Maternal Factors of Newborn Low Birthweight in Malaria Endemic Settings of Nanoro, Rural Burkina Faso

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Abstract

Background. In sub-Saharan Africa, the intermittent preventive treatment of malaria in pregnancy with sulphadoxine pyrimethamine (IPTp-SP) strategy is recommended to limit malaria consequences on birth outcomes. Ten year after IPTp-SP was adopted in Burkina Faso, we assessed the magnitude of low birthweight (LBW) and its maternal factors in Nanoro.

Methods. A secondary analysis of data from a cross-sectional study was carried out in women who gave birth at Nanoro peripheral health centers using a binary multivariate logistic regression. Maternal socio-demographic factors, gyneco-obstetrical history and relevant medical characteristics were evaluated to identify associated factors. A p-value less than 0.05 was considered statistically significant.

Results. Of 291 delivery records examined, 14 % of women received three or more doses of SP while 80% used bed nets the night before their admission for delivery. Malaria was detected in 36.1% and anemia in 52.9% of women. The average neonate birthweight was 2933 g and 12 % of them were born with a low birthweight. After multivariate analysis, first delivery (OR = 8.84, [95% CI: 3.72-21.01]), and being multiparous with history of stillbirth (OR = 5.03, [95% CI: 1.54-16.40]) were significantly associated with an increased risk of LBW.

Conclusion. LBW is still prevalent in rural Nanoro and the uptake of three or more doses of SP for the IPTp was low. In addition, to improving the coverage of IPTp-SP to improve birthweight, an extension of the target of antenatal care to other known causes of LBW including curable sexually transmitted infections may be necessary.

1. Introduction

Despite halving the global neonatal mortality rate from 36.6 to 18.0 per 1000 livebirths between 1990 and 2017 [1], an estimated 2.5 million neonates died in the world in 2018 and this situation threatens the achievement of the third sustainable development goal (SDG), to end preventable child deaths by 2030 [2]. Low birthweight (LBW) - a birthweight below 2500 grams - is an important risk factor of neonatal deaths [3, 4], and is prevalent in sub Saharan Africa although half of infant birthweight is not recorded [5]. Noteworthy, neonate who survive from low birthweight immediate consequences, still present higher risk of short and long term health consequences such as stunted growth [6], lower intelligence quotient (IQ, an IQ test score of 70 or below) [7, 8] or adult-onset chronic conditions [9]. Regional data suggest that the global burden of LBW is heavily skewed towards sub-Saharan Africa and south Asia due to high risk of infections [3, 10]. Maternal infections including malaria and sexually transmitted infections are important risk factors of low birthweight through intrauterine growth retardation (birthweight below the 10th percentile for the gestational age) or prematurity (birth before 37 weeks of gestational age) [11–18]. Maternal malaria causes 20% of LBW in malaria endemic area and 6% neonatal deaths [18]. Potentially, 100,000 infant lives could be saved each year if adequate malaria prevention measures were implemented during pregnancy.

Sulfadoxine-pyrimethamine (SP) is recommended to prevent malaria adverse effects on pregnancy in sub Saharan Africa through the intermittent preventive treatment of pregnant women (IPTp) [19]. However, the spread of *P. falciparum* resistance to SP threatens the antimalarial effectiveness of the IPTp-SP strategy [20].

In Burkina Faso, IPTp-SP was adopted in 2005 starting at the second trimester of pregnancy with the requirement of 3 doses of SP [21]. Seven years later, the magnitude of LBW did not decrease significantly (from 15.8% in 2005 to 13.4% in 2012) and since then no other evaluation was carried out although it is still the recommended strategy [22, 23]. A reevaluation of the impact of the current IPTp strategy is needed to understand its utility and prevent the effects of non-efficacy. The main goal of this analysis was to measure the prevalence of term LBW and to identify associated risk factors in Nanoro ten years after IPTp-SP policy was adopted.

2. Methods

2.1. Study site: The study was conducted in Nanoro demographic and health surveillance system (HDSS) area**,** a sentinel site for the "*Roll Back Malaria*" initiative. It is situated in the centre-west region of Burkina Faso at about 90 km from Ouagadougou the capital city with a population of 63,000 inhabitants [24]. Malaria transmission is holo-endemic, with transmission peaking during the rainy season (June-October). The commonest malaria vectors are *Anopheles gambiae*, *A. funestus* and *A. arabiensis* and *P. falciparum* is the predominant malaria parasite. Malaria is the main reason for visiting health centres with a case-fatality rate between 5% and 30% [25].

2.2. Study design: A secondary data analysis was conducted from data originally collected to evaluate malaria infection among women who recently gave birth in Nanoro health centers through a cross sectional survey. Nursing mothers and their babies were enrolled into the study. Data on demographic, gyneco-obstetric characteristic and relevant medical history were collected from the mothers onto a case report form. The participant antenatal care (ANC) cards were reviewed and data extracted from September 2013 to March 2014.

2.3. Inclusion/exclusion criteria: Women were eligible if they were aged between 16 and 45 years and gave birth to a neonate within the last 24 hours from a pregnancy with a minimum gestational age of 37 weeks (using last menstrual period or the Ballard score)[26], lived in Nanoro HDSS, and have signed an inform consent form. Mothers who delivered twin babies, presented a post-partum hemorrhage were not eligible. Of the 323 women, 9.9% (32/323) were not included, due to reasons including 4 (1.2%) multiple pregnancies, 6 (1.8%) stillbirths, 3 (0.9%) neonate deaths in the first two hours of life, 2 (0.6%) very ill newborns, 5 (1.5%) missing birthweight records, 3 (0.9%) concurrent participation to other study and 9 (2.3%) delivery before 37 weeks of gestational age. Finally, 291 (90.1%) women were included. In this analysis, term low birthweight, birthweight between 500 and 2500 grams from a gestational age over 37 weeks was considered the main outcome.

2.4 Sample size: At the time of policy change, LBW proportion was 15.8% [23]. We hypothesized that the policy change would reduce this proportion to 10% within the ten-year period of implementation. The sample size was estimated to test the hypothesis, with a precision i = 3.5%, a confident interval of 95 % (α = 0.05, with a critical value Z^2 =1.96), the minimum sample size required was n = 282 participants using the following formula $n = Z^2 * p * (1-p)/i^2$. This was a secondary analysis of database collected on 291 participants recruited to estimate malaria prevalence. Therefore, the available sample size was adequate to test the hypothesis.

2.5 Data collection procedures and variables collected. Data were collected from the health center birth registries, the antenatal care cards and by neonate examination. Information not available in these documents were collected by one-on-one interviews using a standardized questionnaire. Neonate examination was conducted within 24 hours of delivery either in the health facility or by home visit. Variables collected for mothers are presented in table 1 and included age, occupation, instruction level, parity, history of abortion, history of stillbirth, the number of living children at the time of the survey, the use of insecticide treated net (ITN) the night before visiting the health facility for delivery, the number of ANC visits performed, knowledge of the recommended protocol of 3 SP received during the pregnancy. Neonate birthweights were measured using calibrated Seca® 384 electronic scale with 10 g resolution and a precision less than 10 grams (seca gmbh & co. kg, Germany). In addition, blood samples were obtained from finger pricks to measure maternal hemoglobin level using a portable spectrophotometer (HemoCue, Ängelholm, Sweden) and a malaria rapid diagnostic test was performed using SD-Bioline Malaria Antigen *Pf®* test strips (sensitivity 99.7% and specificity of 99.5 %) for the identification of *P. falciparum*.

Table 1. List of exploratory variables

No	Variable	Definition	Categories
Socio-demographic's characteristics			
1	Age	Mother age (years)	15 – 19 ; 20 – 34 ; and 35 - 42
2	Instruction	Educational level	None, primary, secondary or higher
3	Occupation	Mother's occupation	Unemployed, farmer-trader, employed/self employed
4	Parity	Number of birth that a woman had after 28 weeks of gestation	1; 2 – 4; 5 or more
5	Stillbirth	Maternal history of stillbirth	Yes / No
6	Abortion	Maternal history of abortion	Yes / No
7	Kids	Number of living kids at the time of the survey	One or two; three or four; Five or more
Attitude and knowledge regarding malaria prevention			
8	Required_IPTp	Knowledge of the minimum required 3 IPTp-SP doses	Yes / No
Use of malaria prevention measures and relevant medical conditions			
9	ITN use	Use of ITN the previous night	Yes / No
10	IPTp-SP	Number of IPTp - SP doses received	1; 2; 3 or more
11	ANC	Number of ANC visits performed	Less than 4; 4 or more
12	Anemia	Anemia (Hemoglobin level < 11g/dL)	No / Yes
13	Malaria	Positive malaria rapid diagnostic test results	No / Yes
14	Birthweight	Weight of neonate at birth in grams	Low (<2500); Normal (>=2500)

ANC: antenatal care, ITN: Insecticide treated bed net, IPTp-SP: Intermittent preventive treatment with sulfadoxine-pyrimethamine, g/dL: Gram per deciliter

2.6. Data processing and analysis: data were entered into a REDCap database, cleaned on Excel 2016 and imported to Stata version 15 (StataCorp. 2017, TX, USA) for analysis. The uptake of IPTp-SP was grouped in one, two, and three or more doses. Anemia was defined as hemoglobin level < 11g/dL, malaria as a positive rapid diagnosis test result. Pregnancy duration was obtained using the last menstrual period (LMP) or the Ballard score obtained by neonate examination whenever there was uncertainty. A term low birthweight was defined as any birthweight from a mono-fetal pregnancy of at least 37 weeks of gestational age that was below 2500 g [16,26]. Odds ratios (OR) of LBW and 95% confident intervals (95% CI) were calculated according to each maternal factor using univariate logistic regression. Adjusted odd ratios (aOR) and 95% CI were derived by a backward elimination regression of variables with a p-values < 0.20 and retention of variables with statistically significant p-values. For the multivariable analysis, variable age was not included due to its strong correlation with the parity. Because of a comparable proportion of LBW if more than one delivery, mothers were subsequently grouped in single and multiple deliveries. In addition, variable history of stillbirth was combined to parity (first delivery, and multiple delivery with history of stillbirth). A p-value < 0.05 was considered statistically significant.

2.7. Ethical considerations: The study protocol was discussed with local health authorities and community leaders to obtain their assent. Permission was obtained from the national ethics committee of Burkina Faso by the principal investigator (CERS 018.6.078). Informed consent was obtained from all women prior to participation. All participants with anemia or positive malaria test were treated according to the national guidelines.

3. Results

3.1. Study participants' characteristics: Table 2 summarizes study participants' characteristics. In brief, of the 291 mothers included, the average age (± standard deviation) was 26 (± 6) years and most of them were housewives. The median parity stood at three births (interquartile range, 2-5 births) and the median number of living children was three. One third of participant were tested positive for peripheral malaria (with a lower percentage among bed net users 33% versus 44% among non-users) and half study participants were anemic. More than 96% of women reported three as the minimum SP doses required during the course of a pregnancy contrasting with the low rate (14%) of those that effectively received at least three doses

Table 2: Socio-demographic, gyneco-obstetric and relevant medical history at inclusion (n=291).

Characteristics	items	Percentage
Age group (years)	< 20	20.3
	20-34	67.7
	>=35	12.0
History of stillbirth	No	89.3
	Yes	10.7
History of abortion	No	84.5
	Yes	15.5
Parity	1	22.7
	2 – 4	49.8
	5 or more	27.5
Anemia	No	47.1
	Yes	52.9
Malaria	Negative	63.9
	Positive	36.1
ITN use	Yes	81.6
	No	18.4
Number of ANC visits performed	≤ 1	5.2
	2	17.5
	≥ 3	77.3
Knowledge of required SP doses	≥ 3	96.6
	< 3	3.4
Number of IPTp-SP doses received	≤ 1	31.3
	2	54.6
	≥ 3	14.1
Instruction level	None,	83.8
	Primary or more	16.2
Mother occupation	Housewives	85.2
	Other	14.8

Abbreviation. ANC: antenatal care, SP: sulfadoxine-pyrimethamine,

3.2. Low birthweight prevalence and maternal factors: Of the 291 neonates, the mean birth weight (± standard deviation) was 2933 ± 390 g and 12.0 % (35/291) were born with a birthweight below 2500 g. This proportion was higher among teenage mothers (28.8%). **Table 3** presents the prevalence of LBW in relation to maternal sociodemographic characteristics, obstetrical history as well as the univariate odds ratios. Younger maternal age, and being primigravid or a multigravida with history of stillbirth were positively associated with the risk of low birthweight, while sleeping under bed net was significantly associated with a lower prevalence. Uptake of more than 3 doses of SP did not show a significant association, however a trend toward a decrease of the prevalence of low birthweight was observed as the uptake of SP increased. The prevalence of low birthweight was higher among anemic mothers although this association was not statistically significant (p=0.052).

Table 3: Low birthweight prevalence and maternal factors, Burkina Faso 2013-14 (n=286)

Characteristics	Total	LBW (%)	OR	95%CI	p. value
Age group (years)	59	28.8	4.0	1.9-8.5	<0.001*
< 20	197	9.2	1.0	ref	
20 - 34	35	0.0	-	-	
≥ 35					
Instruction level	244	11.5	0.7	0.3-1.8	0.509
None	47	14.9	1.0	Ref	
Primary or more					
Occupation	248	12.5	1.0	Ref	0.539
Housewives	43	9.3	0.7	0.3-2.1	
Others					
Parity	61	29.5	8.8	3.7 – 21.0	<0.001*
Primipara	26	19.2	5.0	1.5 – 16.4	
Multipara with history of stillbirth	199	4.5	1.0	Ref	
Multipara					
History of abortion	246	11.4	1.0	Ref	0.443
No	45	15.6	1.4	0.6-3.5	
Yes					
Anemia	137	8.0	1.0	Ref	0.052
No	154	15.6	2.1	0.9-4.5	
Yes					
Malaria	186	10.8	1.0	Ref	0.378
No	105	14.3	1.4	0.7-2.8	
Yes					
ITN use	227	9.7	1.0	Ref	0.018*
yes	51	21.6	2.6	1.2-5.7	
No					
Number of ANC visits	15	13.3	1.2	0.3-5.5	0.902
≤1	51	13.7	1.2	0.5-3.0	
2	225	11.5	1.0	Ref	

≥3					
Number of SP doses received	91	14.3	1.5	0.5-5.1	0.703
≤ 1	159	11.3	1.2	0.4-3.7	
2	41	9.8	1.0	Ref	
≥3					

Legend: ***statistically significant

Abbreviations. SP: sulfadoxine-pyrimethamine; CI: confidence interval; ANC: antenatal care; LBW: low birthweight; Ref: reference group, ITN: insecticide treated bed nets,

The multivariate analysis showed that the first delivery (OR = 8.83, [95% CI: 3.71-21.01]), or the subsequent deliveries when there is an obstetrical history of stillbirth (OR = 5.03, [95% CI: 1.54-16.40]) were significantly associated with an increased risk of LBW.

4. Discussion

Low birthweight prevalence was still high in Nanoro particularly given that low birthweight from preterm births were not counted. However, the observed prevalence was 3.8 percentage points lower than the 15,8% reported among term neonates at the start of the new strategy in the same region [23]. Lower prevalence than that reported in Nanoro was observed in other African countries with a similar malaria patterns and comparable intervention packages for antenatal care services. Indeed, in Ethiopia (10%) in 2014 [27], and Nigeria (7%) in 2013 [28] the reported prevalence was lower than that of the current evaluation. However these estimates could be understated as in the Nigerian's study, data were collected retrospectively from the routine surveillance system and it is reported that half of delivery data in Africa is not recorded due to weaknesses in the reporting system [5]. Similarly, the study in Ethiopia was carried out in an urban area where the economic level of women tend to be higher than those from the rural area and the impact of better economic status on the prevalence of low birthweight is already described [29, 30]. In contrast, rate in excess were reported in South Africa (38.5%) in 2014 [31], and in a study conducted in Zimbabwe (16.7%) [32]. The reason behind this higher prevalence in the South African and Zimbabwean studies could be related to the higher prevalence of human immuno-deficiency virus (HIV) infection [33]. HIV is reported in many African studies as a possible risk factor of LBW although the mechanism has not yet been fully elucidated [32, 34]. This illustrates the importance of testing HIV when evaluating the impact of interventions allocated to pregnant women.

It is reported that the maternal obstetrical history and events occurring during the course of the pregnancy impact the outcome of pregnancies. However, the specific factors reducing the birthweight are not always identified. Our results showed that combined parity and obstetrical history of stillbirth were significantly associated with the occurrence of low birthweight in rural Burkina Faso. Similarly to Hoquet *et al*. report, our study showed that the risk of LBW was significantly increased for the first delivery [34]. The impact of primiparity on low birthweight neonates was reported by several authors [35–37]. The biological ground for first delivery children to be at higher risk of low birthweight may be related to some physiologic changes occurring during pregnancy to facilitate fetal growth with the process incompletely reversing in postpartum thereby creating a more efficient environment for subsequent fetuses [38]. Indeed, uteroplacental blood flow, which is responsible for delivering oxygen and nutrients to the fetus, is greater during subsequent pregnancies compared to the first pregnancy [39, 40]. In addition, there may be structural factors that limit the uterine capacity in the first pregnancy as described in animal models [41]. Furthermore, infants born from first pregnancy may have developed in a different maternal immune environment, contributing to relative growth restriction, compared to subsequent pregnancies [42]. Along with primiparity, mother with multiple pregnancy and an obstetrical history of stillbirths also presented a higher risk of delivering low birthweight neonates compared to multiple pregnancy without history of stillbirths. Similar observation was reported by Chen *et a*l. in 2018 and Rozi *et al*. in 2016 [43, 44]. Ahrens *et al*. have noticed that the risk of low birth weight was highest after history of three stillbirths [45]. Particular attention to pregnant women with such background characteristics during their antenatal care visits could be of greater impact in mitigating the risk of low birthweight among them.

Poor maternal nutritional status is also described as a key factor of poor intrauterine fetal growth [46]. Even though that characteristic was not assessed in the current study, the high prevalence of anemia could indicate a poor nutritional status [47]. Indeed, a study conducted in the same area showed that low maternal weights, low maternal body mass indexes and low brachial perimeters were significantly associated with anemia [42]. In the current study, anemia was positively associated with an increased risk of low neonate weights at univariate analysis ($p = 0.052$) however that trend weakened with adjustment to parity during multivariate analysis and also because of reduced sample size secondary to missing values. Further assessment building on the scope of this finding may be necessary to show the adequate impact of anemia and poor nutritional status on the risk of the occurrence of LBW.

Studies reported that using bed net throughout pregnancy reduces the risk of adverse delivery outcomes including low birthweight [48]. A similar trend was observed by univariate analysis in the current study ($p = 0.018$) which showed bed net use to efficaciously prevent adverse birth outcomes by reducing up to 11% of malaria infections. However, this could not be confirmed by multivariate analysis because of the reduced sample size due to missing values. Studies building on a larger sample size may be required to assess the actual impact of ITN use on the reduction of LBW

A number of limitations in this study are worth noting. The study was conducted on women who have delivered at term excluding low birthweight from preterm deliveries and that could understate the actual extent of the problem. It remains to bear in mind that gestational age record was collected from parental assessment of last menstrual period (LMP), which could be prone to some errors, as majority of the study population did not recall their LMP. Although the analysis had limitations, it is worthy identifying the population that need special attention during antenatal care. Larger studies building on the scope of these factors examined in this report will be valuable in guiding efforts to curtail the impact of low birthweight in sub-Saharan Africa.

5. Conclusions

This report showed that low birthweight prevalence remained high among neonates in rural Nanoro although its magnitude has considerable decreased. It also showed that the intake of IPTp-SP was still low among the women. In addition, to improve the coverage of IPTp to reduce the magnitude of LBW, perhaps it would be important to associate interventions targeting other known causes of adverse birth outcome such as bacterial vaginosis and poor nutritional status.

List Of Abbreviations

SP: sulfadoxine pyrimethamine, **IPTp**: intermittent preventive treatment in pregnancy, **LBW**: low birthweight, **ANC**: antenatal care, **OR**: odds ratio, **CI**: confident interval, **SDG**: sustainable development goals, **NMR**: neonatal mortality rate, **SGA**: small-for-gestational-age, **HDSS**: health and demographic surveillance system, **HIV**: human immunodeficiency virus, **WHO**: world health organization, **LMP**: late menstrual period,

Declarations

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Competing interests

The authors declare that they have no competing interests.

Authors' contribution

ML, DV, IV and HT have conducted the study, conceptualized and written large parts of the manuscript. ML, MWD, and AR performed the statistical work. MS, SOS AR, MWD and DP have made important comments to the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

The dataset used and analyzed during the current study is available from the corresponding author.

Ethics approval, consent to participate

The study was approved by the national ethics committee of health science research of Burkina Faso (CERS-201-6-078)

Consent to publication

Not applicable

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