

Low Birth Weight and Prematurity in Teenage Mothers in Rural Areas of Burkina Faso

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Abstract

Background: Adolescence is associated with adverse fetal outcome, particularly in resources limited settings. We assessed the association between mother's age and low birth weight or prematurity in Nanoro, a rural health district of Burkina Faso.

Methods: We collected data on mothers and their newborns in the framework of the "Safe and Efficacious Artemisinin-based Combination Treatments for African Pregnant Women with Malaria" clinical trial. Low birth weight or prematurity was defined as adverse fetal outcome. Logistic regression was used to compare its occurrence in teenagers and in women aged ≥ 20 years.

Results: From June 2010 to November 2013, 870 pregnant women enrolled in the PREGACT study were treated for a *Plasmodium falciparum* infection and followed up until delivery.

Of the 823 women with singleton live-borns, 205 (24.9%) were teenagers of whom 44 (5.3%) were minors (15-17 years). Up to 91.7% of adolescents presented with anemia at entry.

The incidence of adverse fetal outcome in teenagers was 39.8%, increasing to 50.0% in minors. Anemic adolescents were significantly at higher risk of delivering low birth weight or preterm babies compared to their older counterparts.

In multivariate analysis, teenagers with both anemia and fever presented the highest and significant odds ratios of adverse fetal outcome, whatever was their BMI: Teenagers with anemia, fever and high BMI at entry, AOR=3.46, 95% CI: (1.40, 8.58), teenagers with anemia, fever and low BMI at entry, AOR=2.86, 95% CI: (1.14, 7.13).

Conclusion: Teenager's pregnancy is associated with adverse fetal outcome in the rural health district of Nanoro, mainly when teenagers experiment anemia and fever. In low resources setting, multidisciplinary approach including education and setting up favorable socio-economic environment are needed to prevent early motherhood.

Keywords: Teenagers; Low birth weight; Preterm birth; Rural; Burkina Faso

Introduction

In 2010, 36.4 million women aged 20-24 years had given birth to a live child before their 18th birthday. This was much more common in West and Central Africa (28%) than in Eastern Europe and Central Asia (4%). Similar proportions were found for giving birth before the 15th birthday, i.e. 6% and 0.2%, respectively. In Burkina Faso, the prevalence of a first birth before 18 was estimated at 28% [1].

Teenage pregnancy is a concern worldwide as it is associated with low birth weight (LBW) and preterm birth (PTB) [2-4]. Pregnancy in teenagers can result in adverse maternal outcome such as severe anemia or death and compromise their socio-economic opportunities [5]. Children from teenage mothers are more likely to be stunted at their second birthday, to develop glucose disorder and problems at school [3]. They are more often hospitalized and will contribute with more than half to the following generation of adolescent mothers [6]. Moreover, PTB complications are one of the main causes of death among children aged less than 5 years [7]. LBW has also been associated to an increased neonatal mortality and hospitalization [8,9]. Premature infant's experience also more temperature instability, hypoglycemia, respiratory distress and jaundice [10]. Later in

life they are more likely to present impaired neurodevelopment, impaired learning capacity, and impaired behavior. Previous studies that reported an association of LBW or PTB with maternal age remains controversial about mechanisms involved [8,11-13].

Studies focusing on adverse fetal outcome in adolescents are scarce in Burkina Faso, despite a high proportion of them that could further increase in the upcoming decades [1]. This study aimed at assessing the prevalence of adolescents' pregnancy in Burkina Faso and its association with LBW or PTB in the rural setting of Nanoro and Nazoanga.

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Materials and Methods

Study settings

This study was nested in the PREGACT multicenter clinical trial (trial registration NCT00852423). Details of the methodology and results have been reported elsewhere [14]. The study was designed to assess the efficacy and the safety of four artemisinin based combinations treatments against malaria in pregnancy. Seven sites in four countries were involved of whom two in Burkina Faso. The present analysis uses data collected from all pregnant women enrolled in Burkina Faso.

Recruitment

Pregnant women attending the antenatal care clinic in Nanoro or Nazoanga were screened for malaria using a rapid diagnostic test. If positive, study protocol and procedures were explained and a written informed consent obtained. Women included in the trial were those residing within the health center catchment zone, aged of at least 15 years, with a pregnancy between 16 and 37 weeks, with *Plasmodium falciparum* infection, a hemoglobin level of at least 7 g/dL, willing to deliver at the health facility, and to adhere to the study required procedures. They should be able to provide written informed consent also. Exclusion criteria were history of illness which may affect pregnancy outcome, history of allergy to the study drugs, history of known obstetric complication or bad pregnancy history, current use of cotrimoxazole or antiretroviral treatment, evidence of intake of antimalarial drug or antimicrobials with antimalarial activity, inability to take oral treatment, or requirement of hospitalization because of serious illness at screening. Women intending to leave the study catchment area prior to delivery and those currently participating to another study were also excluded. In Burkina Faso, women were randomized to one of the three following treatments: Artesunate-Amodiaquine (ASAQ), Arthemether-Lumefantrine (AL) and Mefloquine-Artesunate (MQAS). Randomization was done using balanced incomplete block design. Participants were treated and observed the first three days by study nurses.

At recruitment study staff recorded demographics, anthropometrics, medical and pregnancy history. A portable ultrasonography device allowed assessment of the fetal viability.

Follow-up

Visits were scheduled over 9 weeks after treatment, at days 3, 7 and then once a week. Subsequently, women were encouraged to attend the antenatal clinic monthly until delivery and at any time they felt unwell, regardless to the schedule.

At each scheduled and unscheduled visit, physical examination was performed. Weight, height and temperature were measured. Signs and symptoms since last visit were collected. A blood sample was taken for malaria smears while hematology was done on days 7, 14, 28 and 63 and biochemistry at days 7 and 14 only.

Recurrent malaria infection was treated as per the malaria national program guidelines. After delivery, the newborn was weighted within 72 h. The gestational age was determined using the Ballard score [15].

Laboratory methods

Thin and thick blood smears were obtained from each participant to determine parasite density. A portable HemoCue device (Hb301 Hemocue, Angelholm, Sweden) was used to determined maternal hemoglobin level. Detail laboratory methods have been published elsewhere [14,16].

Ethics

The PREGACT study was approved by the ethics committee of the University of Antwerp, Belgium, the Institutional Ethics committee of Centre Muraz and the Ethics committee of the Ministry of Health, Burkina Faso [16]. All data were coded, and no participant's identifiers appeared either in the study case report form, database and previous publications. Informed consent was obtained from the study participants and, for those minor of age, from their representatives

Definitions and statistical analysis

Maternal age was determined at entry from the date of birth in the health booklet or self-reported by the participant. Teenager was defined as an individual between the age of 15 and 19 years according to the WHO definition [17]. Teenagers were divided in two subgroups: 15-17 and 18-19 years old.

The dependent variable was adverse fetal outcome defined as the occurrence of LBW (<2500 g) and/or PTB (gestational age<37 weeks). The weight was measured within 72 h after birth using digital scales and Ballard score was assessed at birth by the study physician [15].

Baseline pregnancy BMI (weight in kg divided by square of height in m), fever (body temperature $\geq 37.5^{\circ}\text{C}$) and anemia (hemoglobin level<11 g/dl) were covariates analyzed along with maternal age.

As part of the PREGACT quality assurance system, all data were entered into an electronic case report form built under MACRO software (InferMed, Kings Clinical Trial Unit, and King's College London, UK). They were checked for consistency and all queries were resolved before locking the database for statistical analysis.

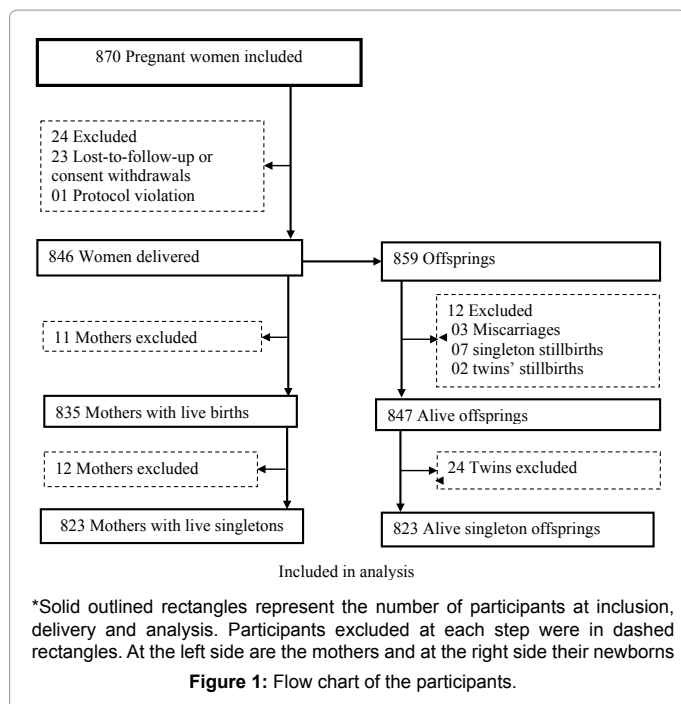
Univariate logistic regression was used to assess whether teenagers had a higher adverse pregnancy outcome than adults at each level of the covariates. Adjustments were then made using a multivariate logistic regression. All covariates and their interaction terms with maternal age were included in the model independently of their statistical significance. The estimated coefficients including those of the interactions, their standard errors and their correlation coefficients were used to derive adjusted odds ratio and 95% confidence interval for each combination of the covariates.

A p-value ≤ 0.05 was considered as a statistical significant result. All analyses were performed with STATA 14.1 IC[®] software (StataCorp LP, Texas USA).

Results

From June 2010 to November 2013, 870 pregnant women in their second or third trimester were enrolled in the trial and randomized to one of the three treatment groups. A total of 846 women delivered while 23 withdrew or were lost to follow-up. One woman was excluded by the investigator because of protocol violation (no malaria infection at inclusion). Among the 859 offspring, 847 were live births including 24 twins. Relationship with adverse fetal outcome was assessed on the 823 singleton live births and their mothers. A total of 14 newborns had missing data: 8 lack information on birth weight and 7 were not assessed for gestational age at birth. The large majority of women (73.0%, 601/823) were in their second trimester of pregnancy, there were 205 (24.9 %) teenagers, including 44 (5.3%) minors (15-17 years). More than a quarter 233 (28.3%) were primigravidae and up to 74.6% had anemia (Figure 1 and Table 1).

Half (50.2 %) of the teenagers had a low BMI ($\leq 21\text{kg/m}^2$), 18.5% had fever at entry. There was a significantly higher proportion of anemia in



	Overall N=823	Maternal age (years)			
		15-17 n=44	18-19 n=161	All teenagers n=205	Adults 20-45 n=618
Recruitment site					
Nanoro	552	33 (6.0)	114 (20.7)	147 (26.6)	405 (73.4)
Nazoanga	271	11 (4.1)	47 (17.3)	58 (21.4)	213 (78.6)
Treatment arm					
ASAQ	278	14 (5.0)	65 (23.4)	79 (28.4)	199 (71.6)
AL	277	13 (4.7)	48 (17.3)	61 (22.0)	216 (78.0)
MQAS	268	17 (6.3)	48 (17.9)	65 (24.3)	203 (75.7)
Pregnancy trimester					
Second	601	36 (6.0)	125 (20.8)	161 (26.8)	440 (73.2)
Third	222	8 (3.6)	36 (16.2)	44 (19.8)	178 (80.2)

*ASAQ: Artesunate-Amodiaquine; AL: Artemether-Lumefantrine; MQAS: Mefloquine-Artesunate

Table 1: Recruitment and randomization characteristics by maternal age group.

teenagers than in adults (91.7% versus 68.9%, p -value<0.001). Among the 823 newborns, 113 (13.9%) were premature and 148 (18.1%) had a LBW (Table 2).

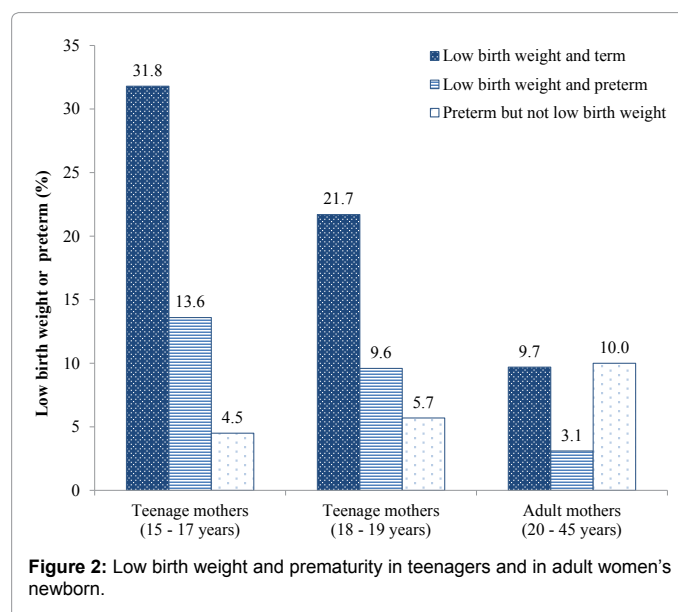
The overall incidence of adverse fetal outcome was 27.1%, increasing up to 39.8% among teenagers and up to 50.0% in minors (15-17 years). In teenagers, most LBW infants were born from pregnancies at term, the highest incidence, 31.8%, being in minors. Teenagers were significantly at higher risk of delivering LBW or PTB babies compared to older women, regardless of their BMI (BMI of 16-21, OR=2.07, 95% CI: (1.30, 3.29), BMI of 21-30, OR=2.56, 95% CI: (1.54, 4.24)). Teenager's babies had also an increased risk of LBW or PTB whatever was the temperature at entry. Newborns from anemic teenage mothers were at higher risk of adverse fetal outcome than those from anemic adults. (OR=2.24, 95% CI: (1.54, 3.25)) (Figures 2 and 3).

In multivariate analysis, teenagers with both anemia and fever

	Overall N=823	Maternal age (years)				p-value*
		Teenagers			Adults	
		15-17 n=44	18-19 n=161	All teenagers n=205	20-45 n=618	
Pregnancy BMI						0.70
16-21	423	24 (54.5)	79 (49.1)	103 (50.2)	320 (51.8)	
21-30	400	20 (45.5)	82 (50.9)	102 (49.8)	298 (48.2)	
Fever at inclusion						0.12
Yes	125	9 (20.5)	29 (18.0)	38 (18.5)	87 (14.1)	
No	698	35 (79.5)	132 (82.0)	167 (81.5)	531 (85.9)	
Anemia at inclusion						<0.001
Yes	614	41 (93.2)	147 (91.3)	188 (91.7)	426 (68.9)	
No	209	3 (6.8)	14 (8.7)	17 (8.3)	192 (31.1)	

*p-value is for all teenagers versus adults; BMI: Body Mass Index (kg/m²)

Table 2: Obstetrical and clinical characteristics of teenagers and adults pregnant women.

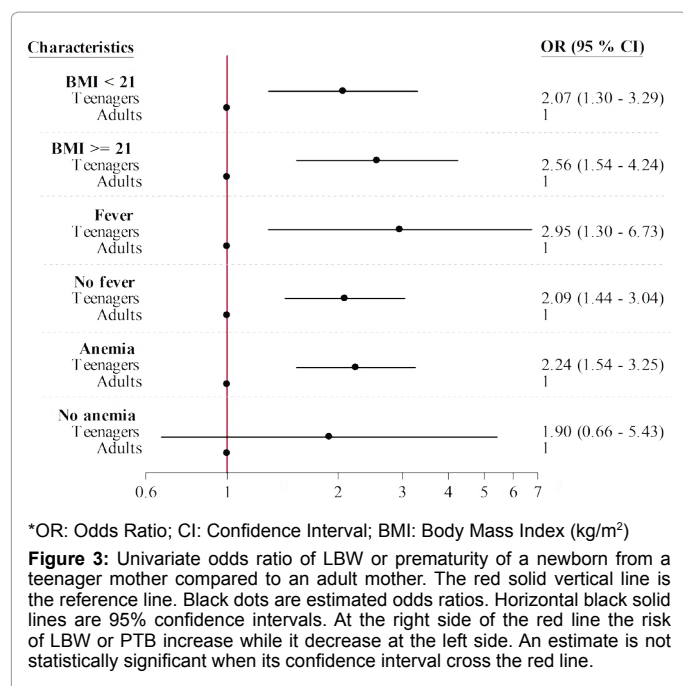


BMI	Adjustment covariates		AOR (95% CI)
	Fever	Anemia	
<21	Yes	Yes	2.86 (1.14-7.13)
<21	Yes	No	2.46 (0.62-9.76)
<21	No	Yes	1.97 (1.19-3.26)
<21	No	No	1.70 (0.54-5.29)
≥ 21	Yes	Yes	3.46 (1.40-8.58)
≥ 21	Yes	No	2.98 (0.79-11.24)
≥ 21	No	Yes	2.39 (1.35-4.22)
≥ 21	No	No	2.06 (0.68-6.26)

*AOR: Adjusted Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index (kg/m²)

Table 3: Multivariate odds ratio of low birth weight or prematurity of a newborn from a teenage mother compared to an adult mother.

presented the highest and significant odds ratios of delivering LBW or PTB babies, regardless of the BMI: Teenagers with anemia, fever and low BMI at entry, AOR=2.86, 95% CI: (1.14, 7.13), teenagers with anemia, fever and high BMI at entry, AOR=3.46, 95% CI: (1.40, 8.58) (Table 3).



Discussion

The analyses nested in the main PREGACT trial offered the opportunity to investigate consequences of teenagers' pregnancies on their offspring. In rural Burkina Faso, in Nanoro and Nazoanga, about a quarter of pregnant women in the study were teenagers. Adverse fetal outcomes, particularly LBW and PTB, were frequent among teenagers, regardless of the BMI. In addition, anemia and fever increased such a risk. Such level of childbearing by adolescents has been reported by studies done in other sub-Saharan countries: 21.1% in Zimbabwe, 24.4% in Cameroon and 24% in a multi-country study in sub-Saharan Africa [12,18,19]. This is also consistent with the distribution of teenage pregnancies in the world, the highest rates being recorded in the developing countries [1].

Some literature shows that teenager's mothers share more unfavorable socio-economic characteristics than adults [11,20]. Most of the time they were unemployed or earned less income, live in rural areas, have low educational level and do not use effective contraceptive methods [20-23]. We did not assess the socio-economic background of our participants. Nevertheless, Burkina Faso like others West African countries is a low resources country where 67 % of the teenage girls aged 15-19 years live in rural areas. A large proportion of rural adolescents (83.3%) are out of school and only 3% use a modern contraceptive method [24]. A study conducted in inpatient neonates in Burkina Faso reported a higher rate (33%) of adolescent mothers [25]. This is in line with publications stating that newborns from adolescent mothers have a higher risk of hospitalization compared to those from non-adolescent mothers [6].

In our study teenagers LBW and PTB deliveries were 34.0% and 16.3%, respectively. In other sub-Saharan countries the rates were lower, but not homogenous [2,12,19,21,26]. This maybe reflects behavioral and cultural diversity among pregnant adolescents across countries [27,28]. Higher proportions (LBW 38.9%, PTB 27.7%) were found in India [29]. We link this to the greater proportion (11% of young teenagers (15-17 years) in this study, given that inverse relationship between maternal age and adverse fetal outcome [4,30,31].

In this study we did not aim at exploring factors associated with LBW or PTB. Our focus was on the potential risk of these adverse fetal outcome associated with the status of being a teenager.

In our univariate analysis adolescence was associated with LBW or PTB, as already demonstrated elsewhere [3,4,18,19,21,30,31]. Conversely studies from Nigeria and Brazil showed no association between maternal age and LBW or preterm birth [32,33]. The urban setting and the hospital-based recruitment in these studies may explain their finding.

In multivariate analysis anemic teenagers delivered more LBW or PTB newborns than their adults counterparts. Indeed anemia is more frequent in adolescents than in adults and it is linked to LBW and PTB [4,8,12,23,27,34]. The high frequency of anemia in teenagers may be explained by the inadequacy of their diet to fill the iron demand induced by their rapid growth and the menstruation's onset [35,36]. Also, adolescents' intake of iron folic acid for anemia prevention is lower compared to adults [29].

The risk of adverse fetal outcome in teenagers was the highest when they presented both anemia and fever. This is not surprising, considering the interplay of fever with anemia, and the role of malaria in the occurrence of fever anemia and LBW in endemic areas [37].

Although low BMI was frequent in teenagers and could indicate biological immaturity, this did not lead to a significant increased risk of adverse fetal outcome in our study as hypothesized elsewhere [2,31,38].

Our analysis excluded twins and this could underestimate the outcome, even if their number is limited. It was also not exhaustive concerning commonly analyzed covariates.

Nevertheless, the prospective design represents strength of our study. In addition, data were collected in an accurate and standardized way.

Importantly, the interplay of maternal age with the covariates was pointed out in our analysis. Inadequate number of antenatal visits has often been cited as deleterious factor of fetal outcome [12,39]. However, a free provision of quality health care including antenatal package was provided throughout the duration of the PREGACT trial.

Conclusion

Being a teenager is associated with adverse fetal outcome in the rural health district of Nanoro, mainly when teenagers experience anemia and episodes of fever. In low resources setting, multidisciplinary approach including education and setting up favorable socio-economic environment are needed to prevent early motherhood.

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Ethics approval and consent to participate

This research has been conducted according to the declaration of Helsinki and to the ICH Good Clinical Practices guidelines. The PREGACT study was

approved from the Ethics committee of the University Hospital, Antwerp, Belgium, the Institutional Ethics committee of Centre Muraz and the Ethics committee of the Ministry of Health, Burkina Faso. All the participants or their representatives gave informed consent before entering the study.

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