ORIGINAL RESEARCH ARTICLE

Prevalence and risk factors for malaria in pregnancy in Vanga, Democratic Republic of Congo

DOI: 10.29063/ajrh2021/v25i5.2

Junior Mudji[1,2], Prince Kabamba Yaka[1,2], Victoria Olarewaju[3,4], Christian Lengeler[3,4]*

Hôpital Evangélique de Vanga, Vanga, Democratic Republic of Congo[1]; Université Protestante au Congo, Kinshasa, Democratic Republic of Congo[2]; Swiss Tropical and Public Health Institute (SwissTPH), Basel, Switzerland[3]; University of Basel, Basel, Switzerland[4]

***For Correspondence:** Email: *christian.lengeler@swisstph.ch*; Phone: +41 61 284 8221

Abstract

The Democratic Republic of Congo (DRC) is the second most malarious country in the world, but little information is available on malaria control measures in pregnancy. We conducted a longitudinal study among 395 women pregnant with singletons in the Vanga and Mayoko health facilities, Vanga Health Zone, Kwilu Province. We recruited 406 pregnant women between April and October 2019. Malaria prevalence at recruitment was 18.8% in Vanga and 30.1% in Mayoko (difference p<0.01). At delivery, malaria prevalence in placental samples was 9.7% in Vanga and 17.7% in Mayoko (difference p=0.04). The overall prevalence of anemia (< 11 g/dl hemoglobin) in both sites was high at recruitment (68.8%) and at delivery (62.9%). Malaria infection rates in the mother were high but decreased between first ANC contact and delivery - from 24.2% to 13.6%. It is unclear whether regular use of ITNs and uptake of IPTp-SP have contributed to that decrease. *(Afr J Reprod Health 2021; 25[5]: 14-24).*

Keywords: Malaria; pregnancy; malaria control; Democratic Republic of Congo

Résumé

La République Démocratique du Congo (RDC) est le deuxième pays le plus impaludé au monde, mais peu d'informations sont disponibles sur les mesures de lutte contre le paludisme pendant la grossesse. Nous avons mené une étude longitudinale auprès de 395 femmes enceintes dans les formations sanitaires de Vanga et Mayoko, Zone de Santé de Vanga, Province du Kwilu. Nous avons recruté 406 femmes enceintes entre avril et octobre 2019. La prévalence du paludisme au recrutement était de 18,8 % à Vanga et de 30,1 % à Mayoko (différence p<0,01). A l'accouchement, la prévalence du paludisme dans les prélèvements placentaires était de 9,7 % à Vanga et de 17,7 % à Mayoko (différence p=0,04). La prévalence globale de l'anémie (< 11 g/dl d'hémoglobine) dans les deux sites était élevée au recrutement (68,8 %) et à l'accouchement (62,9 %). Les taux d'infection palustre chez les mères étaient élevés mais ont diminué entre le premier contact prénatal et l'accouchement - de 24,2 % à 13,6 %. Il n'est pas clair si l'utilisation régulière des MII et l'utilisation de prophylaxie ont contribué à cette diminution. *(Afr J Reprod Health 2021; 25[5]: 14-24).*

Mots-clés: Paludisme; grossesse, contrôle; République Démocratique du Congo

Introduction

Pregnant women are three times more likely to have severe malaria than their non-pregnant counterparts. Malaria in pregnancy has been associated with an increased risk of maternal anemia, low birth weight, in utero death and maternal mortality[1,2]. Depending on the endemicity of malaria in an area, up to 50% of pregnant women may be infected but asymptomatic[2]. In areas with moderate to high transmission, the World Health Organization (WHO) recommends the use of insecticide-treated bed nets (ITNs) and intermittent preventive treatments during pregnancy (IPTp), with a dose of sulfadoxine-pyrimethamine at each antenatal scheduled visit for malaria prevention3. This is because pregnant women on antimalarial chemoprophylaxis are less likely to be infected, while sleeping under ITNs reduces human contacts with the vector Anopheles mosquitoes. Both preventive measures have been shown to contribute significantly to reducing the incidence, morbidity, mortality and other adverse effects of malaria in pregnancy1–4. The Democratic Republic of the Congo (DRC) is the second country in the world in terms of malaria burden[3]. Asymptomatic malaria is

common in the general population, where the local prevalence can be as high as 48.2%5. The national average prevalence of malaria is 37.2%[6]. The prevalence of measured malaria parasites was higher among first-time mothers (26.5%) than among multiparas (18.8%) in four maternities in Kinshasa in 2006[7].

The malaria situation in DR Congo is poorly understood, despite the high endemicity and the risk it represents for the lives and health of the Congolese people. The same applies to the rural Health Zone of Vanga, Kwilu Province, which is an area holo-endemic for malaria transmission. Data on asymptomatic and symptomatic malaria in pregnant women is usually available in the frame of clinical care and ANC; however, recurrent disruption of Rapid Diagnostic Test (RDT) supplies and high cost of blood smears (BS) prevent regular diagnosing and hence reporting. Similarly, little is known about the level of malaria control measures and their impact on the health of pregnant women.

The purpose of this study was to: (1) assess the prevalence of malaria and anemia in pregnant women attending ANC in Vanga and Mayoko, and (2) describe the coverage and potential preventive impact of insecticide-treated nets (ITNs) and intermittent preventive treatment during pregnancy with sulfadoxine-pyrimethamine (IPTp-SP).

Methods

Study setting

The study was conducted in the Vanga Health Zone (Vanga and Mayoko health facilities) between April and October 2019 in the Kwilu Province, one of 519 health zones in the DRC, and one of the 26 integrated disease surveillance sentinel sites of malaria in the country. It is located around 560 Km from the capital city Kinshasa, covering both banks of the Kwilu River. The two sites have ANC and delivery services. However, the Vanga Hospital is the general referral hospital of the Vanga Health Zone. The roads around the Vanga health facilities are better accessible than the areas around the Mayoko health facilities. In addition, there is more economic activity in Vanga compared to Mayoko.

Study design

Longitudinal study following women pregnant with singletons in the Vanga Health Zone, who attended either the Vanga or the Mayoko antenatal care clinic (ANC). This cohort of pregnant women were followed from the time of first ANC visit to one month post-delivery.

Study population and sample size

The study population were pregnant women recruited from the two sites. We used an online calculator (www.openepi.com) to calculate the required sample size, based on an estimate that pregnant women have a 35% malaria prevalence rate, which was to be measured with an 8% precision and an alpha error of 5%. This gave a minimum sample size of 135. To compare the two sites for malaria prevalence, we assumed a 15% prevalence difference with 80% power, 5% error margin and 30% loss of follow-up to birth, giving a sample size of 200 per study site.

Recruitment

We recruited two midwives from the existing staff in each health facility and trained them specifically for the needs of the study. The midwives recruited the pregnant women on the day of their regular prenatal consultation in a way that an *ad hoc* representative geographic sample was obtained at each site. All pregnant women in the second and third trimesters expecting only one child were eligible, regardless of their age. Informed consent was obtained before inclusion in the study. Pregnant women for whom the age of pregnancy could not be determined with precision (up to a week later), or with complications such as high blood pressure or very low haemoglobin levels (<8g/dl), or who had particular problems with the unborn child, or who did not give an informed consent, were excluded.

Data collection

We used a paper questionnaire to collect socio-demographic information, knowledge on malaria and use of insecticide treated nets (ITNs) from the participants during the antenatal visit. Other information such as obstetrical history, history of malaria during the current pregnancy, use of IPTp-SP, use of iron and folic acid were taken from the participant's prenatal care chart. A blood sample was taken to perform a haemoglobin analysis, and malaria was tested by RDT as well as by a thick and thin smear. We assessed the presence of mosquito

bed nets in each participant's house through a home visit. Each participant was given a study enrolment card entitling her to free ANC services including delivery. Clinic appointments were made according to routine antenatal schedules. Details of the delivery such as the method of delivery, childbirth status, birthweight, gestational age, haemoglobin level and malaria test result were recorded on a separate form.

The age of pregnancy was calculated using the date of the start of the last normal menstrual period. Symptomatic malaria was defined through corresponding clinical symptoms and a positive RDT or blood smear result. Anaemia was defined as haemoglobin <11.0 g/dl, and severe anemia as haemoglobin <8.0 g/dl. A delivery before 37 weeks was considered as preterm, and a newborn with a birthweight ≥2.5 Kg was considered as normal birthweight.

Laboratory methods

We tested for malaria with Rapid Diagnostic Tests (RDT) using CareStart™ kits detecting Plasmodium falciparum HRP2 antigen (Access Bio Inc. Somerset, NJ 08873, USA). In addition, we did a standard Giemsa staining on thin and thick slides. A positive result of either test would define malaria positivity status. At inclusion, blood was collected from the participants at the finger, while at delivery it was collected from the intervillous space of the placenta. The ethics committee did not allow to collect a second blood sample from the finger at the time of birth.

Hemoglobin was measured by a HemoCue Hb201+ point-of-care-analyser (HemoCueAB, Ängelholm, Sweden). We used a body meter Seca model 2101821009 to measure the height, and a Seca model 725 10210090 to measure the birthweight within 24 hours of birth.

Statistical analysis

We entered the data collected in Excel with a double check of all entries. The data were then imported into STATA version 12.0 (Stata Corp, College Station, TX, USA) for analysis. Descriptive analysis of the sample was done by calculating the frequencies and percentages, with their confidence intervals. The averages and standard deviations of selected variables were calculated, as appropriate. Data was summarized in frequency tables and proportions were compared between the two sites using a Chi-square test. We used the average, standard deviation and student-t test to summarize the continuous variables and reported the corresponding p values for differences.

We used bivariate logistic regression analysis to assess associations between a number of parameters/risk factors and the four main outcomes: (1) malaria prevalence among study participants at first ANC visit, and (2) at birth, (3) anaemia of the mother at birth, and (4) birthweight of the child. Explanatory variables with a p value <0.05 in the bivariate analysis were included in a multivariate analysis by logistic regression to further examine the association. The odds ratio (OR), their 95% confidence intervals (CI) and p values were reported for the final multivariate models.

Results

General characteristics of participants (Table 1)

We recruited 406 pregnant women between April and October 2019, 213 in Vanga and 193 in Mayoko. A total of 11 women were lost to follow-up, resulting in 395 women analysed: 208 in Vanga (52.7%) and 187 in Mayoko (47.3%). The majority of the women were aged 20-34 years (63.2% and 71.1% in Vanga and Mayoko, respectively), and the mean age was 27.6 ± 6.9 years, with no difference between sites (Table 1). The majorits of the women were married (83.7% and 86.3%), had not completed high school education (68.2% and 82.3%), had agriculture/gardening as the main source of income (62.2% and 81.3%) and lived in houses with walls made of bamboo or earth (90.9% and 100%) in Vanga and Mayoko, respectively. Overall, the level of poverty was high in both settings.

Obstetrics characteristics of pregnant women and newborn at delivery (Table 2)

More than half of the participants were multiparous with more than 3 children already (50.6% in Vanga and 66.1% in Mayoko) (Table 2).

Table 1: Socio-demographic characteristics of pregnant women attending antenatal care (ANC) in Vanga and Mayoko health centers, Kwilu Province, DR Congo

Characteristics	Center of recruitment					
	Vanga		Mayoko		Total	
	N	%	N	%	N	%
Age category (years)						
<20	33	15.8	16	8.6	49	12.4
20-34	132	63.2	133	71.1	265	66.9
35 and above	43	20.6	38	20.3	81	20.5
Average Age (SD)	27.4 ± 7.1		27.9 ± 6.8		-	-
Marital status						
Single	34	16.4	20	10.7	54	13.7
Married	174	83.7	167	86.3	341	86.3
Education						
Never been to school	10	4.8	11	5.9	21	5.3
Attended primary school	30	14.4	32	17.1	62	15.7
Went to high school but not completed	102	49.0	111	59.3	212	53.6
Gone to high school	55	26.4	32	17.1	87	22.0
Higher education	11	5.3	1	0.5	12	3.0
Source of Income						
Agriculture/Gardening	130	62.2	152	81.3	282	71.2
Work at home	38	18.2	5	2.7	43	10.9
Private sector	12	5.7	11	5.9	23	5.8
Public sector	18	8.6	14	7.5	32	8.1
No stated source of income	11	5.3	5	2.6	16	4.1
House wall type						
Earth/Bamboo	189	90.9	187	100.0	376	95.2
Brick	19	9.1	0	0.0	19	4.8

Slightly over one-fifth reported having had a child from previous pregnancies born alive, but now deceased: 23.1% and 26.7% in Vanga and Mayoko, respectively. The first antenatal visit during the current pregnancy took place during the first trimester in only 0.9% and 10.7% of the participants in Vanga and Mayoko. The average gestational age at delivery was 38.8 ± 2.2 weeks in Vanga and 38.7 ± 2.6 weeks in Mayoko. The average birthweight was 2.9 ± 0.5 Kg in Vanga and 2.6 ± 0.4 Kg in Mayoko. Seven babies were dead upon delivery in Vanga versus only one in Mayoko. Rather than reflecting the risk associated with a particular center, this probably reflects the fact that high-risk pregnancies were often referred to Vanga Hospital, which is a bigger and better equipped health facility.

Prevalence of malaria and anaemia (Table 3)

In total 106 participants, 32.2% in Vanga and 20.9% in Mayoko reported having malaria during the current pregnancy (Table 3). At inclusion, overall measured malaria prevalence was 24.2%, which differed significantly between the two sites: 18.8% in Vanga compared to 30.1% in Mayoko (p= 0.01). At delivery, the overall malaria prevalence was 13.6%, with 9.7% in Vanga and 17.7% in Mayoko (p= 0.04). Hence, the average prevalence had been reduced by more than 10 absolute percent between recruitment and birth.

The average maternal hemoglobin levels at inclusion were similar in both sites: 10.5 g/dl ± 1.2 in Vanga and 10.2 g/dl ± 1.2 in Mayoko but the distribution of anemia was different between the two sites (p<0.03). At delivery, Hb levels were again similar: 10.3 g/dl ± 1.6 in Vanga and 10.4 g/dl ± 1.4 in Mayoko. Severe anemia defined as Hb below 8 g/dl was observed among 7.4% and 2.2% of the participants in Vanga and Mayoko, respectively. Overall, 68.0% of the women were anemic at first ANC visit (inclusion) and 62.9% were anemic at delivery, a slight improvement.

Usage of insecticide treated nets (ITNs)

Participants in the study had a high awareness about malaria with 95% reporting mosquito bites as the source of malaria. Almost all the participants had ITNs: 97.1% in Vanga and 95.6% in Mayoko.

Table 2: Obstetrics characteristics of pregnant women having delivered in Vanga and Mayoko

Characteristics	Center of recruitment						P value
	Vanga		Mayoko		Total		
	n	%	n	%	N	%	
Parity							
N	207		186		393		
No children before	54	26.1	35	18.8	89	12.4	0.09
Between 1 and 2 children	37	17.9	28	15.1	65	66.9	
More than 3 children	116	56.0	123	66.1	239	20.5	
Number of children from previous pregnancies born alive but currently dead							
N	208		187		395		
None	160	76.9	137	73.3	297	75.2	0.19
Between 1 and 2 children	46	22.1	44	23.5	90	22.8	
More than 3 children	2	1.0	6	3.2	8	2.0	
Gestational age at first ANC visit for current pregnancy							
N	208		187		395		
First trimester	2	0.9	20	10.7	22	5.6	0.001 *
Second trimester	153	73.6	112	59.9	265	67.1	
Third trimester	53	25.5	55	29.4	108	27.3	
Gestational age at birth (weeks)							
N	186		175		361		
Preterm (<37weeks)	34	18.3	34	19.4	68	18.8	
Full-term ((≥ 37weeks)	152	81.7	141	80.6	293	81.2	0.49
Average gestational age	38.8 ± 2.2		38.7 ± 2.6				
Birthweight (Kg)							
N	190		184		374		
Very low (<2.5)	24	12.6	42	22.8	66	17.7	
Low (2.5-2.9)	84	44.2	96	52.2	180	46.1	
Normal (≥3.0)	82	43.2	46	25.0	128	34.2	0.001 *
Average birthweight (Kg)	2.9 ± 0.53		2.6 ± 0.46				
Child alive at delivery							
N	186		175		361		
Yes	179	96.2	174	99.4	353	97.8	0.06
No	7	3.8	1	0.6	8	2.2	

Total numbers may differ for certain variables due to missing data. N=sample size for variable. P values given for differences between the two sites

Most ITNs were obtained at the ANC clinic (35.2% and 9.1%) and during distribution campaigns: 43.9% in Vanga and 90.3% in Mayoko. More than half the women reported daily use of an ITN: 76.6% in Vanga and 66.6% in Mayoko. When asked about reasons for not using an ITN, suffocation was indicated by some respondents (12.8% and 6.9% in Vanga and Mayoko) but the main reason was the perceived absence of mosquitoes (87.2 and 93.1%, respectively). The vast majority of the respondents reported sleeping under a mosquito net the night before the survey: 93.1% and 94.9% (p= 0.37).

Uptake of IPTp-SP (Table 4)

A high 97.4% of the participants had heard about IPTp-SP. A total of 303 women had taken at least some SP during their pregnancy (91.6% in Vanga, 66.9% in Mayoko, total 80.2%). Only 56 (18.5%) in both sites had taken the first dose within the recommended time limit of 16 weeks (Table 4). The average number of received doses was 2.9 ± 0.7 in Vanga and 2.1 ± 0.9 in Mayoko (difference p<0.03). Almost all doses of SP were taken in the presence of a health care worker: 96.8% in Vanga, 98.3% in Mayoko.

Logistic regression analysis of the association of malaria at birth, birthweight, maternal Hb with selected risk factors (Table 5)

Malaria infection at birth (Table 5). The only significant risk factor we found was a parity of 1-2 children (OR= 0.20, 95% CI= 0.05- 0.77). Three and more children seemed also to be protective, but the effect was not significant (OR=0.57, 95% CI 0.24-1.35).

Table 3: Prevalence of malaria and anemia among pregnant women attending antenatal clinics in Vanga and Mayoko

Characteristics	Center of recruitment						P value
	Vanga		Mayoko		Total		
	N	%	N	%	N	%	
Suffered from malaria in this pregnancy?							
N	208		187		395		
Yes	67	32.2	39	20.9	106	26.8	0.01 *
No	141	67.7	148	79.1	289	73.2	
If suffered from malaria, place of treatment?							
N	67		39		106		
Health facility	65	97.0	36	92.3	101	95.3	0.27
Self-medication	2	2.9	3	7.7	5	4.7	
Type of medication taken							
N	67		38		105		
Quinine	52	77.6	33	86.8	85	80.9	0.45
SP	8	11.9	2	5.3	10	9.5	
ACT	7	10.5	3	7.9	10	9.5	
Malaria test result at inclusion							
N	208		183		392		
Positive	39	18.8	55	30.1	95	24.2	0.01 *
Negative	169	81.3	128	69.9	297	75.8	
Malaria test at delivery							
N	186		175		361		
Positive	18	9.7	31	17.7	49	13.6	0.04 *
Negative	168	90.3	144	82.3	312	86.4	
Maternal Hemoglobin level at inclusion (g/dl)							
N	208		183		391		
Severe	0	0	0	0	0	0	0.03 *
Moderate Anemia	133	63.9	136	74.3	269	68.0	
Normal Hb	75	36.1	47	25.7	122	31.2	
Average Hb	10.5 ± 1.2		10.2 ± 1.2				
Maternal Hemoglobin level at delivery (g/dl)							
N	190		185		375		
Severe	14	7.4	4	2.2	18	4.8	
Moderate Anaemia	107	56.3	111	60.0	218	58.1	0.06
Normal	69	36.3	70	37.8	139	37.1	
Average Hb	10.3 ± 1.6		10.4 ± 1.4				

Anemia defined as severe (< 7.9 g/dl haemoglobin), moderate (8-10.9 g/dl) and normal (≥11g/dl). SP=Sulphadoxine-pyrimethamine. N=sample size for variable. P values given for differences between the two sites.

Low birthweight (Table 5). There was a slight trend for younger ages to be protective, but this was not statistically significant. Strangely, a malaria positive slide at birth seemed to be protective, and this effect was statistically significant (OR=0.34, 95% CI 0.17-0.70). This could well be a chance finding since it is well-known that a malaria infection can lead to anemia. The use of an ITN last night was found to be protective, but not significantly so (OR=0.44, 95% CI 0.09-2.04). Disappointingly, no level of IPTp doses seemed to offer significant protection.

Maternal hemoglobin. No significant risk factor was found for maternal hemoglobin at birth (Results not shown).

Discussion

We conducted a longitudinal study in Vanga Health Zone (Vanga and Mayoko health centers) to assess the prevalence of malaria and anemia, as well as the coverage and impact of malaria control with Insecticide-treated mosquito nets (ITNs) and intermittent preventive treatment with sulfadoxine-pyrimethamine (IPTp-SP) during pregnancy.

Malaria prevalence and anemia

The overall malaria prevalence among pregnant women attending ANC in both sites was 24.1% at recruitment and 13.6% at birth, similar to the reported prevalence of 14.9% in Mwene Ditu, DRC, 18.6% in Cameroon, 19.2% in Tanzania, and

Table 4: Uptake of Intermittent Preventive Treatment with Sulphadoxine-pyrimethamine among pregnant women attending antenatal clinics in Vanga and Mayoko

Characteristics	Center of recruitment						P value
	Vanga		Mayoko		N		
	n	%	N	%	N	%	
Heard of intermittent preventive treatment with SP?							
N	203		175		378		
Yes	199	98.0	169	96.6	368	97.4	0.26
No	4	1.9	6	3.4	10	2.7	
Have taken the tablets for malaria prevention in current pregnancy?							
N	203		175		378		
Yes	186	91.6	117	66.9	303	80.2	0.001 *
No	17	8.4	58	33.1	75	19.8	
If not, why?							
N	17		59		76		
Not available	12	70.6	55	93.2	67	88.2	0.31
Not aware of SP	5	29.4	2	3.4	7	9.2	
Side effects	0	0.0	2	3.4	2	2.6	
When was the first dose received?							
N	186		117		303		
Taking the SP dose within the time limit (at 16 weeks)	20	10.8	36	30.7	56	18.5	0.001 *
Delay in taking the SP dose (after 16weeks)	166	89.3	81	69.2	247	81.5	
Doses of SP received at time of delivery, for those have received at least one dose							
N	186		117		303		0.03 *
	2.9 ± 0.7		2.1 ± 0.9				

P values given for differences between the two sites

Table 5: Logistic regression analysis to assess risk factors for (1) malaria infection in mothers at birth and (2) low birthweight (less than 2.5 Kg) versus normal birthweight (>2.5 Kg)

	Malaria infection			**Low birthweight**		
Characteristics	Odds Ratio	95% CI	P value	Odds Ratio	95% CI	P value
Age of mother						
<20 years	1.00			1.00		
20-34 years	1.05	0.36 - 3.08	0.92	1.18	0.44 - 3.16	0.74
≥ 35 years	1.21	0.32 - 4.62	0.77	2.71	0.73 -10.17	0.14
Education						
Never been to school	1.00			1.00		
Attended primary school	0.38	0.08 - 1.95	0.25	0.86	0.19 – 3.80	0.85
Gone to high school or higher	0.81	0.22 - 3.05	0.75	1.04	0.27 – 3.97	0.95
Parity						
No children before	1.00			1.00		
Between 1 and 2 children	0.20	0.05 - 0.77	0.01 *	1.11	0.43 - 2.88	0.81
Between 3 and 11 children	0.57	0.24 - 1.35	0.20	1.26	0.54 - 2.89	0.59
Net use last night						
No	1.00			1.00		
Yes	0.80	0.24 - 2.64	0.72	0.44	0.09 - 2.04	0.29
Malaria test result at delivery						
Negative	-			1.00		
Positive	-	-	-	0.34	0.17 - 0.70	0.003 *
Total number of IPTp-SP doses received						
0	1.00			1.00		
1	0.95	0.09 - 9.70	0.97	1.06	0.18 - 6.46	0.94
2	0.97	0.10 - 9.21	0.98	0.92	0.16 - 5.25	0.92
3	1.16	0.13 - 10.41	0.89	1.77	0.32 – 9.85	0.51
4	0.54	0.05 - 6.30	0.62	3.57	0.46 - 27.63	0.22

18.1% in Burkina Faso[8–11]. A significantly higher prevalence was reported in Kisangani 27.6%, Nigeria 41.6%, and 2 regions in Ghana 57.4% and 42.6%[12–14]. The variation in prevalence observed across these studies most certainly reflects the differences in overall level of malaria risk, as well as the ecological contexts (rural and urban). Importantly, the overall prevalence in both sites decreased from 24.2% at inclusion to 13.6% at delivery, with significant differences between Vanga (9.7%) and Mayoko (17.7%). An explanation for this may be the better IPTp-SP uptake for preventive treatment of malaria in Vanga compared to Mayoko, as there was no significant difference in ITNs usage in both sites (p= 0.17). Another explanation might be the higher level of socio-economic status in Vanga, but this could not be assessed formally in this study. Only *Plasmodium falciparum* infections weres found in all the participants that tested positive for malaria, and this is consistent with reports from previous studies[2,15].

Anemia in pregnancy increases the risk of poor birth outcomes and maternal mortality, since blood loss in anemic pregnant women could have more severe medical consequence[16,17]. In this study, the overall prevalence of maternal anemia was 62.9% for Hb<11g/dl. This finding is similar to the result of a study conducted in South Kivu province in the eastern Democratic Republic of Congo [16]. The 2007 and 2008, DRC national DHS estimated an anemia prevalence of 57% and 60% respectively among women of reproductive age. This level of anemia prevalence was categorized as severe according to WHO and is a public health concern [17]. Although malaria has been associated with anemia in pregnancy, there are other etiological factors with complex interactions [2,11]. Some of these factors are nutritional deficiencies (iron), genetic disorders and other parasitic infections, suggesting the need for further research on the anemia prevalence in the study area[18]. The average gestational age at delivery was not significantly different in both sites (p= 0.49) with most of the deliveries above 37 weeks.

Utilization of ITNs

Regular use of ITNs is the most prominent large-scale preventive measure against malaria infection, in particular in areas with high endemicity[19,20]. ITNs coverage among the participants from Vanga and Mayoko was high since every household had a mosquito net. The utilization rate was high as well, with 93.9% of the participants reporting to have slept under a mosquito net the previous night. This finding is similar to reports from a study conducted among pregnant women in Sierrea Leone with an ITNs utilization rate of 87.6%, in Ethiopia 91.0% and in Togo 96.7%[21,22]. However, it is higher than the 60% utilization rate reported previously among pregnant women in DRC in 2016[23]. In this study, the high reported coverage of ITNs was linked to mass distribution campaigns accompanied by sensitization programs organized by the DRC National Malaria Control Program (PLNP), in partnership with international aid agencies [16]. The malaria prevalence reported in this study (13.6%) could be considered as relatively low, and this could be seen as evidence of the positive health impact of ITNs utilization in Vanga and Mayoko. But our risk factor analysis was inconclusive.

Uptake of IPTp-SP

The effectiveness of IPTp-SP in the prevention of adverse birth outcomes associated with malaria in pregnancy have been reported widely[10,24,25]. The DRC, like many other countries in SSA, have adopted the WHO recommendation of administering IPTp-SP after the first trimester at every ANC visit through directly observed therapy (DOT)[26,27]. In this study, a total of 303 women had taken at least some SP during their pregnancy (91.6% in Vanga, 66.9% in Mayoko, total 80.2%). Of these, only 56 participants (18.6%) had initiated an ANC visit in the first trimester in both sites. This low value for early IPTp initiation is consistent with findings of a study in Tanzania, where it was reported that uptake of the first IPTp-SP dose is determined by timely registration for ANC[28].

The key reason given by the few participants who had not received any dose of IPTp-SP was non-availability at the facility, which is similar to findings from previous studies[28,29]. There was a significant difference in the average number of doses received by delivery (2.9 in Vanga versus 2.1 doses in Mayoko, p= 0.03). A major reason for this may be the frequent stock-out situation at the Mayoko facility, which is a publicly funded facility, unlike the Vanga Hospital, which is a private not-for-profit religious health facility with its own

system of drug procurement. Unfortunately, from our data it is unclear whether IPTp has provided any protection to these women.

Limitations

This study has a number of limitations. Firstly, while we did a sample size calculation to plan the study, subsequently a number of risk factors were showing some protective trend but were not significant, presumably because the sample size was too small for a stratified analysis. We also controlled for a number of obvious confounders in the statistical analysis, but we failed for example to assess socio-economic status with a validated indicator. Finally, the participants were recruited during ANC visits, thus pregnant women who did not visit the clinic for antenatal care were not assessed. These results are therefore not entirely representative of the pregnant women in the Vanga Health Zone. Despite these limitations, we believe the present study makes an important contribution to better understanding of the malaria situation in DR Congo, the second most malarious country in the world.

Ethical consideration

We submitted the research proposal to the ethics committee of the Protestant University of Congo, and received the approval number CEUPC 0057. To participate in this study, the pregnant women had to sign the informed consent form after explanation of the purpose, benefits and risks of participation. Participants who tested positive for malaria were treated with a full oral dose of the DRC-recommended artemisinin-based combination therapy (ACT): either artesunate-amodiaquine or artemether-lumefantrine. All costs for care, including diagnostic tests, as well as for childbirth were covered from the study budget. The confidentiality of the patient data was ensured by collecting information on paper forms that were kept in locked cabinets. The principal investigator conducted the data entry and kept it on a password-protected computer. Personal identifiers (required to follow-up the women at home) were removed for data analysis.

Conclusion

In this study, the overall prevalence decreased between recruitment (24.2%) until delivery (13.6%), and it differed significantly between the two study sites, both at inclusion and at delivery. This reduction could be related to a high coverage and utilization of ITNs among the participants. Early uptake of IPTp-SP was low in both sites due to late ANC initiation, and there was a significant difference in the total number of doses in Vanga and Mayoko. The main reason for this was non-availability of SP. While there are some encouraging results, much remains to be done in protecting pregnant women against the deleterious effects of malaria in the DR Congo.

Contributions of authors

JM: Conception and design of study, data collection, analysis, interpretation and manuscript preparation. PKY: design of the study and implementation of the interventions for the pregnant women; review of the manuscript. VO: Data analysis, interpretation and manuscript preparation. CL: overall supervision and work on the manuscript. All authors read and approved the manuscript.

Competing interests

The authors declare that they have no competing interests.

Acknowledgements

The authors want to thank all the pregnant women who volunteered to participate in this study, as well as the mid-wives in the Vanga and Mayoko health centers. We want also to thank the Vanga and Mayoko local health authorities and particularly the Médecine-Chef de Zone, Dr. Blaise Mumbungu and the malaria responsible Pitshou Mubima.

This study was supported by a grant from the International Society for Infectious Diseases (ISID), as well as from the Swiss Tropical and Public Health Institute. We gratefully acknowledge the support of these institutions. Finally, we gratefully acknowledge the inputs into the proposal by Prof. Jennifer Goldcamp (University of St Louis) and Prof. Frederick N. Baliraine (LeTourneau University, Texas, USA).

References

1. Desai M, ter Kuile FO, Nosten F, McGready R, Asamoa K, Brabin B and Newman R. Epidemiology and burden of malaria in pregnancy. Lancet Infect Dis.

2007; 7: 93-104. doi: 10.1016/S1473-3099(07)70021-X.
2. Parise M, Nahlen B, Menendez C and Steketee R. The burden of malaria in pregnancy in malaria-endemic a reas. Am J Trop Med Hyg. 2001; 64: 28–35.
3. World Health Organization. World malaria report 2020. Available from: https://www.who.int/publications/i/item/9789240015791
4. Agomo C and Oyibo W. Factors associated with risk of malaria infection among pregnant women in Lagos, Nigeria. Infect Dis Poverty. 2013; 2: 19. doi: 10.1186/2049-9957-2-19
5. Mvumbi DM, Bobanga TL, Melin P, De Mol P, Kayembe JN, Situakibanza HN, Mvumbi GL, Nsibu CN, Umesumbu SE and Hayette M. High prevalence of *Plasmodium falciparum* infection in asymptomatic individuals from the Democratic Republic of the Congo. Malar Res Treat. 2016; 1–4. doi: 10.1155/2016/5405802.
6. Taylor S, Van EA, Hand C, Mwandagalirwa K, Messina J, Tshefu A, Atua B, Emch M, Muwonga J, Meshnick S and Kuile F. Quantification of the burden and consequences of pregnancy-associated malaria in the Democratic Republic of the Congo. The Journal of Infectious Diseases. 2011; 204: 1762-1771. doi: 10.1093/infdis/jir625
7. Lukaka K, Fumie O, Mulumbu M, Lokombe BJ and Muyembe TJ. Malaria prevalence at delivery in four maternity hospitals of Kinshasa city, Democratic Republic of the Congo. Bull Société Pathol Exot. 2006; 99: 200–1.
8. Jean-Claude MK, Bienfait MM, Simon IK and Jean-Baptiste KSZ. Epidemiological aspects of malaria in pregnant women: Prevalence and risk factors in Mwene Ditu, DR Congo. OALib. 2018 ; 05:1–4.
9. Ouédraogo CMR, Nébié G, Sawadogo L, Rouamba G, Ouédraogo A and Lankoandé J. Étude des facteurs favorisant la survenue du paludisme à *Plasmodium falciparum* chez les femmes enceintes dans le district sanitaire de Bogodogo à Ouagadougou, Burkina Faso. J Gynécologie Obstétrique Biol Reprod. 2011; 40: 529–34. doi: doi.org/10.1016/j.jgyn.2011.03.005
10. Mpogoro FJ, Matovelo D, Dosani A, Ngallaba S, Mugono M and Mazigo. Uptake of intermittent preventive treatment with sulphadoxine-pyrimethamine for malaria during pregnancy and pregnancy outcomes: a cross-sectional study in Geita district, North-Western Tanzania. Malar J. 2014; 13: 455.
11. Olliaro PL, Delenne H, Cisse M, Badiane M, Olliaro A, Vaillant M and Brasseur P. Implementation of intermittent preventive treatment in pregnancy with sulphadoxine/pyrimethamine (IPTp-SP) at a district health center in rural Senegal. Malar J. 2008; 7: 234.
12. Otuli NL, Nguma JB, Alongo MM, Bosunga GK, Mukonkole JM, Likwela JL and Okenge JM. . Prevalence of congenital malaria in Kisangani, a stable malaria transmission area in Democratic Republic of the Congo. Infect Dis Obstet Gynecol. 2020; 2020: 1–7.
13. Fana SA, Bunza MDA, Anka SA, Imam AU and Nataala SU. Prevalence and risk factors associated with malaria infection among pregnant women in a semi-urban community of northwestern Nigeria. Infect Dis Poverty. 2015; 4: 24.
14. Dako-Gyeke M and Kofie HM. Factors influencing prevention and control of malaria among pregnant women resident in urban slums, southern Ghana. African Journal of Reproductive Health March 2015; 19: 44
15. Guyatt HL and Snow RW. Impact of malaria during pregnancy on low birth weight in sub-Saharan Africa. Clin Microbiol Rev. 2004; 17: 760–9.
16. Inungu JN, Ankiba N, Minelli M, Mumford V, Bolekela D, Mukoso B, Onema W, Kouton E and Raji D. Use of insecticide-treated mosquito net among pregnant women and guardians of children under five in the Democratic Republic of the Congo. Malar Res Treat. 2017; 5923696. doi: 10.1155/2017/5923696.
17. World Health Organization. The global prevalence of anaemia in 2011. Geneva: WHO. 2015. Available from: https://www.who.int/nutrition/publications/micronutrients/global_prevalence_anaemia_2011/en/
18. Balarajan Y, Ramakrishnan U, Özaltin E, Shankar AH and Subramanian SV. Anaemia in low-income and middle-income countries. The Lancet. 2011; 378: 2123–35.
19. Lengeler C. Insecticide-treated bed nets and curtains for preventing malaria. Cochrane Infectious Diseases Group, editor. Cochrane Database Syst Rev. 2004; 2. doi: 10.1002/14651858.CD000363.pub2
20. Lim SS, Fullman N, Stokes A, Ravishankar N, Masiye F, Murray CJL and Gakidou E. Net benefits: a multi-country analysis of observational data examining associations between insecticide-treated mosquito nets and health outcomes. PLoS Med. 2011; 8: e1001091.
21. Bennett A, Smith SJ, Yambasu S, Jambai A, Alemu W, Kabano A and Eisele TP. Household possession and use of insecticide-treated mosquito nets in Sierra Leone 6 months after a national mass-distribution campaign. PLoS One. 2012; 7: e37927.
22. Stevens ER, Aldridge A, Degbey Y, Pignandi A, Dorkenoo MA and Hugelen-Padin J. Evaluation of the 2011 long-lasting, insecticide-treated net distribution for universal coverage in Togo. Malar J. 2013; 12: 162.
23. USAID. Malaria Operational Plan FY 2016. DRC; 2016. Available from: https://reliefweb.int/sites/reliefweb.int/files/resources/fy-2016-democratic-republic-of-the-congo-malaria-operational-pan.pdf
24. Hommerich L, von Oertzen C, Bedu-Addo G, Holmberg V, Acquah PA, Eggelte TA, Bienzle U and Mockenhaupt FP. Decline of placental malaria in southern Ghana after the implementation of intermittent preventive treatment in pregnancy. Malar J. 2007; 6: 144.
25. Gross K, Alba S, Schellenberg J, Kessy F, Mayumana I and Obrist B. The combined effect of determinants on coverage of intermittent preventive treatment of

malaria during pregnancy in the Kilombero Valley, Tanzania. Malaria Journal 2011; May 21; 10:140. doi 10.1186/1475-2875-10-140.

26. World Health Organization. Updated WHO Policy Recommendation: Intermittent Preventive Treatment of malaria in pregnancy using Sulfadoxine-pyrimethamine (IPTp-SP). Geneva. 2012. URL: https://www.who.int/malaria/iptp_sp_updated_policy_recommendation_en_102012.pdf
27. World Health Organization. The world health report; Make every mother and child count. Geneva; 2005. p. 229.
28. Protas J, Tarimo D and Moshiro C. Determinants of timely uptake of ITN and SP (IPT) and pregnancy time protected against malaria in Bukoba, Tanzania. BMC Res Notes. 2016; 9(1): 318.
29. Mbaye A, Richard K, Balajo B, Dunyo S and Shulman CGB. Malaria in pregnancy. Lancet Infect Dis. 2007; 7: 1–7.