Interventions, surveillance and monitoring of malaria in pregnancy in rural southern Malawi
Msyamboza, K.P.

Citation for published version (APA):

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SUMMARY

Malaria in pregnancy is a significant cause of maternal and infant morbidity and mortality. In sub-Saharan Africa, coverage and use of the three effective interventions for prevention and control of malaria in pregnancy; intermittent preventive treatment with sulfadoxine pyrimethamine (IPTp-SP), case management and vector control (insecticide treated nets or indoor residual spray) are generally lower than the recommended 60%. Alternative supplementary approaches of delivery, monitoring and evaluation could improve coverage and use of these interventions, particularly IPTp-SP.

Chapter 1: General Introduction and study objectives

Background information on the burden of malaria in pregnancy and their increased risk of malaria, consequences of malaria in pregnancy and evidence on the effectiveness of IPTp-SP is presented. Evidence is also provided on the effectiveness of IPTp-SP in areas with high (>10%) prevalence of HIV and/or high (>25%) resistance of SP in children with symptomatic malaria. Operational challenges for low IPTp-SP (≥2 doses) in the presence of high (>90%) antenatal care clinic coverage are highlighted. Study objectives are outlined.

Chapter 2: Community-based distribution of sulfadoxine-pyrimethamine for intermittent preventive treatment of malaria during pregnancy improved coverage but reduced antenatal attendance in southern Malawi

Objective: To evaluate the impact of a 2-year programme for community-based delivery of sulfadoxine-pyrimethamine (SP) on intermittent preventive treatment during pregnancy coverage, antenatal clinic attendance and pregnancy outcome.

Methods: Fourteen intervention and 12 control villages in the catchment areas of Chikwawa and Ngabu Government Hospitals, southern Malawi, were selected. Village-based community health workers were trained in information, education and counselling on malaria control in pregnancy and the importance of attending antenatal clinics and promoted these messages to pregnant women. In the intervention group community health workers also distributed SP to pregnant women.

Results: In the control area, coverage of intermittent preventive treatment during pregnancy (>2 doses) was low before (44.1%) and during the intervention (46.1%). In the intervention area, coverage increased from 41.5% to 82.9% (P < 0.01). Antenatal clinic attendance (>2 visits) was maintained in control villages at above 90%, but fell in intervention villages from 87.3% to 51.5% (P < 0.01). Postnatal malaria parasitaemia prevalence fell in women from both study areas during the intervention phase (P < 0.05). Increasing the coverage of intermittent preventive treatment during pregnancy to >40% did not significantly improve maternal haemoglobin or reduce low birthweight prevalence.

Conclusions: Better coverage of community-based intermittent preventive treatment during pregnancy can lower attendance at antenatal clinics; thus its effect on pregnancy outcome and antenatal attendance need to be monitored.
Chapter 3: Trends in pregnancy outcomes in Malawian adolescents receiving antimalarial and haematinic supplements

Objective: To describe pregnancy outcomes of adolescent and adult primigravidae receiving antimalarials and haematinic supplementation and compare findings with a survey in this area a decade earlier.

Methods: Data on antenatal attendance, uptake of intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP), place of delivery, birthweight, malaria, anaemia were collected from study sites (community) and health facility.

Results: Fewer adolescent than adult primigravidae received ≥2 IPTp-SP doses (66 vs. 77.2%, p < 0.001), although more attended for two or more antenatal visits (92.0 vs. 76.7%, p < 0.001). Only 24.1% of adolescent primigravidae attended for hospital delivery. Women resident in intervention sites receiving IPTp-SP community distribution were more likely to choose a community delivery (p < 0.01), and have higher uptake of IPTp-SP (p = 0.036) than women not resident in these villages. Postnatal malaria prevalence was low and did not differ by age or place of delivery. Postnatal anaemia and low birthweight prevalence were higher in adolescents with community deliveries. Maternal anaemia and low birthweight prevalence were lower amongst adolescents in this study compared to estimates from the same population a decade previously.

Conclusions: Adolescents had higher anaemia risk, lower IPTp-SP uptake than adults and under a quarter had a hospital delivery. Pregnancy outcomes improved compared to the survey a decade earlier. Monitoring and surveillance is required to reinforce to policy makers the need to improve adolescent coverage for available interventions.

Chapter 4: In-vivo parasitological response to sulfadoxine-pyrimethamine in pregnant women in southern Malawi

Background: Malaria in pregnancy is a significant cause of maternal and infant morbidity and mortality. Malawi adopted intermittent preventive treatment with sulfadoxine-pyrimethamine (SP) for the control of malaria in pregnancy in 1993.

Methods: We conducted a cross-sectional and prospective cohort study of women attending an antenatal care clinic at Montfort Hospital in the Lower Shire Valley, Malawi in order to determine the prevalence of malaria and anaemia at the first antenatal visit, and the rate of parasitological failure to SP in pregnancy.

Results: Of 961 pregnant women screened, 9% were parasitaemic, 77% had mild anaemia (Hb <11.0g/dl), 24% moderate anaemia and 6% had severe anaemia (<7.0g/dl). Malaria parasitaemia was significantly more frequent in primigravidae, the second trimester and in the post- rainy season (all p <0.05). Moderate anaemia (Hb ≤ 9.0g/dl) was significantly more common in adolescents and primigravidae (both p <0.05). In the in vivo follow up study, 6 of 77 women (7.8%) had parasitological failure at day 7, 8 of 73 (10.9%) women who completed the day 14 follow up had parasitological failure, and at day 28, 12 of 61 (19.7%). Parasitological failures were all R1 category except for one participant with R2 failure.

Conclusion: Anaemia prevalence was high at first antenatal visit. Parasitological failure to SP in pregnant women increased in this area from 5% in 1996 to 19.7% in 2004.
Chapter 5: Maternal anaemia as an indicator for monitoring malaria control in pregnancy in sub-Saharan Africa.

**Background:** Malarial anaemia is a major problem in many developing countries and often occurs more frequently in first pregnancies, as primigravidae are more susceptible to Plasmodium falciparum malaria and are at excess risk of malarial anaemia.

**Objective and methods:** To analyse the excess risk of anaemia in primigravidae as a potential indicator of malaria control and exposure in pregnant women living in sub-Saharan Africa. The sensitivity, specificity and predictive values for anaemia in first compared with later pregnancies are calculated for 27 studies from malarious and 7 studies from non-malarious areas.

**Results:** In malarious areas, the weighted odds ratio for excess anaemia (haemoglobin Hb <11 g/dl) in primigravidae compared with multigravidae for all studies was 1.34 (95% CI 1.14-1.58). At an Hb cut off below 8 g/dl, the weighted odds ratio was 1.79 (95% CI 1.52-2.10). In non-malarious areas, there was no increased risk of anaemia in primigravidae with Hb below 11 g/dl (OR 0.80; 95% CI 0.63-1.90) or below 8 g/dl (OR 0.82, 95% CI 0.51-1.28).

**Conclusions:** In view of the consistency of results across highly malarious areas compared with nonmalarious areas, maternal anaemia has the potential to be used for surveillance of malaria control in pregnancy. Based on the analysis, an anaemia nomogram is developed for use as a surveillance indicator in malarious areas in sub-Saharan Africa.

Chapter 6: Estimation of effectiveness of interventions for malaria control in pregnancy using the screening method.

**Background:** The evaluation of the effectiveness of antimalarial drugs and bed net use in pregnant women is an important aspect of monitoring and surveillance of malaria control in pregnancy. In principle the screening method for assessing vaccine efficacy can be applied in non-vaccine settings for assessing interventions for malaria control in pregnancy.

**Methods:** In this analysis field data on the proportion of placental malaria cases treated with two doses of sulphadoxine-pyrimethamine (SP) and the uptake of two doses of SP in the antenatal clinic was used in a case-coverage method to assess the protective effectiveness (PE) of intermittent preventive treatment with SP for malaria control in pregnancy. PE was assessed using placental malaria, low birthweight and maternal anaemia at delivery as outcome variables. The method was also applied to an evaluation of the protective effectiveness of self-reported use of impregnated bed nets (ITNs).

**Results:** Effectiveness was highest for reduction of low birthweight in multigravidae (87.2%, 95% CI, 83.2-91.3%). PE was lower for placental malaria (61.6% primigravidae, 28.5% multigravidae), and maternal anaemia (Hb < 8.0 g/dl, 37.8% primigravidae, 29.6% multigravidae). Estimates for PE of self-reported use of ITNs gave values for all three outcome parameters that were much lower than for SP use. For women of all parties effectiveness estimates for reduction of low birthweight were 22% (95% CI, 17.7-26.4), prevention of placental malaria (all types) 7.1% (95% CI, 4.4-9.8), prevention of active placental infection 38.9% (95% CI, 27.4-50.4), and for maternal anaemia 8.8% (95% CI, 0-20.0).

**Conclusions:** The case-coverage method could provide a useful and practical approach to routine monitoring and evaluation of drug interventions to control malaria in pregnancy and has potentially wide applications. Effectiveness estimates related to
reported ITN use in pregnancy may be less reliable. The method should be further evaluated using currently available data sets.

Chapter 7: Integrated sentinel surveillance of malaria, lymphatic filariasis and neglected tropical diseases in rural southern Malawi

Background: Malaria and lymphatic filariasis (LF) are global priority diseases because of their significant morbidity and mortality. These diseases share vectors presenting an opportunity for integration and co-implementation of effective vector control interventions.

Objective: To establish baseline database for integrated surveillance and monitoring of malaria and LF control in southern Malawi.

Methods: In preparation for the first mass drug administration for the LF elimination programme, a baseline survey was conducted in six sentinel sites in the southern Malawi, amongst adult participants and children aged over five years. A questionnaire was used to obtain data on socio-demographic factors, ownership and use of bed nets and previous ingestion of Ivermectin. Finger prick blood samples were collected between 22:00 hours to 01:00 hours for LF microscopy, malaria smears and haemoglobin estimation. Stool and urine samples were collected for examination of soil transmitted helminths and schistosomiasis.

Results: A total of 1,903 participants were enrolled. Bed net use was lower than ownership (17.4% vs 23.1%) and in some districts less than half of the nets were used. Prevalence of malaria parasitaemia, microfilaraemia, soil transmitted helminths and urinary schistosomiasis were lower than previously reported in the same area. This could be explained by improved ITN coverage and the ongoing mass drug administration programme for onchocerciasis. Anaemia prevalence was high (19.2%).

Conclusion: Promotion of bed net use and interventions aimed at improving nutrition could maximise the benefits of ITN coverage on both malaria and LF in these sentinel sites.

Chapter 8: General Discussion

The main findings of the study and their public health importance and possible relevance for future directions, and malaria control in pregnancy strategies are discussed.