BASELINE IMMUNITY OF THE POPULATION AND IMPACT OF INSECTICIDE-TREATED CURTAINS ON MALARIA INFECTION

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Abstract. It has been shown that insecticide-treated bed nets or curtains may reduce morbidity and mortality from malaria in hyper-holoendemic areas of sub-Saharan Africa. This protection could partially depend on the transitory imbalance between the anti-malaria immunity acquired by the population before the intervention and the lowered sporozoite load resulting from the anti-vector measure. To verify if the efficacy of the intervention is influenced by the baseline immune status of the population, we compared the protective effect of permethrin-impregnated curtains (PIC) against malaria infection among groups with different baseline levels of anti-malaria immunity. We analyzed the impact of PIC on the Plasmodium falciparum infection rate in two rural villages of Burkina Faso inhabited by three ethnic groups: the Fulani, Mossi, and Rimaibé. These have been previously shown to differ for several malarialogic indices, with the Fulani being characterized by lower infection and disease rates and by higher immune response to P. falciparum with respect to the other ethnic groups. The PIC were distributed in June 1996 and their impact on malaria infection was evaluated in groups whose baseline levels of immunity to malaria differed because of their age and ethnic group. Age- and ethnic-dependent efficacy of the PIC was observed. Among the Mossi and Rimaibé, the impact (parasite rate reduction after PIC installation with respect to the pre-intervention surveys) was 18.8% and 18.5%, respectively. A more than two-fold general impact (42.8%) was recorded in the Fulani. The impact of the intervention on infection rates appears positively correlated with the levels of anti-malaria immunity. Since decreased transmission entails a reduction of immunity, the efficacy of the intervention in the long term cannot be taken for granted. The expected complementary role of a hypothetical vaccine is stressed by these results, which also emphasize the importance of the genetic background of the population in the evaluation and application of malaria control strategies.

The most recent estimates of the global malaria morbidity and mortality are 300–500 million clinical cases and 1–2.8 million deaths per year. The parasite drug resistance, the constraints in the use of anti-vector measures associated with limited resources, and capabilities for program implementation represent the main obstacles in malaria control. The very high transmission rates in sub-Saharan Africa present a major challenge for effective interventions. Several studies have recently shown the impact of insecticide-impregnated bed nets or curtains on morbidity and mortality in the short-term, whereas no data are yet available on the long term. The possibility exists that in areas characterized by very high inoculation rates the impact on morbidity and mortality is not sustained. The initial protection could be mostly associated to the rapid reduction of transmission after the installation of the control measure and to the consequent imbalance between the high baseline immunity of the population and the comparatively low sporozoite load resulting from the intervention. The benefit of this initial favorable imbalance would be only transitory if the acquired immunity against malaria is short term. With the aim of contributing to the analysis of this strategic issue, we examined the relation between the immune status and the protective efficacy of permethrin-impregnated curtains (PIC). The impact of the vector control measure on P. falciparum infection rates was compared among individuals belonging to different age classes and to sympatric ethnic groups characterized by different levels of anti-malaria immunity.

MATERIALS AND METHODS

Study area and subjects. The study was carried out in two rural villages 35 km northeast of Ouagadougou, the capital city of Burkina Faso, in a shrubby savanna of the Mossi plateau (about 300 meters above sea level) belonging to the Sudan-Sahelian ecoclimatic zone (isohyets = 600–900 mm). A description of the area has been reported elsewhere. The two villages, Barkoumbilen and Barkoundouba, are respectively inhabited by a Mossi-Rimaibé community (about 1,300 inhabitants) and by a Fulani-Rimaibé community (about 600 inhabitants). The Mossi and Rimaibé are Sudanese negroid populations with a long tradition of sedentary farming; the Fulani are nomadic pastoralists partly settled and characterized by non-negroid features of possible Caucaoid origin. Both communities have settled in the area for more than 30 years. Very intense P. falciparum transmission is recorded during the June–October rainy season, frequently reaching mean sporozoite inoculation rates well above one infective bite/person/night. The main malaria vectors are Anopheles gambiae, An. arabiensis, and An. funestus. Entomologic surveys conducted in the study area during 1994 and 1995 showed similar P. falciparum inoculation rates for the three ethnic groups.

Malarialogic cross-sectional surveys performed in the two villages during 1994 and 1995 showed considerable variations in the inoculation rates between the two high transmission seasons but substantial stability of the parasitologic indices. In all surveys and in all age groups the Fulani had lower P. falciparum parasite rates compared with the Mossi and Rimaibé. The differences were particularly marked in the older age groups and in the period of lower transmission. The comparative analysis of the humoral immune responses against P. falciparum antigens in the three ethnic groups have also been reported. For all antigens tested (circumsporozoite protein, thrombospondin-related...
FIGURE 1. *Plasmodium falciparum* inoculation rates based on indoor vector collections in the compounds of the three ethnic groups (Mossi, Rimaibé, and Fulani) in the Barkoundouba area of Burkina Faso from August 1994 to October 1996. Permethrin-impregnated curtains were installed in June 1996.

**RESULTS**

**Entomology.** A total of 14881 *Anopheles* were collected: 7,277 in 1994, 6,977 in 1995, and 627 in 1996. The *P. falciparum* indoor inoculation rates in 1994, 1995, and 1996 are compared in Figure 1. The variation between 1994 and 1995 was probably due to differences in the amount and distribution of rainfalls (860 mm in 1994, 609 mm in 1995, and 637 mm in 1996). A striking reduction of the indoor inoculation rates was observed, as expected, after the installation of PIC (June 1996), with a similar impact in the three ethnic groups. The reduction can be safely estimated to more than 90% of the levels recorded in the two previous years. The decrease of transmission was due to a decrease in the mean seasonal daily indoor human biting rate (5.9 in 1994, 4.0 in 1995, and 0.6 in 1996) and to a minor extent, to a lowering in the seasonal sporozoite indices (0.122 in 1994, 0.083 in 1995, and 0.054 in 1996). Consequently, the outdoor transmission was presumably much less affected.

**Parasitology.** The results of the three parasitologic surveys performed in August 1994, 1995, and 1996 analyzed by ethnic and age group are presented in Table 1. In 1995, in spite of lower values of inoculation rates compared with 1994, a small but significant increase in the *P. falciparum* parasite rates was recorded. The overall *P. falciparum* parasite rate was 70.7% (556 of 786) in August 94 and 76.3% (907 of 1,189) in August 95 (chi square, Yates’-corrected *P* = 0.007). A remarkable reduction in the *P. falciparum* parasite rate was observed in August 96 after PIC installation; the *P. falciparum* parasite rate was 54.2% (396 of 731) with a general impact of 26.9% (chi square, Yates’-corrected, *P* < 0.0001) compared with the mean 1994–1995 parasite rate.


As shown in Figure 2, the general impact on the *P. falciparum* parasite rate was not uniformly distributed by age and ethnic group. In all three ethnic groups a positive correlation was recorded between age and PIC efficacy (Pearson’s *r* and *P* with 3 df = 0.93 and 0.02 in the Mossi; 0.99 and 0.01 in the Rimaibé; 0.95 and 0.01 in the Fulani; total sample with 13 df = 0.85 and 0.0001). As to the ethnic group variable, the impact observed in the Fulani (42.8%)
was more than two-fold as compared with the Mossi and Rimaïbè (18.8% and 18.5%, respectively). No evident inter-ethnic differences in the reduction of the PPD were noted; on the contrary, intra-ethnic age dependent differences in the reduction of the PPD were noted in each ethnic group; an obvious decrease of the PPD was observed in the 0–10 years age group of the Mossi and Rimaïbè and in the 0–5 years age group of the Fulani, whereas no significant variations were recorded in higher age classes.

**DISCUSSION**

The influence of the immune status on the efficacy of vector control measures reducing the sporozoite inoculation rates, can be evaluated by comparing the protective effect on malaria infection among groups with different baseline levels of anti-malaria immunity, living in the same epidemiologic context. Following this rationale, we analyzed the impact of PIC on *P. falciparum* parasite rates in individuals of different age, belonging to three sympatric ethnic groups exposed to the same level of transmission but characterized by different baseline levels of anti-malaria immunity. In each ethnic group a marked association between age and efficacy was observed, and, in spite of similar reduction of the indoor inoculation rates for the three ethnic groups, striking inter-ethnic differences in the protective effect were recorded. In the Fulani, who are characterized by higher humoral responses to *P. falciparum*, we observed a protective effect more than two-fold higher than in the Mossi and Rimaïbè. The different impact according to ethnic and age group could not be interpreted in terms of parasite exposure heterogeneities. The three ethnic groups had similar pre-intervention inoculation rates and the reduction afforded by PIC was equivalent. Exposure could also be a confounder for age differences, but only if adults were less exposed than children while the reverse appears to be the case. Thus, two variables, i.e., age and ethnic group, independent from each other but both associated with the immune status, influenced concurrently the impact of PIC on malaria infection. These findings support the view of a direct association between the efficacy of PIC (and possibly of any measure aimed at reducing malaria transmission), and the pre-intervention immune status of the population. If this is the case, it may be expected that the post-intervention conspicuous reduction of transmission, entailing a progressive decay of immunity to malaria, may gradually reduce the overall protective effect. The immediate impact on malaria morbidity and mortality obtained in large-scale trials of insecticide-treated fabrics might have been the consequence of a transitory favorable imbalance between the immune status of the population and the suddenly lowered transmission. However, this impact could fade off with time, as the imbalance disappears. Though not conclusive, the results of the Burkina Faso large-scale PIC trial point in this direction. The similar incidence of severe malaria in epidemiologic contexts characterized by largely different levels of transmission also supports the hypothesis that the immune status tends to be proportional, over a wide range, to the intensity of transmission.

The association between immune status and efficacy of vector control measures boosts the potential value of a hypothetical integrated strategy combining insecticide-treated fabrics and a vaccine. This may be particularly true for a pre-erythrocytic vaccine applied in areas of very high transmission, where this single tool may be deemed to be insufficient. Finally, the present data show that in the experimentation of malaria control strategies, the possible role of human heterogeneities in the response to the disease should be carefully considered; actually, in our case, the same control strategy, applied to populations with different genetic backgrounds in the same epidemiologic context, resulted in different impact values. The difference we observed is probably a consequence of genetically-based interethnic heterogeneities in the immune reactivity to malaria; in other situations, sociocultural factors may also influence the efficacy of a control measure.
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