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Malaria incidence during early childhood in rural Burkina Faso: Analysis of a birth cohort protected with insecticide-treated mosquito nets

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ABSTRACT

Background: Even in the high transmission areas of sub-Saharan Africa (SSA), the incidence of falciparum malaria varies greatly depending on factors such as age, rainfall pattern, distance to breeding places, quality of houses, and existing vector control measures. Insecticide-treated mosquito nets (ITN) have now become the vector control standard in nearly all of SSA. This study aims to describe and analyse the incidence of malaria in a cohort of young children protected with ITN in rural West Africa.

Methods: Data of a subsample from a large community trial in rural north-western Burkina Faso consisting of 420 children were analysed. The main aim of the trial was to evaluate the long-term effects of ITNs in two groups of new-borns; Group A was protected with ITN from birth onwards while Group B was protected only from month six onwards. The primary objective of this study was to describe malaria incidence in detail with an analysis of the impact of potentially relevant determinants of malaria incidence, in particular age, sex, ITN protection, village, month and season as secondary objective. Bivariate negative binomial regression analysis was used to calculate incidence rate ratios of malaria incidence. Moreover, relevant variables were included in a multivariate negative binomial regression model to examine possible risk factors for malaria.

Results: Out of the 420 study children 387 (92.1%) developed a total of 1822 falciparum malaria episodes; the malaria incidence rate was 7.6 per 1000 child days. Group A children had lower malaria incidence rates compared to group B, but only in early infancy. Malaria incidence varied significantly between villages and increased with age, but no sex-specific differences were observed; these findings were confirmed in the multivariate analysis. Malaria incidence peaked sharply towards the end of the rainy season in September but there were no differences in the seasonal pattern by study group.

Conclusions: The study, carried out in a high-transmission West African area, shows that malaria incidence remains high in spite of maximum ITN coverage.

1. Background

Global estimates of the World Health Organization (WHO) have recently shown a reduction of malaria incidence of around 40% between 2000 and 2015, with mortality rates roughly halved during this time period (WHO, 2015a). Despite these promising developments, malaria remains the fourth major cause of death in children under 5 years, with most of these deaths occurring in sub-Saharan Africa (SSA) (WHO, 2015a). However, developments were not equal over SSA with a number of high-transmission countries having shown no significant decrease in the malaria burden despite increased control efforts (WHO, 2015a).

Over the last 20 years, insecticide-treated mosquito nets (ITNs) have become the most widespread vector-control intervention in malaria-endemic areas (Bhatt et al., 2015). ITN programs are associated with a reduction in all-cause childhood mortality around 20% and in malaria morbidity around 50% (Müller, 2011). However, ITN coverage is not complete in vulnerable populations and compliance is not always guaranteed (WHO, 2015a; Müller, 2011). Despite such shortcomings, it has been shown that ITN programmes largely reduce malaria transmission intensity even in the high transmission areas of SSA (Müller, 2011).

The risk for malaria disease depends on many factors, ranging from more proximal determinants such as individual behaviour and access to

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health services to more distal determinants such as environmental changes and poverty (Müller, 2011). While the beneficial effects of ITNs on the malaria burden were already confirmed in numerous studies (Lindblade et al., 2015; Lengeler, 2004; Eisele et al., 2010; Chitnis et al., 2010), future research will focus more on the sustainability of ITN programmes and on their effects at the local level under consideration of different biological, social and environmental factors (Bhatt et al., 2015).

There are large variations in malaria transmission pattern in SSA, ranging from areas with unstable transmission (e.g. the North and the South of the continent and highland areas) to hyper/holoendemic areas (e.g. in the savannah areas of West and Central Africa) (Müller, 2011). Burkina Faso is an example of a continuously high malaria burden in SSA despite a major roll-out of control interventions (De Allegri et al., 2013; Louis et al., 2015). Malaria has remained the main cause of death in children under 5 years in this country (WHO, 2015b; Hammer et al., 2006).

This study aims at describing the malaria incidence in young children in a cohort of young children enrolled into an ITN trial. As secondary objective, potentially relevant determinants of malaria incidence, in particular age, sex, ITN protection, village, month and season were examined.

2. Methods

2.1. Study design

This is a sub-group analysis of data from a birth cohort enrolled for a randomized controlled trial (RCT) on the long-term effects of ITN protection in an area of high malaria transmission in Burkina Faso (Müller et al., 2006; Louis et al., 2012).

In brief, neonates from 41 villages of the rural research zone of the *Centre de Recherche en Santé de Nouna* (CRSN) were randomized either to ITN protection from birth or to ITN protection from the age of six months until their fifth birthday (Fig. 1). Primary outcomes of the main trial were all-cause mortality in all study children (n = 3387) and falciparum malaria incidence in a subsample of the study population (n = 420). This subsample forms the study population for the analysis presented in this paper.

2.2. Study area

The study took place in the study area of the CRSN in Nouna Health District (NHD), north-western Burkina Faso. This is an area of dry orchid savannah mainly populated by subsistence farmers of different ethnic groups. The CRSN is situated in Nouna Town, the capital of NHD. Malaria has been characterised as hyper/holoendemic in this part of the country (Traoré, 2003). However, this was before a major out roll-out of ITNs took place in the study area and the whole of Burkina Faso.

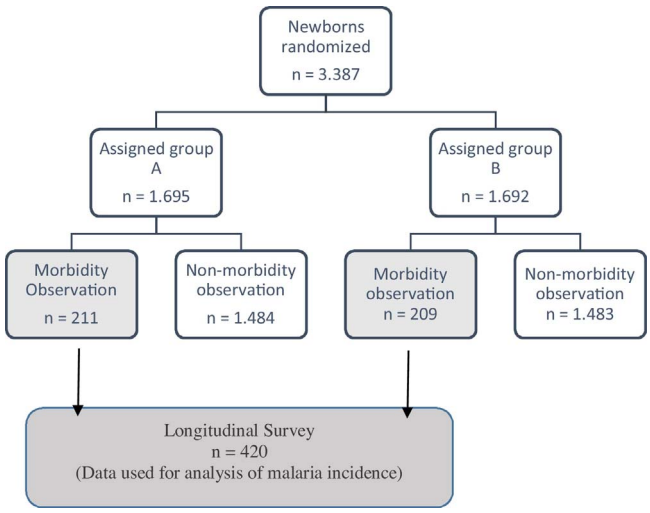

Fig. 1. Trial profile (Müller et al., 2006).

2.3. Study procedures

The 420 children of the subsample from the six sentinel villages under intense surveillance were visited every second day by trained village-based field staff to interview the families and to examine the study children. Axillary temperature, symptoms reported by parents, as well as received treatments were investigated during the visits and documented in a structured questionnaire. In cases of increased temperature (≥ 37.5 °C) or a history of fever in the past 48 h, the fieldworkers were instructed to take finger-prick blood samples and to prepare thick and thin blood films. Ill children received either adequate treatment according to national guidelines or were referred to governmental health services in case of severe illness. Study nurses performed monitoring visits twice-weekly. Blood films were transported under controlled conditions to the CRSN laboratory in Nouna Town. Slide reading was done by two experienced laboratory technicians supervised by the head of the laboratory, who decided in case of discordance. To assure quality, 10% of the blood films were randomly selected for re-examination at the laboratory at Heidelberg University resulting in 100% concordance for all slides with a parasite density above 5000 per µl blood. In slides with lower parasite densities, 7% were false-negatives and 11% false-positives. The collected study data was entered into Microsoft Access, version 97. Data management procedures were supervised by scientists from the Heidelberg University to assure high data quality (Müller et al., 2006).

2.4. Statistical analysis

For this study, incidence rates per 1000 child days were calculated for children in both study groups, with separate calculations by sex and by village. Moreover, all analyses were done for three defined age periods (0–5 months, 6–12 months and > 12 months) to describe the malaria incidence in this birth cohort in more detail. For hypothetical testing of a significant difference in malaria incidence of children not protected by mosquito nets during the first months of life (study group B) compared to children with a protection by the intervention from birth (study group A), we used negative binomial regression instead of Poisson regression to account for over-dispersed count outcome variables and estimated a possible difference in malaria risk with the calculation of Incidence Rate Ratios between the two study groups. Additionally, we included the variables study group, sex and village in a multivariable model to investigate possible risk factors for malaria within each age period. The log observation time was used as an offset term in the regression analysis.

To avoid inclusion of recrudescent malaria episodes, 20 days for each defined falciparum malaria episode were subtracted from the individual observation time.

We delineated the temporal dynamics of malaria incidence during the observation period with a detailed listing of the number of malaria episodes per each study month. The respective malaria definition of the previous study was used: “A malaria episode was defined as fever (axillary temperature (≥37.5 °C) accompanied by ≥5000 *P. falciparum* parasites per µl) in the presence or absence of *P. malariae* or *P. ovale* parasites, with no other obvious cause of fever.” (Müller et al., 2006).

All analyses were done with SAS® Studio (University Edition).

2.5. Ethical aspects

As this study is based on a secondary analysis of existing data from a clinical study which had already received ethical approval from all relevant ethical committees, no further ethical approval was needed.