

# Intermittent Preventive Treatment in Pregnancy with Sulphadoxine-Pyrimethamine Does Not Have Effect on Maternal Hemoglobin at Delivery and Birth Weight in Kisangani, Democratic Republic of Congo

Labama Otuli Noël<sup>1\*</sup>, Bosenge Nguma Jean-Didier<sup>1</sup>, Maindo Alongo Mike-Antoine<sup>1</sup>, Losimba Likwela Joris<sup>2</sup>, Manga Okenge Jean-Pascal<sup>1</sup>

<sup>1</sup>Department of Gynecology-Obstetrics, Faculty of Medicine and Pharmacy, University of Kisangani, Kisangani, Democratic Republic of Congo

<sup>2</sup>Department of Public Health, Faculty of Medicine and Pharmacy, University of Kisangani, Kisangani, Democratic Republic of Congo

Email: \*labama.otuli@unikis.ac.cd

**How to cite this paper:** Noël, L.O., Jean-Didier, B.N., Mike-Antoine, M.A., Joris, L.L. and Jean-Pascal, M.O. (2019) Intermittent Preventive Treatment in Pregnancy with Sulphadoxine-Pyrimethamine Does Not Have Effect on Maternal Hemoglobin at Delivery and Birth Weight in Kisangani, Democratic Republic of Congo. *Journal of Biosciences and Medicines*, 7, 168-180.

<https://doi.org/10.4236/jbm.2019.712014>

**Received:** November 10, 2019

**Accepted:** December 10, 2019

**Published:** December 13, 2019

Copyright © 2019 by author(s) and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

## Abstract

**Background:** The consequences of malaria during pregnancy are different regarding local conditions of malaria transmission. In stable malaria areas, the main complications are maternal anaemia and fetal growth restriction. This study aims to determine if pregnancy-associated malaria is associated with the risk of the above-mentioned complications and to determine if IPTp-sp reduces them in Kisangani. **Methods:** It is a cross-sectional analytical study conducted in parturients, in 6 medical facilities of Kisangani, from January 1st to September 30th, 2017. At delivery we measured their hemoglobin, we performed the thick blood smear of their peripheral blood and placental apposition; and we weighed their newborns at birth. **Results:** Risk of anaemia at delivery increased with malaria access during pregnancy ( $p = 0.0056$ ; OR: 1.4221, 95% CI: 1.0851 - 1.8638) and peripheral parasitaemia at delivery ( $p = 0.0000$ ; OR: 6.3855, 95% CI: 4.5552 - 8.9512). LBW increased with peripheral parasitaemia at delivery ( $p = 0.0000$ ; OR: 3.5299, 95% CI: 2.4424 - 5.1015) and placental parasitaemia ( $p = 0.0000$ ; OR: 18.3247, 95% CI: 12.5141 - 26.8332). IPTp-sp did not have effect on maternal hemoglobin at delivery ( $p = 0.1546$ ; OR: 0.7553, IC à 95%: 0.4414 - 1.2923) and the birth weight ( $p = 0.1225$ ; OR: 0.6638, IC à 95%: 0.3375 - 1.3056). **Conclusion:** In Kisangani, pregnancy-associated malaria is associated with maternal anaemia at delivery and LBW. IPTp-sp does not reduce the risk of these complications.

---

Therefore, studies evaluating IPTp alternatives are required in malaria endemic areas.

## Keywords

Intermittent Preventive Treatment in Pregnancy, Sulphadoxine-Pyrimethamine, Pregnancy-Associated Malaria, Maternal Anaemia at Delivery, Low Birth Weight, Kisangani

---

## 1. Introduction

Malaria remains a major public health problem. According to the World Health Organization (WHO), sub-Saharan Africa is the region of the world bearing the heaviest burden in terms of cases of malaria and associated deaths. In 2017, sub-Saharan African accounted for 92% of malaria cases and 93% of malaria-related deaths in the world [1] [2].

Malaria is endemic in most African countries, including the Democratic Republic of Congo (DRC), the 2nd sub-Saharan African country most affected by malaria after Nigeria [3]. According to WHO, in 2017, 25% of malaria cases in the world were recorded in Nigeria and 11% in DRC [2]. In the province of Tshopo, in the north of the DRC, malaria is the cause of consultation of 37% of all pathologies and the cause of death at the level of 30%. Children under 5 and pregnant women continue to pay the highest price for this disease. It has also been noted that children under 5 years old are twice as likely to die as the rest of the population. In Kisangani, administrative center of Tshopo Province, in 2010, there were 11.9523 new cases of malaria that caused 288 deaths [4] [5].

Malaria is a socio-economic burden for hundreds of millions of Africans and a factor of poverty and underdevelopment. According to the 2011 WHO report, economic losses due to malaria were enormous: up to US\$12 billion annually [6]. These directly cover individual and public expenditures for the prevention and treatment of the disease; and indirectly the loss of productivity or income when one considers the losses caused by medical care, absenteeism from school and work, funeral expenses, with an annual growth deficit estimated at 1.3% and a GDP decline of 32% [6] [7] [8].

Every year in Africa, more than 30 million pregnant women live in malaria-endemic areas. The prevalence of malaria during pregnancy varies from 5% to 40% depending on the country [7]. Malaria infestation of pregnant women is a major public health problem, as it is a threat to themselves and their children [1] [9]. The pregnant woman is particularly vulnerable: the pregnancy weakens the woman and makes her more susceptible to malaria infection, increases the risk of the disease, severe anaemia and death. For the unborn child, malaria increases the risk of spontaneous abortion, stillbirth, preterm birth and low birth weight (LBW), one of the main causes of child mortality [1] [10]-[17]. Lukuka *et al.* [18] had found in 2006, in four maternity departments in the City of Kinshasa

(DRC), that 11.3% of newborns of malarious mothers suffered of LBW.

Depending on the local conditions of malaria transmission, the consequences of this medical condition during pregnancy are different. Acute and severe complications, including maternal mortality and pernicious access, are limited to unstable endemic areas, low or epidemic transmission, where pregnant women are not immunized against malaria and cases are less frequent outside epidemic episodes. On the other side, in areas of stable malaria, with moderate to high transmission, pregnant women are semi-immune to malaria and there are essentially problems of maternal anaemia and fetal growth restriction responsible for a LBW, particularly marked in primigesta [13].

In view of the above, considering that Kisangani is a malaria-endemic area and due to the lack of data on malaria complications during pregnancy in Kisangani, we conducted this study to determine if in this city, pregnancy-associated malaria is associated with maternal anaemia at birth and LBW and to determine if intermittent preventive treatment in pregnancy with Sulphadoxine-Pyrimethamine (IPTp-sp) reduces these complications.

## 2. Methods

### 2.1. Type, Framework and Period of Study

From January to September 2017, we have conducted a cross-sectional analytic study. This study was multi-center and conducted in Kisangani, a highly endemic malaria area which is in north of the DRC. Six hospitals served as a study framework. These hospitals were selected regarding their high attendance by pregnant women and the availability of laboratories accredited by the provincial health division for biomedical tests. In all these hospitals, the WHO recommendations on prevention of malaria during pregnancy, use of insecticide-treated mosquito nets (ITNs) and IPTp-sp, are applied.

### 2.2. Population

We had exhaustively recruited all pregnant women who were admitted for labor, parturients, into our research sites during the period of our study.

#### 1) Inclusion criteria

The participants were parturients who:

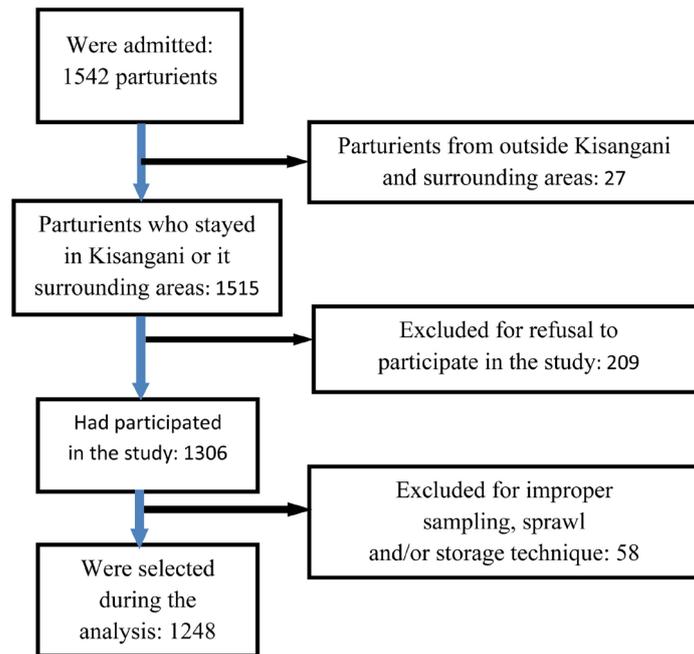
- have been staying in or around Kisangani for more than 2 weeks before delivery;
- have signed their informed-consent form.

Parturients who did not fulfill at least one inclusive criteria were excluded.

#### 2) Recruitment of the respondents (Figure 1)

1542 parturients were admitted to our research sites during our study period. Of these, we first excluded 27 who had not been staying to Kisangani or the surrounding area in the 2 weeks before delivery. Then, we excluded 209 parturients who had not given their informed-consent. Then we excluded 209 parturients who did not give their informed-consent. Finally, we had put aside 58 for im-

proper sampling technique, spreading for thick drop smear and/or blade preservation. Thus, at the time of data analysis, we selected a sample of 1248 parturients.



**Figure 1.** Recruitment of the respondents.

### 2.3. Data Collection

#### ▪ Data collection tools

To collect the data, we used a data collection form.

#### ▪ Data collection technique

Data collection was prospective. It was performed when parturients were admitted to the labor room. We performed interview, physical examination and laboratory investigations in parturients. Data related to the evolution of pregnancy were collected from ANC form.

Our survey team consisted of twelve midwives or nurses (two per site), six medical biologists (one per site) and one supervisor. Before starting the data collection, the nurses or midwives had attended training sessions to standardize the interview procedure as well as physical examination of parturients and newborns. Medical biologists were briefed on hemoglobin measurement techniques using the Hemocue Hb analyzer, peripheral blood sampling and slide spreading techniques for thick blood smear, and its transport after spreading. In addition, they were briefed on HIV rapid testing and trained in placental apposition technique. The supervisor was trained on all the steps of our research.

At the admission of parturients in the labor room, nurses or midwives interviewed the parturients. They attributed a unique code to each parturient and asked them questions related to their socio-demographic parameters such as age, education level, profession, commune of residence, their gynecological and ob-

stetric history, and their preventive measures of malaria, in particular the use of the ITNs and IPTp-sp. The interview was followed by a physical examination of these parturients. After obtaining their consent, the medical biologists proceeded to parturients HIV rapid testing, maternal hemoglobin testing and peripheral blood sampling followed by slide spreading to prepare thick drop smear test. Hemoglobin determination was performed using the Hemocue Hb Analyzer, following the manufacturer's instructions; and any result below 11gr/dl was considered as case of anaemia.

Immediately after giving birth, medical biologists performed placental apposition for thick drop smear test, while nurses or midwives thoroughly examined the newborns and weighed them using an electronic scale table SH-8008 (this scale is made in China by Jiangsu Suhong Medical Instruments Co. Ltd). Thereby, a weight less than 2500 gr at birth was considered as LBW. To perform placental appositions, medical biologists cleaned the placenta, superficially cut its maternal surface and applied a blade on the incised placental surface.

The study supervisor transported, according to the standards, the smear spread on slides to the Provincial Public Health Laboratory for thick drop smear test. Thereby, the smears were stained for 10 minutes to 10% diluted giemsa solution before being read by microscopy 100× objective. The thick drop smear test was considered when trophozoites or other plasmodium development stages were present in the sample. So, a positive thick drop test in peripheral blood was considered as peripheral parasitaemia whereas placental malaria was defined as a positive thick drop test in placental appositions. Association “malaria access during pregnancy—peripheral parasitaemia at delivery—placental malaria” was considered as pregnancy-associated malaria.

## 2.4. Data Analysis

The collected data were first stripped and then analyzed using the software Epi info version 7.2.2.6.

For the Sample Description, we calculated frequency and percentage as well as averages. To compare proportions, we calculated Pearson's chi squared and fisher's exact at the level of significance < 0.05. To measure the strength of association, we calculated odds ratio (OR) and its 95% confidence interval (CI).

## 3. Results

### 3.1. Characteristics of Study Respondents

The characteristics of study respondents are presented in **Table 1**.

170 respondents (13.62%) were under the age of 19; 24.36% of the participants were primigravida; 95.03% of them used the ITNs; 95.27% used IPTp-sp; the proportion of respondents with HIV serology positive was 3.37%; 23.88% of the respondents suffered from malaria access during pregnancy, 15.22% had peripheral parasitaemia at delivery and 14.90% had placental malaria; the prevalence of maternal anaemia at delivery was 32.85% while the prevalence of LBW was 13.46% (**Table 1**).

**Table 1.** Characteristics of study respondents.

Characteristics	n	%	95% CI
<b>Age (years) (Average: 25.39 ± 6.24)</b>			
≤18	170	13.62	11.79 - 15.68
19 - 34	950	76.12	73.64 - 78.44
≥35	128	10.26	8.66 - 12.11
<b>Gravidity N = 1248</b>			
Primigravida	304	24.36	22.06 - 26.82
Multigravida	944	75.64	73.18 - 77.94
<b>VIH serology N = 1248</b>			
Negative	1206	96.63	95.48 - 97.50
Positive	42	3.37	2.50 - 4.52
<b>Use of IPTp-sp N = 1248</b>			
No	59	4.73	3.68 - 6.05
Yes	1189	95.27	93.95 - 96.32
<b>Number of IPTp-sp doses N = 1248</b>			
0 - 2	299	23.96	21.67 - 26.40
3 - 4	949	76.04	73.60 - 78.33
<b>ITNs N = 1248</b>			
No	62	4.97	3.89 - 6.32
Yes	1186	95.03	93.68 - 96.11
<b>Arterial hypertension during current pregnancy N = 1248</b>			
No	1200	96.15	94.94 - 97.09
Yes	48	3.85	2.91 - 5.06
<b>Malaria access during pregnancy N = 1248</b>			
Negative	950	76.12	73.68 - 78.40
Positive	298	23.88	21.60 - 26.32
<b>Peripheral parasitaemia at delivery N = 1248</b>			
Negative	1058	84.78	82.68 - 86.66
Positive	190	15.22	13.34 - 17.32
<b>Placental malaria p N = 1248</b>			
Negative	1062	85.10	83.01 - 86.96
Positive	186	14.90	13.04 - 16.99
<b>Maternal Hb at delivery (gr/dl) N = 1248</b>			
≥11	838	67.15	64.49 - 69.70
<11	410	32.85	30.30 - 35.51
<b>Birth weight of newborn (gr) N = 1248</b>			
≥2500	1080	86.54	84.53 - 88.32
<2500	168	13.46	11.68 - 15.47

### 3.2. Effect of Pregnancy-Associated Malaria and IPTp-sp on Maternal Hemoglobin at Delivery

We present the effect of pregnancy-associated malaria and IPTp-sp on maternal hemoglobin at delivery, in **Table 2**.

**Table 2.** Effect of pregnancy-associated malaria and IPTp-sp on maternal hemoglobin at delivery.

Characteristics	Hb < 11 gr/dl	Hb ≥ 11 gr/dl	p-value	OR (IC à 95%)
<b>Use of IPTp-sp</b>				
<b>No</b>	23 (38.98%)	36 (61.02%)	0.1546	0.7553 (0.4414 - 1.2923)
<b>Yes</b>	387 (32.55%)	802 (67.45%)		
<b>Number of IPTp-sp doses</b>				
<b>0 - 2</b>	104 (34.78%)	195 (65.22%)	0.2077	0.8923 (0.6783 - 1.1738)
<b>3 - 4</b>	306 (32.24%)	643 (67.76%)		
<b>Malaria access during pregnancy</b>				
<b>No</b>	294 (30.95%)	656 (69.05%)	0.0056	1.4221 (1.0851 - 1.8638)
<b>Yes</b>	116 (38.93%)	182 (61.07%)		
<b>Peripheral parasitaemia at delivery</b>				
<b>No</b>	278 (26.28%)	780 (73.72%)	0.0000	6.3855 (4.5552 - 8.9512)
<b>Yes</b>	132 (69.47%)	58 (30.53%)		

While reading **Table 2**, we notice that the risk of anaemia at delivery increased with malaria access during pregnancy ( $p = 0.0056$ ; OR: 1.4221, 95% CI: 1.0851 - 1.8638) and peripheral parasitaemia at delivery ( $p = 0.0000$ ; OR: 6.3855, 95% CI: 4.5552 - 8.9512) while use of IPTp-sp did not have effect on maternal hemoglobin at delivery ( $p = 0.1546$ ; OR: 0.7553, 95% CI: 0.4414 - 1.2923) (**Table 2**).

### 3.3. Effect of Pregnancy-Associated Malaria and IPTp-Sp on Birth Weight of Newborns

**Table 3** shows the effect of pregnancy-associated malaria and IPTp-sp on birth weight of newborns.

**Table 3.** Effect of pregnancy-associated malaria and IPTp-sp on birth weight of newborns.

Characteristics	Weight < 2500	Weight ≥ 2500	p-value	OR(95% CI)
<b>Use of IPTp-sp</b>				
<b>No</b>	11 (20%)	48 (80%)	0.1225	0.6638 (0.3375 - 1.3056)
<b>Yes</b>	157 (13.13%)	1032 (86.87%)		
<b>Number of IPTp-sp doses</b>				
<b>0 - 2</b>	48 (16.05%)	251 (83.95%)	0.0687	0.7569 (0.5264 - 1.0885)
<b>3 - 4</b>	120 (12.64%)	829 (87.36%)		
<b>Malaria access during pregnancy</b>				
<b>No</b>	126 (13.26%)	824 (86.74%)	0.3537	1.0729 (0.7364 - 1.5632)
<b>Yes</b>	42 (14.09%)	256 (85.91%)		
<b>Peripheral parasitaemia at delivery</b>				
<b>No</b>	112 (10.59%)	946 (89.41%)	0.0000	3.5299 (2.4424 - 5.1015)
<b>Yes</b>	56 (29.47%)	134 (70.53%)		
<b>Placental malaria p N = 1248</b>				
<b>No</b>	66 (6.21%)	996 (93.79%)	0.0000	18.3247 (12.5141 - 26.8332)
<b>Yes</b>	102 (54.84%)	84 (45.16%)		

**Table 3** shows us that the risk of LBW increased by the peripheral parasitaemia at delivery ( $p = 0.0000$ ; OR: 3.5299, 95% CI: 2.4424 - 5.1015), the placental parasitaemia ( $p = 0.0000$ ; OR: 18.3247, 95% CI: 12.5141 - 26.8332) while use of IPTp-sp did not have effect on the birth weight ( $p = 0.1225$ ; OR: 0.6638, 95% CI: 0.3375 - 1.3056) (**Table 3**).

## 4. Discussion

### 4.1. Pregnancy-Associated Malaria and Maternal Anaemia at Delivery

We have found in our research that the risk of anaemia at delivery increased with malaria access during pregnancy ( $p = 0.0056$ ; OR: 1.4221, 95% CI: 1.0851 - 1.8638) and peripheral parasitaemia at delivery ( $p = 0.0000$ ; OR: 6.3855, 95% CI: 4.5552 - 8.9512).

Our results join those of Cottrell *et al.* [15] in Benin, Matangila *et al.* [16] in the DRC, of Lufele *et al.* [19] in New Guinea, from Samia *et al.* [20] in Sudan and Botolahy *et al.* [21] in Madagascar. These authors found that malaria during pregnancy was associated with anaemia. In their meta-analysis, Steketee *et al.* [22] also met the same findings.

Anaemia in case of pregnancy-associated malaria is due to hemolysis caused by Plasmodium falciparum infection. In addition, Kisangani being a stable malaria transmission area, parturients might have an antimalarial premunition. Therefore, anaemia would be one of the complications of malaria encountered in this case [13].

### 4.2. Pregnancy-Associated Malaria and LBW

LBW increased with peripheral parasitaemia at delivery ( $p = 0.0000$ ; OR: 3.5299, 95% CI: 2.4424 - 5.1015) and placental parasitaemia ( $p = 0.0000$ ; OR: 18.3247, 95% CI: 12.5141 - 26.8332).

Our result match with those found by Cottrell *et al.* [15] in Benin, Egata and Bafa [17] in southern Ethiopia, Lufele *et al.* [19] in New Guinea, Samia *et al.* [20] in Sudan, Botolahy *et al.* [21] in Madagascar, Kapisi *et al.* [23] in Uganda, Mohammed *et al.* [24] in central Sudan and Albiti *et al.* [25] in Yemen. All these authors found that pregnancy-associated malaria was associated to LBW. After a meta-analysis, Steketee *et al.* [22] found that malaria was associated with LBW. In addition, Guyatt *et al.* [26] reported that in sub-Saharan Africa malaria was associated with LBW. By contrast, Rulisa *et al.* [27], in Rwanda, reported that the incidence of malaria during pregnancy had no influence on birth weight.

The association of LBW with peripheral parasitaemia and placental parasitaemia, found in our study like in studies of other authors, is related to placental parasitaemia. Indeed, in areas of stable malaria transmission, placental parasitaemia and maternal anaemia are predominant [13]. This leads to placental lesions responsible of uteroplacental insufficiency, which causes intrauterine growth restriction which results in LBW. LBW in our study was also due to maternal anaemia.

### 4.3. Effect of IPTp-Sp on Maternal Hemoglobin at Delivery and Birth Weight of Newborns

We found in our research that use of IPTp-sp did not have effect on maternal hemoglobin at delivery ( $p = 0.1546$ ; OR: 0.7553, 95% CI: 0.4414 - 1.2923) and the birth weight ( $p = 0.1225$ ; OR: 0.6638, 95% CI: 0.3375 - 1.3056). In addition, number of use of IPTp-sp did not reduce the risk of these complications.

Our results join those of Braun *et al.* [28] in Uganda. They found that use of IPTp-sp did not reduce maternal anaemia at delivery and LBW risk.

By contrast, Our results did not match with those of Losimba *et al.* [29] in DRC, Olliaro *et al.* [30] in Senegal, and Mace *et al.* [31] in Zambia. They found that IPTp-sp reduced the LBW risk. Falade *et al.* [32] in Nigeria found that the prevalence of maternal anaemia was lower among pregnant women who received IPTp-sp. Valea *et al.* [33] in Burkina Faso found that LBW and anaemia had trend to decrease in group of pregnant women who received 3 doses of IPTp-sp.

Our results would be due to the resistance of parasites to SP; indeed, cases of resistance to SP have been reported in DRC [34].

## 5. Conclusion

In Kisangani, pregnancy-associated malaria is associated with maternal anaemia at delivery and LBW. IPTp-sp does not reduce the risk of these complications. Therefore, studies evaluating IPTp alternatives are required in malaria endemic areas.

## Acknowledgements

We are grateful to the Faculty of Medicine and Pharmacy of University of Kisangani for sponsoring this study. We also thank the heads of the health facilities our research site and the provincial laboratory of Tshopo where the parasitological analyses will be carried out. We are grateful to all pregnant women who agreed to participate in these trials. Finally, we thank the entire investigative team.

## Authors' Contributions

Doctors Labama and Bosenge conceived the protocol. Professor Losimba has enriched the protocol. Professor Manga validated the protocol. Doctors Labama and Bosenge were responsible for collecting the data. Doctors Bosenge and Maindo contributed to review the text. Doctors Labama, Bosenge and Maindo wrote the manuscript. All authors enriched the manuscript. Professors Manga and Losimba validated the manuscript.

## Ethics Approval and Consent to Participate

The study protocol has been approved by the Ethics Committee of University of Kisangani.

Before participating in the study, parturients signed an informed-consent form. Parturients who were diagnosed HIV-positive were referred to services of HIV prevention of mother-to-child transmission and those with gestational malaria were treated with quinine.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

### References

- [1] World Health Organization (2017) World Malaria Report 2017. WHO, Genève.
- [2] World Health Organization (2018) World Malaria Report 2018. WHO, Genève.
- [3] World Health Organization (2008) World Malaria Report 2008. WHO, Genève.
- [4] Programme national de lutte contre le paludisme/Province orientale (2009) Rapport annuel 2009 des activités antipaludiques en Province orientale. PNLP, Ministère de la santé, RDC.
- [5] Programme national de lutte contre le paludisme/Province orientale (2011) Rapport annuel 2011 des activités antipaludiques en Province orientale. PNLP, Ministère de la santé, RDC.
- [6] World Health Organization (2011) World Malaria Report 2011. WHO, Genève.
- [7] Programme national de lutte contre le paludisme (2009) Faire reculer le paludisme, Plan stratégique 2009-2013. PNLP, Ministère de la santé, RDC.
- [8] Organisation Mondiale de la Santé (2003) Le sommet d'Abuja sur le projet Faire Reculer le Paludisme. Secrétariat du partenariat Faire Reculer le Paludisme. Genève: OMS.
- [9] Organisation Mondiale de la Santé. Des vies en danger: Le paludisme pendant la grossesse. <http://www.who.int>
- [10] Nosten, F., Rogerson, S.J., Beeson, J.G., McGready, R., Mutabingwa, T. and Brabin, B. (2004) Malaria in Pregnancy and the Endemicity Spectrum: What Can We Learn? *Trends in Parasitology*, **20**, 425-432. <https://doi.org/10.1016/j.pt.2004.06.007>
- [11] Haghdoosta, A.A., Alexander, N. and Smith, T. (2007) Maternal Malaria during Pregnancy and Infant Mortality Rate: Critical Literature Review and a New Analytical Approach. *Journal of Vector Borne Diseases*, **44**, 98-104.
- [12] Cot, M. and Deloron, P. (2003) Paludisme associé à la grossesse: Conséquences et perspectives d'intervention in Mère et enfant en milieu tropical. *Médecine tropicale*, **63**, 369-380.
- [13] Okoko, B.J., Enwere, G. and Ota, M.O.C. (2003) The Epidemiology and Consequences of Maternal Malaria: A Review of Immunological Basis. *Acta Tropica*, **87**, 193-205. [https://doi.org/10.1016/S0001-706X\(03\)00097-4](https://doi.org/10.1016/S0001-706X(03)00097-4)
- [14] Tiono, A.B., Ouedraogo, A., Bougouma, E.C., *et al.* (2009) Placental Malaria and Low Birth Weight in Pregnant Women Living in a Rural Area of Burkina Faso Following the Use of Three Preventive Treatment Regimens. *Malaria Journal*, **8**, 224. <https://doi.org/10.1186/1475-2875-8-224>
- [15] Cottrell, G., Moussiliou, A., Luty, A.J.F., Cot, M., Fievet, N., Massougbedji, A., *et al.* (2015) Submicroscopic *Plasmodium falciparum* Infections Are Associated with Maternal Anaemia, Premature Births, and Low Birth Weight. *Clinical Infectious*

- Diseases*, **60**, 1481-1488. <https://doi.org/10.1093/cid/civ122>
- [16] Matangila, J.R., Lufuluabo, J., Ibalanky, A.L., da Luz, R.A.I., Lutumba, P. and Van Geertruyden, J.-P. (2014) Asymptomatic *Plasmodium falciparum* Infection Is Associated with Anaemia in Pregnancy and Can Be More Cost-Effectively Detected by Rapid Diagnostic Test than by Microscopy in Kinshasa, Democratic Republic of the Congo. *Malaria Journal*, **13**, 132. <http://www.malariajournal.com/content/13/1/132>  
<https://doi.org/10.1186/1475-2875-13-132>
- [17] Egata, A.D. and Bafa, T.A. (2019) Predictors of Low Birth Weight in Newborn Delivered in Public Hospital of Gurage Zone, Southern Ethiopia: A Case-Control Study. *Food and Nutrition Sciences*, **10**, 428-438.  
<https://doi.org/10.4236/fns.2019.104032>
- [18] Lukuka, K.A., Fumie, O.S., Mulumbu, M.R., Lokombe, B.J. and Muyembe, T.J.J. (2006) Prévalence du paludisme à l'accouchement dans quatre maternités de la ville de Kinshasa, République Démocratique du Congo. *Bulletin de la Société de Pathologie Exotique*, **99**, 200-201.
- [19] Lufele, E., Umbers, A., Ordi, J., Ome-Kaius, M., Wangnapi, R., Unger, H., *et al.* (2017) Risk Factors and Pregnancy Outcomes Associated with Placental Malaria in a Prospective Cohort of Papua New Guinean Women. *Malaria Journal*, **16**, 427.  
<https://doi.org/10.1186/s12936-017-2077-4>
- [20] Samia, A.O., Hagir, E.I., Ishag, A., Mutasim, A., Ali, N.N., Abdelrahim, M.A., *et al.* (2017) Placental Malaria and Its Effect on Pregnancy Outcomes in Sudanese Women from Blue Nile State. *Malaria Journal*, **16**, 374.  
<https://doi.org/10.1186/s12936-017-2028-0>
- [21] Botolahy, Z.A., Randriambelomanana, J.A., Imbara, E., Rakotoarisoa, H. and Andrianampalinarivo, H.R. (2011) Aspects du paludisme à *Plasmodium falciparum* pendant la grossesse selon les cas observés au CHU de Toamasina Madagascar. *Revue d'Anesthésie-Réanimation et de Médecine d'Urgence*, **3**, 23-26.
- [22] Steketee, R.W., Nahlen, B.L., Parise, M.E. and Menendez, C. (2001) The Burden of Malaria in Pregnancy in Malaria-Endemic Areas. *American Society of Tropical Medicine and Hygiene*, **64**, 28-35. <https://doi.org/10.4269/ajtmh.2001.64.28>
- [23] Kapisi, J., Kakuru, A., Jagannathan, P., *et al.* (2017) Relationships between Infection with *Plasmodium falciparum* during Pregnancy, Measures of Placental Malaria, and Adverse Birth Outcomes. *Malaria Journal*, **16**, 400.  
<https://doi.org/10.1186/s12936-017-2040-4>
- [24] Mohammed, A.H., Salih, M.M., Elhassan, E.M., *et al.* (2013) Submicroscopic *Plasmodium falciparum* Malaria and Low Birth Weight in an Area of Unstable Malaria Transmission in Central Sudan. *Malaria Journal*, **12**, 172.  
<http://www.malariajournal.com/content/12/1/172>  
<https://doi.org/10.1186/1475-2875-12-172>
- [25] Albiti, A.H., Adam, I. and Ghouth, A.S. (2010) Paludisme Placentaire, anémie et faible poids à la naissance au Yémen. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, **104**, 191-194. <https://doi.org/10.1016/j.trstmh.2009.07.004>
- [26] Guyatt, H.L. and Snow, R.W. (2004) Impact of Malaria during Pregnancy on Low Birth Weight in Sub-Saharan Africa. *Clinical Microbiology Reviews*, **17**, 760-769.  
<https://doi.org/10.1128/CMR.17.4.760-769.2004>
- [27] Rulisa, S., Mens, P.F., Karema, C., Schallig, H.D., Kaligirwa, N., Vyankandondera, J., *et al.* (2009) Malaria Has No Effect on Birth Weight in Rwanda. *Malaria Journal*, **8**, 194. <https://doi.org/10.1186/1475-2875-8-194>
- [28] Braun, V., Rempis, E., Schnack, A., Decker, S., Rubaihayo, J., Tumwesigye, N.M., *et*

- al.* (2015) Lack of Effect of Intermittent Preventive Treatment for Malaria in Pregnancy and Intense Drug Resistance in Western Uganda. *Malaria Journal*, **14**, 372. <https://doi.org/10.1186/s12936-015-0909-7>
- [29] Losimba, L.J., d'Alessandro, U., Labama, L.B., Mugisha, S.E., Gasana, G., Kakoma, J.B. and Wilmet, D. (2010) Effet du traitement préventif intermittent (TPI) de la femme enceinte à la Sulfadoxine-Pyriméthamine (SP) sur le poids de naissance des enfants dans un milieu à résistance élevée du *Plasmodium falciparum* à la SP à l'Est de la République Démocratique du Congo (RDC). *Rwanda Medical Journal*, **68**, 10-15.
- [30] Olliaro, P.L., Delenne, H., Cisse, M., Badiane, M., Olliaro, A., Vaillant, M., *et al.* (2008) Implementation of Intermittent Preventive Treatment in Pregnancy with Sulphadoxine/Pyrimethamine (IPTp-SP) at a District Health Centre in Rural Senegal. *Malaria Journal*, **7**, 234. <https://doi.org/10.1186/1475-2875-7-234>
- [31] Mace, K.E., Chalwe, V., Katalenich, B.L., Nambozi, M., Mubikayi, L., Mulele, C.K., *et al.* (2015) Evaluation of Sulphadoxine-Pyrimethamine for Intermittent Preventive Treatment of Malaria in Pregnancy: A Retrospective Birth Outcomes Study in Mansa, Zambia. *Malaria Journal*, **14**, 69. <https://doi.org/10.1186/s12936-015-0576-8>
- [32] Falade, C.O., Yusuf, B.O., Fadero, F.F., Mokuolu, O.A., Hamer, D.H. and Salako, L.A. (2007) Intermittent Preventive Treatment with Sulphadoxine-Pyrimethamine Is Effective in Preventing Maternal and Placental Malaria in Ibadan, South-Western Nigeria. *Malaria Journal*, **6**, 88. <https://doi.org/10.1186/1475-2875-6-88>
- [33] Valea, I., Tinto, H., Drabo, M.K., Huybregts, L., Henry, M.-C., Roberfroid, D., *et al.* (2010) Intermittent Preventive Treatment of Malaria with Sulphadoxine-Pyrimethamine during Pregnancy in Burkina Faso: Effect of Adding a Third Dose to the Standard Two-Dose Regimen on Low Birth Weight, Anaemia and Pregnancy Outcomes. *Malaria Journal*, **9**, 324. <http://www.malariajournal.com/content/9/1/324> <https://doi.org/10.1186/1475-2875-9-324>
- [34] Ruh, E., Bateko, J.P., Imir, T. and Taylan-Ozkan, A. (2018) Molecular Identification of Sulfadoxine-Pyrimethamine Resistance in Malaria Infected Women Who Received Intermittent Preventive Treatment in the Democratic Republic of Congo. *Malaria Journal*, **17**, 17. <https://doi.org/10.1186/s12936-017-2160-x>

## **Abbreviations**

CI: confidence interval

DRC: Democratic Republic of Congo

GRH: general reference hospitals

IPTp-SP: intermittent preventive treatment in pregnancy with Sulphadoxine-Pyrimethamine

HA: healthcares area

ITNs: insecticide-treated mosquito net

LBW: low birth weight

OR: odds ratio