the proportions of presumptive and clinically confirmed malaria cases. Once irrigated rice farming was resumed, there was an increase in entomological and parasitological parameters of malaria. In Tiémélékro, despite the significant increase in the EIR from the year 2002 to 2005 (Koudou et al., 2005, 2007), the malaria prevalence rates, and the presumptive and clinical malaria cases decreased. Hence, the reduction of malaria transmission in endemic areas does not necessary reduce the incidence of clinical malaria episodes (Charwood et al., 1998), highlighting the complex relationship between these parameters. Hence, a better understanding of the local epidemiology of malaria might assist in tailoring setting-specific control interventions that are needed to reduce the intolerable burden of malaria in rural parts of Africa.

**Acknowledgements**

We thank the village authorities of Tiémélékro and Zatta, the health personnel of Dimbokro and Yamoussoukro and the participating children and their parents for their commitment. Special thanks are addressed to Mahamadou Traoré, senior technician, for help with the field work and the preparation and reading of the malaria slides. This study received financial support from the ‘Fonds Ivoiro-Suisse de Développement Economique et Social’ (FISDES), the Swiss Academy of Natural Sciences (SANW), the Swiss Federal Commission for Fellowships for Foreign Students (CFBEE) and the National Centre of Competence in Research (NCCR) North–South, programme entitled “Research Partnerships for Mitigating Syndromes of Global Change”. J. Keiser (project no. PPOOA–114941) and J. Utzinger (project no. PPOOB–102883 and PPOOB–119129) are grateful to the Swiss National Science Foundation for financial support.

**References**


