

# **Adolescent Pregnancies in Central Gabon: A Description of Epidemiology and Birth Outcomes**

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Dekan: Professor Dr. I. B. Autenrieth

1. Berichterstatter: Professor Dr. P.G. Kremsner

2. Berichterstatter: Professor Dr. C. Reisenauer

# **Adolescent Pregnancies in Central Gabon: A Description of Epidemiology and Birth Outcomes**

Supervisor: Prof. Dr. P. G. Kremsner

Co-Supervisor: Assoc. Prof. Michael Ramharter

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## Abbreviations

**AIDS** Acquired Immune Deficiency Syndrome

**ANC** Antenatal care

**BMI** Body mass index

**CHRGR** Centre Hospitalier Régional Georges Rawiri, Lambaréné

**CI** Confidence interval

**CMF** Centre Médical de Fougamou, Fougamou

**CSA** Chondroitin sulfate A

**CV** Curriculum vitae

**ELBW** Extremely low birth weight

**FAO** Food and Agriculture Organization of the United Nations

**GDP** Gross domestic product

**HAART** Highly active antiretroviral therapy

**HAS** Hôpital Albert Schweitzer, Lambaréné

**HIV** Human immunodeficiency virus

**IPTp** Intermittent preventive treatment in pregnancy

**ITN** Insecticide-treated bed net

**IUGR** Intrauterine growth restriction

**LBW** Low birth weight

**MDG** Millennium development goal

**MiPPAD** Malaria in pregnancy preventive alternative drugs

**MQ** Mefloquine

**N** Number

**OR** Odds Ratio

**SD** Standard deviation

**SGA** Small for gestational age

**SP** Sulfadoxine-Pyrimethamine

**STI** Sexually Transmitted Infection

**UN** United Nations

**UNSD** United Nations Statistics Division

**VLBW** Very low birth weight

**WHO** World Health Organization

# 1 Introduction

## 1.1 Background

Sub-Saharan Africa suffers high rates of maternal, neonatal and childhood mortality and morbidity. While the WHO states that 99% of maternal deaths occur in middle and low income countries, half of them is reported to take place in sub-Saharan Africa [1].

Adolescents are particularly prone to adverse pregnancy outcomes and it is postulated that both mortality and morbidity is higher among adolescents when compared to adult pregnant women [1], including (among other aspects) anemia, malaria and HIV [2]. In the same way, rates of low birth weight (LBW) and prematurity have been reported to be higher among children of adolescent mothers [3]. But most data on adolescent pregnancy and its relation to birth outcomes are reported from industrialized nations and rarely concern sub-Saharan Africa in general and the study area in particular.

“Improve Maternal Health” is one of the eight UN Millennium Development Goals (MDGs) [4]. One of the indicators for achieving this goal is the adolescent birth rate [5], which is considered to reflect the access to reproductive health. The considerably high rate of adolescent mothers in many regions of sub-Saharan Africa [5] reflects the need for assessing the prevalence of adolescent pregnancies in the study area as well as their influence on obstetric outcomes and the necessity of analyzing further associated risk factors.

## 1.2 Adolescent Pregnancy

The definition of ‘adolescent pregnancy’ varies. Often, the term ‘teenage pregnancy’ is used similarly. While the term ‘teenage’ formally refers to the age of 13 to 19 years, it is also commonly used to describe a state of somatic development or legal minority. The terms ‘teenage pregnancy’ or ‘adolescent pregnancy’ sometimes refer to women, who have not yet reached their 20<sup>th</sup> birthday at the time when pregnancy ends (according to the definition of ‘teenage’ being the age between 13 and 19 years and including the rare cases of delivery at an age of 12 years or below). But ‘teenage pregnancy’ as well as ‘adolescent

pregnancy' can also be considered to be the pregnancy of unmarried women or women who are, depending on the country's laws, not yet legally adult.

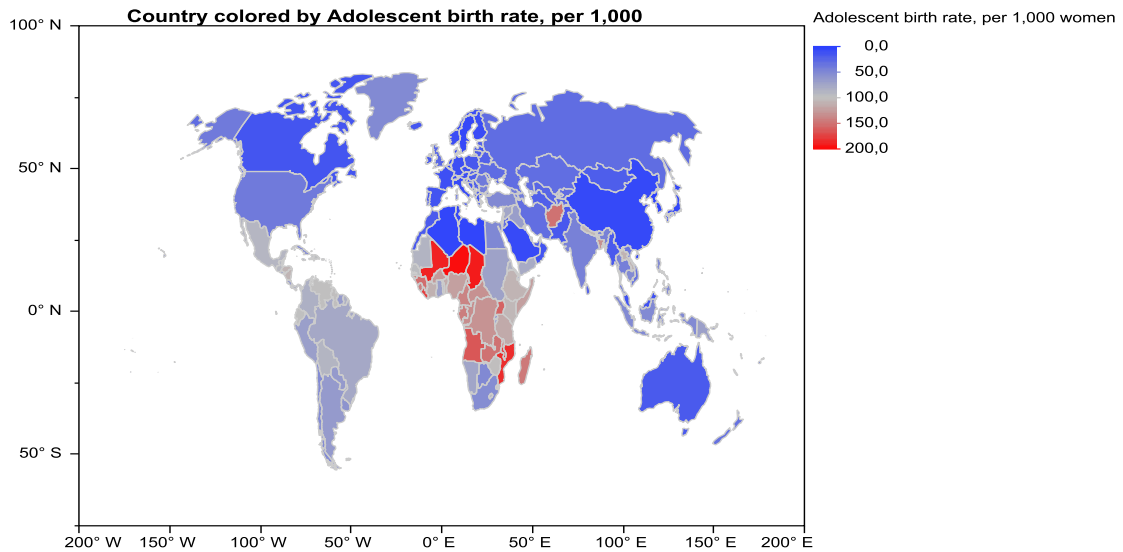
Following the most common definition, 'adolescent pregnancy' will – in this text – be considered as gestation of a woman, who has not yet reached the age of 20 years at time of delivery or end of pregnancy and 'teenage pregnancy' will be used synonymously.

'Very young adolescent pregnancy' will be defined as pregnancy of a girl who has not yet reached her 16<sup>th</sup> birthday by the time when pregnancy ends.

The rates of adolescent pregnancy differ significantly around the world. Adolescent birth rates per 1,000 adolescent women range from under six (for example in South Korea, Switzerland, Japan, Netherlands, Algeria) to over 150 in many African countries [5]. Even though the frequency of adolescent pregnancy has decreased over the past two decades in most countries worldwide, rates still remain high in many countries. The highest rates tend to be found in low and middle income countries, especially in sub-Saharan Africa, where high rates of adolescent pregnancy as well as very young adolescent pregnancy subsist [6].

Figure 1 shows the distribution of adolescent birth rate per 1,000 adolescent women among the world's countries and regions. Data was drawn from the United Nations Statistics Division (UNSD) publications on the MDGs indicators. For each country, the most recent available data was applied.





**Figure 1: Adolescent birth rates worldwide [5].**

The start of sexual activity of girls depends strongly on the cultural setting, on factors as marital status, education and the socioeconomic context (such as a rural or urban setting for example) [7]. Personal, familiar and social perception of early pregnancy also varies according to country, culture and community, including positive as well as negative aspects [8]. While socioeconomic consequences of young motherhood therefore differ widely, the impact on the mother's health is more commonly thought to be disadvantageous [2] and maternal mortality was reported to be higher for adolescent mothers [1, 9, 10]. Early sexual activity might not only lead to pregnancy and its complications, but also bears the risk of acquiring sexually transmitted infections (STI) such as HIV/AIDS. Furthermore, in areas where contraception and sexual education are not frequently available, unsafe and (depending on the nation's laws) illicit abortion can become another major risk, especially for unmarried teenagers, who might choose this alternative to avoid social stigma and early school dropout [11]. Considering these factors, pregnancies among adolescent girls form an important public health issue in the developing world. Awareness among families, communities, health workers and governmental structures is required to improve the situation for young mothers [2, 11].

## **1.3 Low birth weight (LBW)**

LBW is defined as birth weight below 2,500 grams. Birth weight is frequently used as obstetric outcome and research parameter and due to the availability of birth weight data in many contexts, the prevalence of low birth weight in a population is commonly used as epidemiological measure [12].

### **1.3.1 Prevalence of LBW**

The proportion of LBW deliveries is estimated at around 15.5% of all births worldwide, though there are significant regional differences [13]. While the highest rates of LBW are found in South-Central Asia (27%), Europe has the lowest incidence (6%), whereas levels in sub-Saharan Africa lay around 13-15% [13] (all data from the year 2004).

### **1.3.2 LBW as birth outcome measure**

The often assumed association with increased neonatal and child mortality and morbidity [14, 15] as well as with poorer health in adulthood [16, 17] together with the relative easiness of measuring and documenting the birth weight turned LBW into an widely used measure of obstetric outcome, especially in low and middle income countries, where other parameters are rarely accessible. Nonetheless, there are limitations and criticism, for example on the causal relation of birth weight and infant morbidity and mortality or on the defined cut-off level of 2,500 grams, that might not sufficiently reflect the distribution of birth weight in all populations and might therefore be inappropriate for some contexts and regions [18, 19]. But in spite of the call for a broader definition of pregnancy outcome [12, 13], LBW remains a commonly accepted indicator not only for prediction of the individual health and survival of a newborn, but also for a wide range of public health concerns, such as maternal nutrition, maternal health, poverty and quality of health care [20]. Another benefit of the well established WHO definition is the assurance of international comparability.

### 1.3.3 Risk factors for LBW

Immediate reasons for LBW are either intrauterine growth retardation (IUGR), low gestational age at birth or both [14]. However, IUGR and preterm delivery can have many different causes. One of the challenges which are faced when using LBW as birth outcome parameter is indeed the long list of risk factors that have been identified. This multitude of factors suspected to influence birth weight brings along a controversy, whether the particular factors have an independent effect on the birth weight, or are rather associated with other factors.

In a pivotal meta-analysis, summarizing the results of 895 publications in the years of 1970 to 1984, Kramer identified 43 potential determinants on birth weight and assessed their effect on IUGR and prematurity, as well as their possible causal relation with LBW [14]. Kramer distinguishes between risk factors playing a role in the context of middle and low income countries and those with more importance in high income countries. Furthermore, he classifies risk factors according to their modifiability. Among major determinants of IUGR in low income countries, he lists poor gestational nutrition, low pre-pregnancy weight, short maternal stature and malaria during pregnancy, all of them being, according to his analysis, factors with a well-established direct causal impact on intrauterine growth. Further factors with well-established causal relation are stated to be the infant's sex, parity, paternal weight and height, alcohol consumption and cigarette smoking, whereas the latter was identified as a major risk factor in high income countries.

More current publications also include a large number of associated – biological as well as socioeconomic – factors. The following section gives a crude (and due to the nature of the subject incomplete) overview on the issue as discussed in current literature.

#### Parity

A recent meta-analysis, evaluating 41 publications on the influence of parity on birth weight comes to the conclusion, that nulliparity is associated with a significantly increased risk for LBW and IUGR, but not for preterm delivery [21].

Other studies suggest similar correlations between parity and the risk of LBW [22, 23].

#### Short or very long interpregnancy interval

A lot has been investigated concerning birth spacing and its influence on perinatal outcome, though it has been discussed if found associations are rather due to confounding risk factors such as mother's characteristics, than due to birth spacing itself [24]. A recent study from Sudan found an increased risk of preterm birth and low birth weight in women with interpregnancy intervals less than 18 months compared to those with an interval of 18 to 30 months [24]. Similar results are presented in a meta-analysis, concluding that interpregnancy intervals shorter than 18 months or longer than 57 months are associated with a higher risk of LBW, small for gestational age (SGA) and preterm birth compared to deliveries after an interpregnancy interval of 18 to 23 months [25].

#### Maternal weight or BMI

Maternal underweight (defined as BMI  $<18.5 \text{ kg/m}^2$ ), either measured before or during pregnancy, was found to be a risk factor for preterm birth as well as LBW, compared to women with normal weight (BMI 20-24.9  $\text{kg/m}^2$ ) [26]. For low and middle income countries, though, the same analysis found only a significantly increased risk for LBW (not for preterm delivery) in underweight women.

A comparable review evaluates the influence of overweight and obesity on preterm birth and LBW [27], coming to the conclusion, that overweight or obese women have an increased risk of induced (not of overall) preterm birth and, especially in low and middle income countries, a decreased risk of delivering an infant with LBW – but increased risk for very low birth weight (VLBW) and extremely low birth weight (ELBW).

#### Paternal birth weight and adult paternal weight, height and body mass index

While paternal height and weight was at times believed to have no or very little influence on their offspring's birth weight (compare [28]), a variety of studies

indicate a significant correlation of the father's stature and the infant's birth weight. After having controlled for maternal size, gestational age, parity, sex of the newborn, parental smoking habits and ethnic origin of the parents, Wilcox demonstrates, that paternal height significantly correlates with birth weight [29] and that this correlation is stronger than the relationship of paternal adult weight with the offspring's birth weight. Klebanoff states, that there is a significant correlation between all three – paternal birth weight, adult paternal weight and adult paternal height – with the newborn's birth weight, hereof paternal birth weight being most strongly associated with the offspring's birth weight [28]. A recent review analyzing 36 publications on paternal factors possibly correlating to their offspring's birth weight, concludes similarly that paternal adult height and paternal birth weight show a correlation with infant's birth weight and indicates a tendency of fathers with higher own birth weight having offspring with higher birth weight [30].

### Socioeconomic factors

The social and economic situation of the mother plays an important role in the development of the child during pregnancy, since it can directly influence the mother's health behavior. A study in Tanzania identified lack of maternal education, single living (compared to married women) and maternal occupation as factors associated with increased risk for LBW [31]. The same study states that the condition of the maternal education and occupation had an influence on LBW analogous to the same factors on the mother's side.

A study from a rural area in Ethiopia also states that poverty contributes to the risk of LBW [32]. Similarly, a retrospective analysis of data from household surveys in Malawi identified low wealth condition as well as lack of formal education as being associated with LBW [23] and states poor diet as a result of low income and low dietary literacy, limited access to prenatal care and lower adherence to health messages as possible explanations for these associations.

### Hypertension, pre-eclampsia and eclampsia

One large retrospective study, including more than 14,000 women of a Chinese population, found no significant differences in mean birth weight of children born to mothers without hypertensive disorders and mothers with either pregnancy induced hypertension, pre-eclampsia or eclampsia [33]. The same study states that pre-eclampsia increases the risk for fetal growth retardation and therefore for SGA, but also increases the numbers of newborns being large for gestational age, the combination resulting in no significant change in mean birth weight. Moreover, the study announces that the effect of pregnancy induced hypertension on birth weight depends on the gestational age, preterm newborns of mothers with hypertensive disorder having a higher risk of LBW.

Another study finds that mothers with hypertensive disorders during pregnancy (including chronic and pregnancy induced hypertension as well as pre-eclampsia) had a higher risk to have SGA neonates, although differences in birth weight could no longer be considered as significant after regression analysis [34].

Hypertensive disorders during pregnancy seem to have influence on fetal growth, but the risk for LBW does not clearly increase due to hypertensive disorders in pregnancy.

### Maternal anemia

The literature on studies concerning the evaluation of maternal anemia shows highly varying results and suggestions. While some publications state an association of maternal anemia with preterm delivery and LBW, others state no or even an inverse relation [35]. Furthermore, comparability of studies remains poor due to methodological and statistical heterogeneity, namely differing in definition of anemia, time points of anemia assessment during pregnancy, control group selection, health and socioeconomic conditions (the majority of studies being carried out in high income countries with quite low prevalence of anemia during pregnancy), ethnicity and documentation of iron supplementation or treatment of anemia [35].

Nevertheless, there are studies strongly suggesting that maternal anemia during pregnancy is an independent risk factor for LBW [36]. A study in Tanzania, conducted in a population with high prevalence of maternal anemia (68%) found the risk for preterm delivery and LBW increased in proportion to the severity of anemia [37]. This result might be – to a certain extent – transferable on the study area, since prevalence of maternal anemia in Gabon was reported to be about 50% [38, 39].

### Malaria in pregnancy

Being associated with maternal anemia, LBW (due to preterm delivery as well as IUGR) and infant mortality, malaria in pregnancy remains a highly important factor for adverse pregnancy outcome, accounting for estimated 75,000 to 200,000 infant deaths every year worldwide [40, 41]. Malaria is suspected to influence the birth weight through a number of effects, mainly through maternal anemia and placental infection [42]. Adhesion of erythrocytes infected with *Plasmodium falciparum* to chondroitin sulfate A (CSA) was identified to trigger placental infection [43] and although placental malaria infection has been recognized as contributor to placental insufficiency and premature deliveries [42], detailed understanding of underlying mechanisms is still to be gained. Recent studies identify various contributory factors, such as cytokines, parasite sequestration or hormones to influence placental functioning [44], also excess expression of complement C5a (being a regulator of placental vascularization) is suggested to result in impairment and dysregulation of placental angiogenesis [45].

Antecedent acquired semi-immunity to malaria can be lost due to pregnancy and especially women in their first and second pregnancy are at high risk for placental malaria [43, 46]. Placental malaria is further associated with young maternal age (after controlling for gravidity) [47, 48] and HIV-infection [47]. HIV infection, maternal malaria and anemia are all possible risk factors for LBW and are contributing to each other [40, 47, 49], which creates a more complex situation. For the study area, microscopic and sub-microscopic infection with *Plasmodium falciparum* has been identified as independent predictor of LBW [50].

### HIV infection

Associations between maternal HIV and adverse pregnancy outcomes, including LBW, were already reported in the late 1980s and early 1990s, as a review on studies from that time shows [51]. The situation might have changed since, mainly due to improved treatment strategies. A study from Tanzania found that mothers with untreated HIV infection had a higher risk of delivering an infant with SGA and preterm birth compared to mothers with no HIV infection [52]. A recent large scale study on birth outcomes among HIV infected mothers in Botswana demonstrates that HIV infection carries a significantly higher risk for adverse pregnancy outcomes, including still birth, SGA and preterm delivery when compared to delivery outcomes of non-infected mothers [53]. Antiretroviral treatment in pregnancy focuses on prevention of mother to child transmission but at the same time might influence birth outcomes itself, as the same study indicates with its findings that use of HAART during pregnancy is independently associated with increased rates of preterm delivery, SGA and stillbirth when compared to women treated with Zidovudine monotherapy in order to prevent mother to child transmission [53].

Additionally, an association of HIV infection and other STI might contribute to the impact of HIV on LBW.

As stated above, HIV, malaria and maternal anemia are all factors which independently contribute to LBW, but also influence each other.

### Antenatal care (ANC)

Few studies suggest that higher rates of babies delivered with LBW can be found in women who did not attend antenatal care compared to women who did [24, 31], while other surveys cannot find a significant association of antenatal care with the risk for LBW [23]. The fact that these studies only compare numbers of antenatal care visits and do not analyze the quality of these visits might partly account for the ambivalence of findings. Another study finds a strong association of lack of adequate antenatal care and risk for LBW, but using a much more extensive definition of adequate antenatal care, including not only the number of



antenatal care visits, but also the intake of a certain amount of iron and folic acid supplementary tablets, the abstinence of hard physical work and an adequate number of hours of sleep per day [54].

### Maternal age

There is not only a controversy, whether adolescent pregnancy is associated with a higher risk for adverse pregnancy outcome and LBW, but also, whether this might be due to the age of the mother itself or rather due to a number of associated socioeconomic factors.

A large number of studies issuing the impact of maternal age on birth weight are available, but mainly being conducted in high income countries, their relevance for this study is to be put into question, since differences in socioeconomic situation and availability of health care among women of lower age might be greater in low and middle income countries than in industrialized nations.

This debate and the findings of this analysis will be portrayed in the discussion.

### Summary of risk factors for LBW

As a conclusion, nulliparity, short (or very long) interpregnancy interval, low maternal weight or BMI as well as paternal height and weight, anemia during pregnancy, maternal malaria during pregnancy, HIV infection, the disease complex of hypertension, pre-eclampsia and eclampsia, certain socioeconomic factors (such as wealth status, maternal education, occupation and marital status) and lack of attendance of antenatal care can (among many others [14]) be considered as established risk factors for LBW and form confounding factors, which should be included in any analysis, as far as data is available.

## **1.4 Study objectives**

The increased risk of poor obstetric performance among adolescent pregnancies compared to pregnancies of woman aged 20 years or older has been reported as well for the study area [55], as for different countries and backgrounds [3, 56,

57]. While the negative impact of early motherhood on perinatal outcome, especially LBW and premature birth remains more or less beyond controversy, results from previous studies have shown conflicting conclusions concerning the question of whether the increased risk accounts to maternal age per se, or is rather related to associated risk factors, such as lack of education, insufficient prenatal care or the poor socioeconomic situation of many young mothers [3]. Many risk factors have been identified so far to contribute to adverse pregnancy outcome, but available data remains insufficient for the area [55].

The present study assesses the prevalence of adolescent pregnancies in a semi-urban and rural region in the Central African country Gabon. Furthermore, it analyzes maternal adolescence among other parameters as a potential risk factor for adverse pregnancy outcome, focusing on LBW.

In order to understand whether adolescence is associated with an independent risk for LBW, several confounding factors were analyzed, since they are known to possibly be associated with a higher risk of poor obstetric outcomes, such as nulliparity [21], poor antenatal care [58] and lack of intake of sulfadoxine-pyrimethamine (SP) as intermittent preventive treatment of malaria during pregnancy (IPTp) according to WHO and national guidelines in Gabon [38].

The retrospective analysis of birth registers in the study area can contribute to identify adolescence and other variables for adverse pregnancy outcomes. The evaluation of parameters such as antenatal care utilization, parity and number of intake of SP as IPTp allows a distinct analysis of risk factors for poor obstetric outcome such as LBW, prematurity and birth asphyxia.

## 2 Material and Methods

### 2.1 Study design

A retrospective cohort study was performed. Data from birth registers from three different health centers in the central African country Gabon were entered in a purpose built database (*Microsoft Office Excel 2007*). All births documented in the birth registers of the health centers were entered in the database, including still births and home deliveries. Abortions, as far as they were documented in the birth registers, were not entered in the database, since abortions were not systematically documented in these registers. A total of 1,972 births were registered in the database, the registered births took place between December 15<sup>th</sup> 2009 and August 29<sup>th</sup> 2011.

The following maternal parameters were collected from the birth records of the three health centers:

- date of the birth
- HIV-status of the mother
- age of the mother at time of delivery or mother's year of birth
- address, area of living
- profession of the mother
- gravidity
- parity
- number of living children and number of children who died
- number of previous interrupted pregnancies due to intrauterine fetal death, extra uterine gravidity or miscarriage
- number of previous stillbirths
- number of previous spontaneous or induced abortions
- date of the first day of last menstrual period
- gestational age at time of delivery
- fundal height at time of delivery
- number of attended prenatal consultations
- number of performed anti-tetanus vaccinations during the pregnancy
- number of intake of SP as IPTp

- participation of the mother in the MiPPAD study

Following data on the birth outcome were gathered:

- birth weight
- head circumference
- thoracic circumference
- mid-upper arm circumference
- length
- sex of the child
- first APGAR score after delivery
- number of born children
- type of delivery (vaginal vs. caesarean section)
- place of delivery
- birth outcome (still birth or live birth)
- further information or comments (for example: performed reanimation, indications for caesarean section, malformations, neonatal death)

The maternal as well as the infant parameters were chosen based on their importance and availability in the birth registers of all three centers.

In case of missing values or illegible parameters, the birth was nevertheless included in the database.

In order to complete information on parity, gravidity, previous pregnancy outcomes and first day of last menstrual period, data from records of prenatal consultations was obtained in cases where this information was not documented in the birth records.

## 2.2 Study location

The study was performed in three different health centers in Gabon:

- *Hôpital Albert Schweitzer*, Lambaréné (HAS)
- *Centre Hospitalier Régional Georges Rawiri*, Lambaréné (CHRGR)
- *Centre Médicale de Fougamou*, Fougamou (CMF)

### 2.2.1 Gabon – country and people

The central African country of Gabon is located on the Gulf of Guinea; bordering countries are Cameroon, Equatorial Guinea and Republic of the Congo. Gabon counts roughly 1.5 million inhabitants on a area of 267,667 km<sup>2</sup>, which reflects a population density of approximately 5.6 inhabitants per km<sup>2</sup>, although more than one third of the country's population lives in the capital Libreville (estimated 619,000 inhabitants in 2009) and the urban population accounts for 86% of the total population [59]. The official language is French. More than 80% of Gabon's surface is covered with tropical rainforest [60]. Situated along the equator, the region is dominated by tropical climate, with two rainy and two dry seasons every year, an annual mean temperature of 26.6°C and an annual average humidity of 83% [61].

Gabon offers a wide cultural diversity with a large number of ethnic groups and languages. Approximately, 65% of the people are Christians, 5% Muslims and 30% animists [61].

Live expectancy at birth amounts to 59 years for women and 55 years for men; mortality rate for children under five years of age is 91 deaths per 1,000 live births (numbers for the year 2004) [62].

Although the GDP – natural resources, most notably oil, timber and manganese account for the largest proportion – is relatively high for the region, major parts of the population remain poor.

Infectious diseases form a major health problem in Central Africa. The study area is characterized by high perennial transmission of *Plasmodium falciparum* malaria with moderate seasonal variations [63] and an entomological inoculation rate of approximately 50 infected bites per person per year [64]. The prevalence of peripheral parasitaemia among pregnant women in the capital (Libreville) was described to be 57% among women in their first and second pregnancy [65].

The HIV-prevalence among Gabonese adults was 8.1% in 2003 and infectious diseases such as AIDS, malaria, measles, tuberculosis and lower respiratory tract infections are among the leading causes for death [62].



Figure 2: Map of Gabon [66].

### 2.2.2 Lambaréné and its hospitals

Lambaréné is the capital of Moyen-Ogooué, one of nine provinces. With estimated 20,000 inhabitants and a distance of about 250 km land inwards from Libreville, Lambaréné can be characterized as a semi-urban area with predominately rural surroundings.

The town counts three hospitals. In 1913, Albert Schweitzer founded the first hospital of Lambaréné, which was replaced by a new construction in 1981. The hospital is administered by the International Foundation of the Albert Schweitzer Hospital. The *Hôpital Albert Schweitzer* (HAS) currently counts about 150 beds and seven physicians and is composed of departments of internal medicine, pediatrics, obstetrics, surgery, public health, dentistry and a mother and child protection program, which focuses on vaccinations and nutrition. The HAS is a

private hospital, but serves the local population and its funding consists of contributions from international donors, from the Gabonese health ministry and treatment fees of patients.

The Centre de Recherches Médicales de Lambaréné is part of the International Foundation of the HAS. Built in 1981 with an extension in 2006, it hosts an international team of researchers. A main focus lies on clinical trials on antimalarial drugs and vaccines [67]. Further objectives are the conduct of research in other infectious diseases and the organizing of trainings [68].

Two governmental hospitals exist in Lambaréné. The *Centre Hospitalier Régional Georges Rawiri* (CHRGR) was inaugurated in 2009, counting 80 beds and currently five physicians. The hospital has departments of internal medicine, pediatrics and neonatology, obstetrics and gynecology and surgery. In many ways, it replaces the older *Hôpital Régional de Lambaréné*, where nowadays no operations or births are performed anymore - focus lies on external consultations, antenatal care visits and vaccination as well as HIV/AIDS programs instead.

### **2.2.3 Fougamou and its health center**

Fougamou is a small town with estimated 5,000 inhabitants, located approximately 90 km inland from Lambaréné in the province Ngounié. Fougamou and surroundings can be considered as a typical rural setting.

The *Centre Médicale de Fougamou* (CMF) is much smaller than the hospitals in Lambaréné. There is a maternity ward, but no operational tract, so that required caesareans have to be transferred to other hospitals and usually are performed in Lambaréné.

### **2.2.4 Maternal and neonatal health and health care in the study area**

Reliable data on quality of antenatal care throughout the country or even specific for the study area is rare, the latest WHO Country Health System Fact Sheet for Gabon was published in 2006 [62] and provides for some basic data.

Maternal mortality in Gabon was estimated by the WHO in 2004 to be 420 per 100,000 live births, which was under the average for the whole region of Africa for the same year (910 per 100,000 live births) [62].

Total fertility rate per women in 2004 was estimated 3.9 and the adolescent fertility proportion in 1998 was estimated to be 16.9% [62].

Contraceptive rates were stated be about 32.7% in 2000, whereas condom use among young people at higher risk sex was 48% for males and 33% for females [62].

#### 2.2.4.1 Antenatal, peri- and postnatal care centers and birth centers in the study area

There are four locations for antenatal care in the study area (HAS, CHRGR, *Hôpital régional de Lambaréné* and CMF), of which three have facilities for births (HAS, CHRGR, CMF) and two are equipped for caesareans (HAS, CHRGR).

University level trained midwives work in all of the centers and only one gynecologist is active in the area (CHRGR). Caesareans are otherwise performed by surgeons in presence of a midwife.

Distance from homes to the health centers differ widely, some women travel long distances for assessment of appropriate antenatal care, whereas women living in Lambaréné or Fougamou itself are very close to the hospitals and centers.

#### 2.2.4.2 Objectives of antenatal, peri- and postnatal care in the study area

Antenatal care in the study area orientates on national programs and WHO recommendations [69], including:

- confirmation of the pregnancy
- monitoring the progress of the pregnancy and monitoring maternal and fetal health
- identification and treatment of complications, such as anemia, hypertensive disorders, bleeding, malpresentations, multiple pregnancies
- anemia prevention and control (nutritional counseling, iron and folate supplementation, hookworm treatment)



- infectious diseases prevention and control, including hepatitis B (testing and mother to child transmission prevention), syphilis (testing and treatment), urinary tract infections (routine testing and treatment), prevention of neonatal tetanus (anti tetanic vaccination during pregnancy), HIV counseling and testing (nationwide free, anonymous and voluntary testing),
- malaria prevention and control during pregnancy (IPTp and distribution of insecticide treated bed nets)
- screening for preeclampsia (periodic measurement of blood pressure and edema) and maternal diabetes (urinary stick testing for glucosuria)
- advice on danger signs and emergency preparedness
- family counseling and planning (education on birth control, including condom use and birth control pills)
- health counseling (nutrition, breast feeding, healthy lifestyle)
- respond to reported complaints
- recording (booklets for pregnancy records are distributed) and reporting (registers for national statistics are completed)

The antenatal care programs in the study area are aiming for at least four antenatal care visits during a complication free pregnancy, following WHO recommendations. This goal of antenatal care coverage is not achieved for all mothers – the WHO states for the year 2000 that as many as 94% of mothers in Gabon received at least one antenatal care visit, but only 63% received four or more antenatal care visits [62]. The number of prenatal care visits is documented in birth registers in order to analyze and on this basis improve the situation.

Peri- and postnatal care includes:

- monitoring maternal and fetal well-being during labor and delivery
- provision of supportive care and pain relief during labor and delivery
- prevention, identification and management of complications
- promotion, protection and support for breastfeeding

- monitoring and assessment of wellbeing, detection of complications (breathing, infections, prematurity, low birth weight, injury, malformation)
- infection prevention and control
- eye care
- information and counseling on home care, breastfeeding, hygiene
- postnatal care planning, advice on danger sign and emergency preparedness
- immunization and vitamin K prophylaxis according to guidelines

According to WHO figures, the percentage of births attended by skilled health staff in Gabon was 86% in 2000 [62]. A similar number is presented by the national statistic agency of Gabon, which states 87.1% of births in 2005 to have been attended by skilled health workers [70]. Another WHO publication estimates the percentage of children who are not weighted at birth to be 9% (in 2000) [13], which can be seen as indirect marker for a fairly high percentage of births being attended by health staff. Interestingly, the percentage of newborns not weighted at birth seems much higher in neighboring countries where it is reported to be about 65% [13].

In 2000, 6% of all births were reported by the WHO to be performed by caesarean section [62].

Figures on neonatal health from the same WHO publication list an infant mortality rate of 59 per 1,000 live births in the year 2004 and a neonatal mortality rate of 31 per 1,000 live births in the year 2000, stating the main neonatal death causes to be preterm birth (31%), followed by diseases of infectious origin (24%) and birth asphyxia (22%) and list congenital abnormalities, diarrheal diseases and neonatal tetanus among others as further death causes [62].

#### 2.2.4.3 Malaria prevention and control during pregnancy

As described earlier, Gabon can be characterized as an area with high perennial transmission of *Plasmodium falciparum* and malaria parasitaemia is highly prevalent, especially among women in their first or second pregnancy [63-65].

WHO recommendations for malaria prevention and control during pregnancy for highly endemic areas include three main fields of intervention [71]:

- administering at least two doses of SP as IPTp after quickening to each pregnant women in an interval of at least one month
- insecticide-treated bed nets (ITNs), distributed to each pregnant women
- effective case management of malaria illness and anemia

These measures reflect the situation in areas with stable malaria transmission, where the level of acquired immunity is high among women, parasitaemia can remain asymptomatic and treatment restricted to symptomatic episodes will miss a large quantity of infections, although subclinical courses of the disease can still result in maternal anemia as well as placental sequestration of parasites (both potentially resulting in LBW or other adverse effects on maternal, fetal or neonatal health) [72].

Although many interventions have been identified and their effectiveness could be demonstrated, the failure of providing them to all pregnant women remains high in its contribution to infant mortality in malaria endemic areas [40]. This failure can be due to a lack of national programs, incomplete implementation of the very or missing acceptance among the population.

Gabon implemented a national IPTp program in 2005 and studies could show that prevalence of malaria in pregnancy decreased since [38, 73].

Data for the study area on the implementation of the three described pillars of intervention was only available partially. While there is documentation on a regular basis concerning the IPTp intake, there is no documentation concerning distribution and use of ITNs or case management of potential malaria cases.

In all three antenatal care centers in the study area, women are free to approach midwives and seek consultation with health problems. The midwives and nurses are trained to diagnose and treat malaria among other diseases, but costs of transportation, consultation, examination, laboratory tests and medication make accessibility limited to women who can afford these costs or at least part of the costs in cases where hospitals insurances cover parts of it.

ITNs were not distributed permanently, but sometimes (depending on availability at the moment). Women were counseled to use ITNs, but compliance, especially due to the matter of costs, might be rather low.

#### 2.2.4.4 Birth record keeping and methods of parameter assessment

Birth registers were completed after birth. In routine practice, the midwife who attended the birth filled in the register. Information on the mother and the antenatal period were taken from the maternity record booklets, which were distributed to each woman at the first antenatal care visit in order to keep record on the antenatal period and on the mother's gynecological and general health condition. Information on the birth and the newborn were taken from birth documentation sheets, which were filled in during the process of delivery or immediately after delivery while measuring and weighing the infant.

The maternal and birth parameters that were recorded in the birth registers were already described earlier (compare chapter 2.1 *Study design*). In general, all information was collected by midwives either during antenatal care or during delivery and later transferred to the birth registers.

The methods of data assessment are listed in table 1. For data not included in the table, assessment was simply by anamnesis (for example date of birth of the mother, area of living, parity, date of the first day of last menstrual period) or by attendance of the birth (for example sex of the child, birth outcome, number of born children).

Table 1 – Methods of data assessment

Parameter	Method of assessment
HIV status of the mother	Voluntary counseling and HIV-testing during routine antenatal care visits was offered to each pregnant woman and was due to governmental programs free of charge. The test result was entered in the mother's pregnancy records booklet and on the day of the birth transferred to the birth register.
Gestational age at time of delivery	Midwives calculated the gestational age from the anamnestic assessed first day of last menses and entered it in the birth registers. When only the first day of last menses was documented, the calculation was performed in Microsoft Office Excel 2007.
Fundal height at time of delivery	Fundal height was measured by midwives and entered in the birth registers.
Number of attended prenatal consultations	Each antenatal consultation that was documented in the mother's pregnancy records booklet was counted and the number entered in the birth registers.
Number of performed anti-tetanus vaccinations during the pregnancy	Anti-tetanus vaccinations were documented in the pregnancy records booklet and the number was transferred to the birth registers.
Number of intake of sulfadoxine-pyrimethamine (SP) as IPTp	Intake of SP was documented in the pregnancy records booklet and the number of intakes was transferred to the birth registers.
Birth weight	Birth weight was measured immediately after birth by midwives and the result was entered in the birth registers.
Head circumference, thoracic circumference, mid-upper arm circumference, length	Head, thoracic and mid-upper arm circumference and length were measured by midwives immediately after birth and results were entered in the birth registers.
First APGAR score after delivery	Soon after delivery, in general during the first minutes, but not at any defined point of time, APGAR score was assessed by midwives.

## 2.3 Outcome variables

In order to assess the differences in adolescent pregnancy outcomes versus pregnancy outcomes of adult women, out of the gathered parameters as listed above, main outcome variables were defined as follows.

Main pregnancy characteristics were:

- age of the mother
- gravidity and parity
- number of prenatal consultations
- number of intake of SP as IPTp
- HIV status
- gestational age at delivery

Main birth outcome variables were:

- birth weight
- birth outcome (live birth vs. stillbirth)
- mode of delivery (caesarean section vs. vaginal birth)
- cranial, thoracic and mid-upper arm circumference
- length
- first APGAR score
- sex of the newborn

Other parameters from birth registers were not considered suitable for further analysis, mainly because of gaps in documentation.

Main outcome variables were included in descriptive statistics of maternal and birth characteristics and in the evaluation of differences in maternal characteristics and birth outcomes of adolescent versus adult women. Since parity is a known risk factor for LBW and nulliparity is more frequent among younger mothers, a separate analysis in the subset of nulliparous women was performed.

To analyze the influence of adolescent pregnancy on birth weight, multivariable logistic regression analysis was performed.

## **2.4 Ethics statement**

The study was conducted according to Good Clinical Practice and the Declaration of Helsinki and in compliance with local regulations.

The study protocol was approved by the Ethics Committee of the International Foundation for the Albert Schweitzer Hospital in Lambaréné, Gabon. All information was treated confidentially, personal data of participants was pseudonymized and each birth is identified by a unique study number, which was given by the investigator. Study unrelated persons cannot view personal data or names of participants. No names of any participants are to be published. Since the study was performed retrospectively, no written informed consent was regarded necessary by the review committee.

## **2.5 Statistical analysis**

Statistical analysis was performed using JMP (JMP 9.0.0, SAS Institute, Inc., NC, USA). Descriptive statistics were calculated for the above mentioned parameters and logistic regression analysis was performed.

### 3 Results

Data was gathered from birth registers of the three health centers in August 2011. Data was then entered in the prepared database between September and November 2011.

#### 3.1 Participants' characteristics

A total of 1,972 births were included in the survey, taking place in the three health centers CHRGR (N=832/1972; 42.2%), HAS (N=710/1972; 36.0%) and Fougamou (N=430/1972; 21.8%). The births took place between December 15<sup>th</sup> 2009 and August 29<sup>th</sup> 2011. 47 pairs of twins were born, and triplets were born once. Therefore, 1923 mothers accounted for the births.

##### 3.1.1 Characteristics of mothers

###### Age distribution

The mean age of pregnant women included in the analysis was 25.6 years (SD=7.2), the youngest being reported to be 12 years old, and the oldest to be 50 years old. Adolescent pregnancy had a prevalence of 23.7% (N=453/1910). Mothers of the age of 16 or younger were found in 5.5% (N=105/1910). Figure 3 shows the age distribution of all mothers.

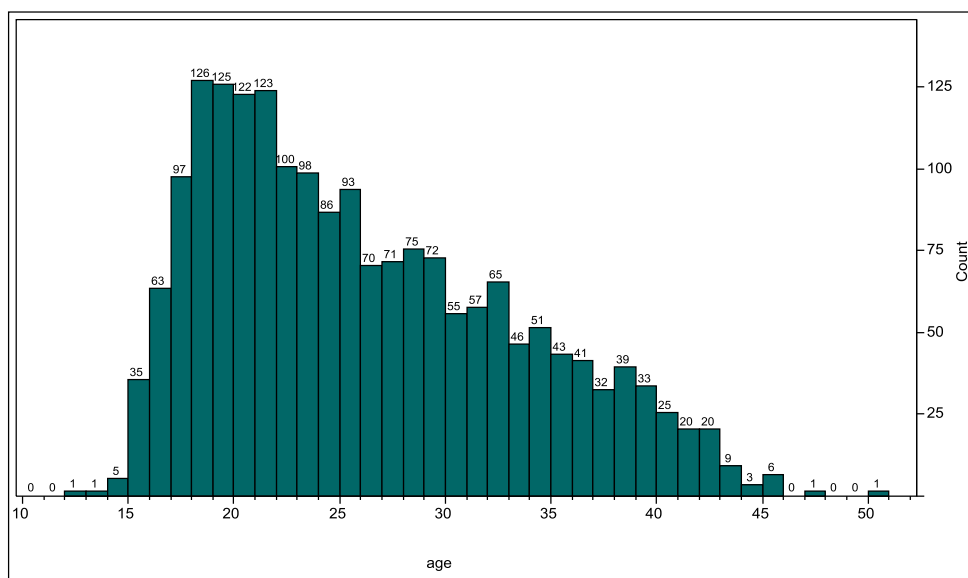


Figure 3: Age distribution of all mothers.



### Parity and previous pregnancy outcomes

Parity ranged from 0 to 12 and 446 of 1,586 mothers with documentation on parity (28.1%) had not given birth before.

A total of 23 previous still births, 7 previous extra uterine pregnancies, 37 previous miscarriages and 8 previous fetal deaths were documented for the study population, but documentation on these parameters can be considered to be incomplete, since in most cases, nothing was reported on the listed previous adverse pregnancy outcomes.

Information on previous abortion, though, was documented for a larger part of women (N=461), but still was considered to be not representative because of incomplete documentation in the birth registers. Among the 461 women with documentation on previous abortions, a total of 688 previous abortions were documented (Mean = 1.5, SD=1.1, range: 0-6). It seems, that these numbers lead to an overestimation, since non-documentation is likely to occur more often in cases, where no previous abortion was reported by the woman, than in cases of one or more reported previous abortions.

### Intermittent preventive treatment of malaria in pregnancy (IPTp)

23.5% of the women (N=451/1923) were participants in the MiPPAD study, where they received either SP or Mefloquine (MQ) as IPTp. They were excluded from analysis of IPTp.

Of the remaining 1,472 women who did not participate in the MiPPAD study, number of intake of SP as IPTp was documented in 1,156 cases.

Intake of at least two doses of SP as IPTp was recorded for 790 women (68.3%). Intake of no IPTp or one dose of IPTp applied to 60 (5.2%) and 306 (26.5%) cases, respectively.

### Antenatal care

For 1664 women, the number of antenatal care visits was available. Of these, 36.2% (N=603/1664) had four or more antenatal care visits performed. A median of 3 (0-10) antenatal care visits was reported.

### Gestational age

Gestational age in weeks as well as last date of menses was reported for most women (N=1667). If last date of menses was available, gestational age was calculated. In cases, where last date of menses was not documented, gestational age as documented in the birth registers was adopted for the database. Mean gestational age was 38.8 weeks post menstruation. In 318 cases (19.1%), delivery took place before completion of 37 weeks of gestation and could therefore be considered as preterm.

### HIV status

Documentation of HIV status was different in the three health centers. While in the birth registers of HAS and Fougamou only HIV positive test results were documented and no differentiation was made between unknown status and negative test result, in CHRGR, every test result was documented as either positive or negative and in case of no available test result, it was recorded as unknown. A total of 77 (4%) HIV positive cases were reported altogether, but these numbers only give an idea of the HIV prevalence among pregnant women in the study area being at least 4%. Table 2 summarizes the mother's characteristics.

<b>Table 2 – characteristics of mothers</b>		
<b>number of mothers</b>		1923
<b>age (years)</b>		25.6 (12-50; 7.2;1910)*
<b>proportion of adults (&gt; 19 years)</b>		1457 (76.3%)**
<b>proportion of adolescents (≤ 19 years)</b>		453 (23.7%)**
<b>proportion of very young adolescents (≤ 16 years)</b>		105 (5.5%)**
<b>gravity</b>		3 (1-14; 1584)***
<b>parity</b>		2 (0-12; 1586)***
<b>    nulliparae</b>		446 (28.1%)**
<b>    primiparae</b>		339 (21.4%)**
<b>    secundiparae</b>		245 (15.4 %) **
<b>    multiparae</b>		556 (35.1%)**
<b>number of prenatal consultations</b>	0	18 (1.1%)**
<b>3 (0-10; 1664)***</b>	1	196 (11.8%)**
	2	335 (20.1%)**
	3	512 (30.8%)**
	>3	603 (36.2%)**
	<b>number of intake of SP as IPTp</b>	0
<b>2 (0-3; 1156)***</b>	1	306 (26.5%)**
	2	775 (67.0%)**
	3	15 (1.3%)**
	<b>positive HIV status</b>	
<b>gestational age at delivery (weeks)</b>		38.8 (3.2; 1667)****
<b>participation in the MiPPAD study</b>		451 (23.5%)**
<p>*Mean (Minimum – Maximum; SD; N)  **N (%)  ***Median (Minimum – Maximum; N)  ****Mean (SD; N)</p>		

### **3.1.2 Birth outcomes and newborn characteristics**

Twins were not excluded for analysis of distribution of birth outcomes.

#### Live births vs. still births

1,920 (97.4%) live births and 52 (2.6%) still births were reported (total number of births in the study: 1972).

#### Sex

More boys than girls were delivered (N=1049; 53.3% versus N=918; 46.7%, respectively).

#### Birth weight and low birth weight

Newborns had a mean birth weight of 2,997.5 grams (SD=522.9). When considering live births only, the mean birth weight was 3,008.1 grams (SD=508.5).

251 of 1,915 live births with documentation of birth weight (13.1%) were classified as presenting with low birth weight (LBW). Still births were excluded from analysis of LBW.

Prevalence of LBW was much higher in twins or triplets. For singleton births only, 196 cases of LBW were reported (196/1828; 10.7%), whereas for twins and triplets, 55 cases of LBW were reported (55/87; 63.2%).

#### Gestational age

Deliveries at a gestational age below 37 weeks after the first day of last menses were classified as being preterm births. Following this definition, 339 (339/1706; 19.9%) newborns were preterm deliveries.

Out of 217 live born children with LBW where information on gestational age was recorded, 127 (58.5%) could be identified as preterm newborns.

Out of 1,444 children without LBW and with available data on gestational age, only 196 (13.6%) were identified as being delivered preterm.

### Anthropometric measures other than weight

Further information on the newborns stature were cranial circumference with  $32.8 \pm 1.9$ cm, thoracic circumference with  $31.8 \pm 2.2$ cm, mid upper arm circumference with  $10.9 \pm 1.1$ cm and length with  $48.9 \pm 2.6$ cm (mean  $\pm$  standard deviation).

### Mode of delivery

A total of 126 (6.5%) caesarean sections were performed. Documented home deliveries (86 deliveries, 4.4%) or deliveries on the way to the health center (15 deliveries, 0.8%) were rare, but total numbers of home deliveries are unknown, since not all children born outside of the hospitals were brought there after delivery.

### APGAR score and birth asphyxia

First measured APGAR after delivery had a median of 9, and 152 (8.8%) of newborns suffered from birth asphyxia (birth asphyxia was considered as such, if first APGAR after delivery was documented to be under 7 or if necessity of reanimation of the newborn was documented). Table 3 summarizes birth outcomes and newborns characteristics.

<b>Table 3 – birth outcomes and newborn characteristics</b>		
<b>Number of born children</b>		1972
<b>live births</b>		1920 (97.4%)*
<b>stillbirths</b>		52 (2.6%)*
<b>preterm deliveries (gestational age &lt; 37 weeks)</b>		339 (19.9%)*
<b>term deliveries</b>		1367 (80.1%)*
<b>birth weight (grams)</b>		2997.5 (650-5540; 522.9; 1957)**
<b>prevalence of LBW</b>		251 (13.1%)*
<b>birth weight &gt;2,499 grams</b>		1664 (86.9%)*
<b>prevalence of preterm delivery among children with LBW (N=217)</b>	preterm	127 (58.8%)*
	term	90 (41.5%)*
<b>prevalence of preterm delivery among children without LBW (N=1444)</b>	preterm	196 (13.6%)*
	term	1248 (86.4%)*
<b>cesarean sections</b>		126 (6.5%)*
<b>vaginal births</b>		1815 (93.5%)*
<b>cranial circumference (cm)</b>		32.8 (15-42.5; 1.9; 1915)**
<b>thoracic circumference (cm)</b>		31.8 (21-38; 2.2; 1912)**
<b>mid upper arm circumference (cm)</b>		10.9 (6-14; 1.1; 1437)**
<b>length (cm)</b>		48.9 (35-58; 2.6; 1882)**
<b>APGAR</b>		9 (0-10; 1719)***
<b>prevalence of birth asphyxia (being defined of APGAR &lt; 7)</b>		152 (8.8%)*
<b>sex</b>	male	1049 (53.3%)*
	female	918 (46.7%)*
<b>place of delivery</b>	health centre	1871 (94.9%)*
	car or on the way to the health centre	15 (0.8%)*
	home	86 (4.4%)*
<b>*N (%)</b>		
<b>**mean (minimum – maximum; SD; N)</b>		
<b>***median (minimum – maximum; N)</b>		

### 3.1.3 The three health centers – distribution of participant's characteristics

Due to the differences in the three health centers concerning the setting being either urban (Lambaréné: HAS, CHRGR) or rural (Fougamou: CMF) and the capacities of care in the health centers as well as possible differences in quality of care and in the socioeconomic spectrum of patients, it seemed appropriate to co-analyze possible relevant discrepancies concerning distribution of maternal age, prevalence of adolescent pregnancy, number of prenatal consultations, number of intake of SP as IPTp and parity, as well as frequency of women's participation in the MiPPAD study. Distribution is shown in Table 4.

<b>Table 4 – distribution of maternal characteristics among the three health centers</b>					
	HAS	CHRGR	CMF	Total	
<b>age (years)*</b>	25.6 (12-50; 7.3; 684)	26.0 (14-45; 7.2; 816)	24.9 (14 -43; 7.0; 410)	25.6 (12-50; 7.2;1910)	
<b>proportion of adolescents (&lt; 20 years)**</b>	170/684 (24.9%)	177/816 (21.5%)	106/410 (25.9%)	453/1910 (23.7%)	
<b>parity**</b>	<b>parity = 0</b>	163/542 (30.1%)	216/727 (29.7%)	67/317 (21.1%)	446/1586 (28.1%)
	<b>parity = 1</b>	127/542 (23.4%)	155/727 (21.3%)	57/317 (18.0%)	339/1586 (21.4%)
	<b>parity = 2</b>	85/542 (15.7%)	103/727 (14.2%)	57/317 (18.0%)	245/1586 (15.4%)
	<b>parity ≥ 3</b>	167/542 (30.8%)	253/727 (34.8%)	136/317 (42.9%)	556/1586 (35.1%)
<b>number of prenatal consultations**</b>	<b>0</b>	0/599 (0.0%)	13/661 (2.0%)	5/404 (1.0%)	18/1664 (1.1%)
	<b>1</b>	80/599 (13.4%)	88/661 (13.3%)	28/404 (6.9%)	196/1664 (11.8%)
	<b>2</b>	176/599 (29.4%)	96/661 (14.5%)	63/404 (15.6%)	335/1664 (20.1%)
	<b>3</b>	223/599 (37.2%)	149/661 (22.5%)	140/404 (34.7%)	512/1664 (30.8%)
	<b>≥ 4</b>	120/599 (20.0%)	315/661 (47.7%)	168/404 (41.6%)	603/1664 (36.2%)
<b>number of intake of SP as IPTp**</b>	<b>0</b>	16/419 (3.8%)	36/624 (5.8%)	8/113 (7.1%)	60/1156 (5.2%)
	<b>1</b>	169/419 (40.3%)	120/624 (19.2%)	17/113 (15.0%)	306/1156 (26.5%)
	<b>2</b>	232/419 (55.4%)	464/624 (74.4%)	79/113 (70.0%)	775/1156 (67.0%)
	<b>3</b>	2/419 (0.5%)	4/624 (0.6%)	9/113 (8.0%)	15/1156 (1.3%)
<b>participation in the MiPPAD study**</b>	139 (20.2%)	13 (1.6%)	299 (71.9%)	451 (23.5%)	
<b>number of mothers**</b>	689 (35.8%)	818 (42.5%)	416 (21.6%)	1923 (100%)	
<b>*Mean (Minimum – Maximum; SD; N)</b>					
<b>**N (%)</b>					

Of all 1,923 mothers who were included in the study analysis, 35.8% (689/1923) gave birth in the HAS, 42.5% (818/1923) in the CHRGR and 21.6% (416/1923) in Fougamou (CMF).

No significant discrepancies were found in the age distribution. Mean age was 25.6, 26.0 and 24.9 years in HAS, CHRGR and CMF (respectively). The prevalence of adolescent pregnancy was similar in the health centers, although being lowest in CHRGR (24.9% in HAS, 21.5% in CHRGR and 25.9% in CMF).

There is a remarkable difference considering participation in the MiPPAD study. While a larger part of women participated in Fougamou (71.9%), percentages of mothers who took part in the MiPPAD study were smaller in Lambaréné (20.2% in HAS and 1.6% in CHRGR).

Differences were also seen in intake of SP as IPTp, parity and number of performed antenatal care visits.

According to guidelines, women are supposed to take SP two times during a pregnancy in order to protect themselves and their offspring from malaria infection and its consequences. Women who participated in the MiPPAD study were excluded from analysis of IPTp. The majority of women received SP two times. Among the health centers, HAS showed the lowest proportion of women who received SP twice during pregnancy (55.4% compared to 74.4% in CHRGR and 70.0% in CMF).

The numbers suggest that parity was higher among the study population in Fougamou. In Fougamou, only 21.1% of women were nulliparous, while in Lambaréné, 30.1% and 29.7% (HAS and CHRGR, respectively) had not given birth before. Parity of three or more was correspondingly higher in Fougamou (42.9%) than in Lambaréné (30.8% and 34.8% in HAS and CHRGR, respectively).

As mentioned above, antenatal health care programs aim for at least four antenatal care visits during pregnancy. This aim was achieved for a total of 36.2% of the study's population (compare Table 1 - Characteristics of mothers).



Distribution among health centers was not equal. While 41.6% of mothers in Fougamou and 47.7% of the mother who gave birth in CHRGR attended four or more antenatal consultation, this applied only to 20% of mothers in HAS.

### **3.2 Univariable analysis of adolescent pregnancies compared to adult pregnancies**

Only singleton births were included in the analysis, because multiple births are associated with an increased risk for LBW. This increase of risk is independent from other risk factors for LBW (such as malaria, parity, maternal anemia or socioeconomic factors) and could therefore conceal effects of different factors on birth weight. Twins and triplets included in this analysis have a significantly increased risk of weighing less than 2,500 grams when compared to singleton newborns (10.7% of singleton newborns compared to 63.2% of twins and triplets presented with LBW,  $p < 0.0001$ ,  $n = 1915$ ).

Mothers of twins or triplets were none the less included in descriptive statistics.

Because of the impact of parity on birth weight, univariable analysis was subdivided into analysis of all mothers and analysis of the subset of nulliparous mothers only.

#### **3.2.1 Analysis of all mothers**

##### Birth weight and low birth weight

The percentage of newborns with LBW was significantly higher in adolescent women. 16.6% (74/445) of newborns to adolescent women presented with LBW, compared to 8.8% (121/1371) in women older than 19 years (OR: 2.1, 95% CI: 1.5-2.8). The mean birth weight of infants born to adolescent mothers was 178.1g lower ( $2896.1g \pm 462.8g$ ), than of those born to adults ( $3074.2g \pm 501.1g$ ) ( $p < .0001$ ,  $n = 1853$ ).

##### Parity

Unsurprisingly, the prevalence of nulliparity was higher among adolescent mothers. 287 of 371 adolescent mothers delivered their firstborn child (77.4%),

while only 115 of 1,172 adult mothers (9.8%) were nulliparous (OR: 22.4, 95% CI: 16.7-30.1).

### Gestational age

There was a minor difference in mean gestational age at delivery between the two groups ( $38.2 \pm 3.7$  weeks vs.  $39.1 \pm 2.9$  weeks, for adolescents and adults, respectively) ( $p < .0001$ ,  $n=1624$ ) and the frequency of preterm births was significantly higher in adolescent pregnancies with 26.1% (99/380) than in adult pregnancies with 15.9% (198/1244) (OR: 1.9, 95% CI: 1.4-2.5).

### Live births vs. still births

Stillbirths occurred less often in adolescent mothers, than in adults (0.9%; 4/449 vs. 2.8%; 40/1414, respectively; OR=0.3; 95% CI: 0.1-0.9).

### Mode of delivery

The percentage of caesarean sections was slightly lower in adolescent mothers when compared to adults, but no significant difference was found (5.2%; 23/444 vs. 6.0%; 84/1392, respectively; OR: 0.9; 95% CI: 0.5-1.4).

### APGAR score and birth asphyxia

Occurrence of birth asphyxia as defined earlier was significantly higher in adolescent pregnancies. The percentage of newborns with birth asphyxia was 12.5% (50/400) in adolescent pregnancies and 7.8% (96/1235) in adult pregnancies (OR: 1.7; 95% CI: 1.2-2.4).

### Intermittent preventive treatment of malaria in pregnancy (IPTp)

Concerning the number of intake of sulfadoxine-pyrimethamine (SP) as antimalarial intermittent preventive treatment, there was a significant difference between the frequency of intake comparing adult women and teenagers. As mentioned previously, SP intake is recommended two times during pregnancy and the health facilities in the study area aim for this. Comparing the number of women who were reported to have been taken the dose at least the recommended two times, it can be seen that adolescent future mothers were less

likely to take the recommended two doses when compared to adults (60.7%; 158/261 vs. 70.9%; 617/870, respectively; OR: 0.6; 95% CI: 0.5-0.8).

### Antenatal care

Similar tendencies were found regarding the frequency of antenatal care visits. A quantity of at least four antenatal care visits is recommended in the study area's context. Comparing the percentage of women who had four or more antenatal care visits during the index pregnancy, it must be stated, that significantly less teenagers achieved the recommended amount, compared to their adult counterparts (28.4%; 111/391 vs. 38.7%; 474/1225, respectively; OR: 0.6; 95%CI: 0.5-0.8).

### **3.2.2 Analysis restricted to nulliparous mothers**

As discussed earlier, first born children are considered to be at higher risk for LBW [21-23] and other adverse pregnancy outcomes. Additionally, pregnant adolescents are more likely to deliver their first child, because they are of younger age and therefore more likely to be at the onset of childbearing. In the study population, adolescents were much more likely to give birth to their first child than adults (77.4%; 287/371 vs. 13.2%; 155/1172, respectively; OR: 0.04; 95%CI: 0.03-0.06).

Therefore, the same univariable analyses were performed for the subset of nulliparous women (N=443).

### Birth weight and low birth weight

The percentage of newborns with LBW was 18.1% (52/287) in adolescent nulliparous women compared to 9.2% (14/153) in women older than 19 years (OR: 2.2, 95% CI: 1.2-4.1). The mean birth weight of infants born to adolescent mothers was 113.3g lower (2876.9g  $\pm$  435.2g), than of those born to adults (2990.2g  $\pm$  416.8g) ( $p < .01$ ,  $n=442$ ).

### Gestational age

There was a slight difference in mean gestational age at delivery between the two groups (38.4  $\pm$  3.4 weeks vs. 39.4  $\pm$  2.8 weeks, for adolescents and adults,

respectively) ( $p < .01$ ,  $n=398$ ) and the frequency of preterm birth was higher in adolescent pregnancies with 23.6% (62/263) than in adult pregnancies with 13.3% (18/135) (OR: 2.0, 95% CI: 1.1-3.6).

#### Live births vs. still births

Only two stillbirths were reported in the subset of nulliparous women, the mothers were in both cases adult women. Statistical analysis was not performed due to the rareness of cases.

#### Mode of delivery

No significant difference was found concerning the mode of delivery, comparing the occurrence of caesarean sections in adults vs. adolescents (10.3%; 16/155 vs. 5.6%; 16/285, respectively; OR: 0.5; 95% CI: 0.3-1.1).

#### APGAR score and birth asphyxia

Occurrence of birth asphyxia was not significantly higher in adolescent first pregnancies. The percentage of newborns with birth asphyxia was 12.0% (32/235) in adolescent pregnancies and 11.1% (16/144) in adult pregnancies (OR: 1.1; 95% CI: 0.6-2.1).

#### Intermittent preventive treatment of malaria in pregnancy (IPTp)

The percentages of women taking at least two doses of SP as IPTp can be regarded similar in the subset of nulliparous women compared to all women. Here again, a significant higher rate of adult women accomplished the goal of at least two intakes. 62.0% of adolescent nulliparous mothers (111/179) were reported to have taken at least two doses of SP, whereas 74.5% of adult nulliparous women (79/106) were reported to have done so (OR: 1.8; 95%CI: 1.1-3.1).

#### Antenatal care

Accordingly, the percentages of women who have attended four or more antenatal care visits are similar in the subset of nulliparous women compared to women of all parities. Among the subset of nulliparous women only, 30.6% of

adolescent mothers (77/252) and 44.2% of adult mothers (61/138) attended at least four times the antenatal care visits (OR: 1.8; 95%CI: 1.2-2.8).

Table 5 summarizes the birth outcomes in adolescent pregnancies compared to those of adult mothers and illustrates the differences between the total population and the subset of nulliparous women.

**Table 5: Univariable analysis of adolescent compared to adult women**

<b>Assessment (Number of Women)</b>	<b>Adolescent women (≤19 years)</b>	<b>Adult women (&gt;19 years)</b>	
<b>All mothers:</b>			
Birth weight (1853)	2896.1g ± 462.8g	3074.2g ± 501.1g	p<.0001
LBW (1816)	16.6% (74/445)	8.8% (121/1371)	OR: 2.1; 95% CI: 1.5-2.8
Gestational age (1624)	38.2 ± 3.7 weeks	39.1 ± 2.9 weeks	p<.0001
Preterm birth (1624)	26.1% (99/380)	15.9% (198/1244)	OR: 1.9; 95% CI: 1.4-2.5
Stillbirth (1870)	0.9% (4/449)	2.8% (40/1421)	OR=0.3; 95% CI: 0.1-0.9
Cesarean section (1836)	5.2% (23/444)	6.0% (84/1392)	OR: 0.9; 95% CI: 0.5-1.4
Birth asphyxia (1635)	12.5% (50/400)	7.8% (96/1235)	OR: 1.7; 95% CI: 1.2-2.4
Intake of two or more doses of SP as iPTp (1132)	60.7% (158/261)	70.9% (617/870)	OR: 0.6; 95% CI: 0.5-0.8
Number of women who attended at least four antenatal care visits (1616)	28.4% (111/391)	38.7% (474/1225)	OR: 0.6; 95% CI: 0.5-0.8
Nulliparity (1543)	77.4% (287/371)	13.2% (155/1172)	OR: 22.4; 95% CI: 16.7-30.1
<b>Primiparous women only:</b>			
Birth weight (442)	2876.9g ± 435.2g	2990.2g ± 416.8g	p<.01
LBW (440)	18.1% (52/287)	9.2% (14/153)	OR: 2.2; 95% CI: 1.2-4.1
Gestational age (398)	38.4 ± 3.4 weeks	39.4 ± 2.8 weeks	p<.01
Preterm birth (398)	23.6% (62/263)	13.3% (18/135)	OR: 2.0; 95% CI: 1.1-3.6
Cesarean section (440)	5.6% (16/285)	10.3% (16/155)	OR: 0.5; 95% CI: 0.3-1.1
Birth asphyxia (379)	12.0% (32/235)	11.1% (16/144)	OR: 1.1; 95% CI: 0.6-2.1
Intake of two or more doses of SP as iPTp (285)	62.0% (111/179)	74.5% (79/106)	OR: 1.8; 95% CI: 1.1-3.1
Number of women who attended at least four antenatal care visits (390)	30.6% (77/252)	44.2% (61/138)	OR: 1.8; 95% CI: 1.2-2.8

### **3.3 Multivariable logistic regression analysis of birth outcomes**

#### **3.3.1 Analysis of potential risk factors for LBW – all mothers**

In order to better assess the influence of adolescence on birth weight, occurrence of LBW was analyzed in multivariable logistic regression analysis. The following dichotomized variables were considered to be potential risk factors for LBW:

- maternal age (adolescent or  $\leq 19$  years vs. adult or  $\geq 20$  years) at time of delivery
- parity status (nulliparity vs. multiparity)
- intake of intermittent preventive treatment of malaria during pregnancy (IPTp) ( $< 2$  doses of IPTp vs.  $\geq 2$  doses of IPTp)
- number of attended antenatal care (ANC) visits ( $< 4$  vs.  $\geq 4$  visits during index pregnancy)
- rural vs. urban health center (Lambaréné (HAS and CHRGR) vs. Fougamou)
- sex (male vs. female)

Gestational age was not included in this analysis. Although being significantly associated with LBW, gestational age is rather to be seen as one mechanism of how a pregnancy can result in the birth of a low birth weight infant than as risk factor for LBW.

Interacting of the considered variables was analyzed. A dependence of number of antenatal care visits and number of intake of IPTp could be demonstrated. Women who attended less than four antenatal care visits had a significantly higher risk of taking SP as IPTp less than two times during pregnancy.

Further, parity status could be verified to be significantly dependent from maternal age. Teenage mothers had a significantly higher risk for delivering their first child compared to adult mothers. Results from analysis of these interactions are shown in tables 6.1 and 6.2.

**Table 6.1 – Interaction of number of antenatal care visits and number of intake of SP as IPTp.**

	number of intake of IPTp <2	number of intake of IPTp ≥2	
<b>number of antenatal care visits &lt;4 (N=687)</b>	309/687 (45.0%)	378/687 (55.0%)	OR: 8.8; 95%CI: 6.0-12.8
<b>number of antenatal care visits ≥4 (N=412)</b>	35/412 (8.5%)	377/412 (91.5%)	

**Table 6.2 – Interaction of age below 20 years and parity status.**

	adolescent women	adult women	
<b>nulliparity</b>	287/442 (64.9%)	155/442 (35.1%)	OR: 22.4; 95%CI: 16.7-30.1
<b>multiparity</b>	84/1101 (7.6%)	1017/1101 (92.4%)	

Number of intake of SP as IPTp and parity were therefore excluded from multivariable logistic regression analysis of risk factors for LBW.

Maternal age, number of attended antenatal care visits, health center and sex showed no significant interactions among each other and were therefore used for logistic regression analysis with the occurrence of low birth weight as dependent variable.

For the same reasons as in univariable analysis, multiple births were excluded from analysis and only singleton births were considered.

The model showed an acceptable fit ( $\chi^2 = 33.4$ ;  $df = 4$ ;  $p < 0.0001^*$ ).

Young maternal age ( $\leq 19$  years) and low number of attended antenatal care visits (<4 visits) could be considered significantly associated with the birth of low birth weight children in univariable and multivariable analysis.



Other parameters (health center (rural vs. urban) and sex of the child) showed no statistically significant impact on the risk for delivering a newborn with low birth weight in multivariable as well as in univariable analysis. Table 7 shows unadjusted and adjusted odds ratio for all variables used in the multivariable logistic regression model.

**Table 7 – Multivariable logistic regression analysis for delivery of an infant with low birth weight.**

Category	Variable	Number of infants with LBW (%)	Univariable OR (95% CI)	adjusted OR (95% CI)	p
<b>Maternal age</b>	≤ 19 years	74/445 (16.6%)	2.1 (1.5-2.8)	1.9 (1.3-2.8)	0.0006*
	≥ 20 years	121/1371 (8.8%)			
<b>Number of attended ANC visits</b>	< 4 visits	126/1007 (12.5%)	2.0 (1.4-3.0)	2.1 (1.5-2.9)	< 0.0001*
	≥ 4 visits	38/542 (7.0%)			
<b>Health center</b>	Fougamou	41/392 (10.5%)	1.0 (0.7-1.4)	1.1 (0.7-1.6)	0.6497
	Lambaréné	155/1436 (10.8%)			
<b>Sex</b>	female	103/849 (12.1%)	1.3 (1.0-1.8)	1.3 (0.9-1.8)	0.1228
	male	93/976 (9.5%)			

### 3.3.2 Analysis of potential risk factors for LBW – subset of nulliparous mothers

For same reasons as stated earlier, analysis was carried out for the subset of mothers who gave birth to their first child. Adolescence ( $\leq 19$  years of age), low number of attended antenatal care visits, area of living and sex were again considered as potential risk factors.

The model showed an acceptable fit ( $\chi^2 = 9.3$ ;  $df = 4$ ;  $p = 0.0531$ ).

Only young maternal age was significantly associated with the risk of delivering an infant with low birth weight both in univariable and multivariable analysis.

Other parameters (number of attended antenatal care visits, health center and sex) showed no significant association with low birth weight.

Table 8 shows unadjusted and adjusted odds ratio for all variables.

<b>Table 8 – Multivariable logistic regression analysis for nulliparous mothers only.</b>					
Category	Variable	Number of infants with LBW (%)	Univariable OR (95% CI)	adjusted OR (95% CI)	p
<b>Maternal age</b>	$\leq 19$ years	52/287 (18.1%)	2.2 (1.2-4.1)	2.2 (1.2-4.6)	0.0164*
	$\geq 20$ years	14/153 (9.2%)			
<b>Number of attended ANC visits</b>	< 4 visits	41/251 (16.3%)	1.4 (0.8-2.5)	1.2 (0.7-2.4)	0.4936
	$\geq 4$ visits	17/137 (12.4%)			
<b>Health center</b>	Fougamou	9/67 (13.4%)	0.9 (0.4-1.8)	0.9 (0.4-1.8)	0.7081
	Lambaréné	57/374 (15.2%)			
<b>Sex</b>	female	36/207 (17.4%)	1.4 (0.8-2.4)	1.5 (0.8-2.7)	0.1649
	male	30/233 (12.9%)			

### 3.3.3 Analysis of potential risk factors for preterm delivery

Low birth weight can either result from preterm delivery or from intra uterine growth restriction. Giving account to this, an analysis was performed considering the same potential risk factors but with the occurrence of preterm delivery as dependent variable.

Once again, only singleton births were considered for analysis.

The model showed an acceptable fit ( $\chi^2 = 100.9$ ;  $df = 4$ ;  $p < 0.0001^*$ ).

Young maternal age ( $\leq 19$  years), low number of antenatal care visits ( $< 4$  visits) and rural area of living (Fougamou) showed a significant association with preterm delivery in both univariable and multivariable analysis. Sex of the child showed no statistically significant impact on the risk for preterm delivery.

Table 9 shows unadjusted and adjusted odds ratio for all variables used in the multivariable logistic regression model.

<b>Table 9 – Multivariable logistic regression analysis for risk factors for preterm delivery.</b>					
Category	Variable	Number of infants with gestational age $< 37$ weeks (%)	Univariable OR (95% CI)	adjusted OR (95% CI)	p
<b>Maternal age</b>	$\leq 19$ years	99/380 (26.1%)	1.9 (1.4-2.4)	1.7 (1.3-2.3)	0.0007*
	$\geq 20$ years	198/1244 (15.9%)			
<b>Number of attended ANC visits</b>	$< 4$ visits	224/896 (25%)	4.4 (3.0-6.3)	4.3 (3.0-6.2)	$< 0.0001^*$
	$\geq 4$ visits	38/537 (7.1%)			
<b>Health center</b>	Fougamou	80/346 (23.1%)	1.5 (1.1-2.0)	1.6 (1.2-2.2)	0.0026*
	Lambaréné	217/1282 (16.9%)			
<b>Sex</b>	female	143/747 (19.1%)	1.1 (0.9-1.5)	1.0 (0.8-1.4)	0.8554
	male	152/877 (17.3%)			

## 4 Discussion

Several studies from the study area and other regions have demonstrated the increased risk of adolescent mothers to deliver an infant with LBW [3, 55-57, 74, 75], but assigned explanations remain diverse.

Our study aimed to analyze the risk of adolescent women to give birth to a newborn with LBW in the Central African country Gabon. Furthermore, we aimed to investigate the influence of potential confounding factors related to adolescence.

Our analysis indicates that the risk to deliver an infant with LBW was distinctly higher for adolescent women compared to adult mothers. Further, it indicates that the risk for preterm delivery was significantly higher among adolescent women.

Besides of young age, low frequency of antenatal care visits could be identified as risk factor for preterm delivery as well as for low birth weight.

### Prevalence of adolescent pregnancy and low birth weight in the study area

The data showed a high prevalence of adolescent pregnancy. 23.7% of all mothers were at the age of 19 years or below, 23.2% of those even aged 16 years or younger. This emphasizes the importance of further analysis of young maternal age as potential risk factor for adverse pregnancy outcome in the study area.

Prevalence of low birth weight was 13.1% in our study and measured 14% by the WHO in the year 2000 [13].

### HIV-prevalence among pregnant women in the study area

The HIV prevalence among child-bearing women in Lambaréné has been estimated to be less than 4% in 2003, but published data is not available [50].

The analysis of HIV prevalence in the study population was highly limited by passive documentation in two of the three health centers, as already described earlier. Nevertheless, 77 (4%) cases of HIV infection were documented and since hospital based testing was the basis for documentation in all three health centers,

this can be considered as reliable data for estimating the minimum of HIV prevalence. Analyzing only the subset of the 815 women who gave birth in the CHRGR, where for each women the HIV status was either documented as negative (N=738; 90.6%), positive (N=33; 4.1%) or unknown (N=44; 5.4%), the findings uncover a fairly higher rate, revealing that the HIV prevalence could be anywhere between 4% and 10%.

This correlates to some extent with official numbers from the UN, positioning the HIV prevalence among Gabon's population aged 15 to 49 years in the year 2009 to be 5.2% [76].

#### Intake of SP as IPTp and number of antenatal care visits

Adolescent mothers were significantly less likely to take at least two doses of SP as IPTp during pregnancy. On the other hand, intake of less than two doses of IPTp often is considered to have an influence on the risk for low birth weight delivery. The efficacy of SP as IPTp is currently discussed in literature and there are reports that its efficacy is decreasing due to resistance [77].

Cohering with the number of intake of malaria prophylaxis is the number of realized antenatal care visits. The percentage of adolescent mothers attending at least four antenatal care visits during pregnancy was lower than the proportion of adult mothers and less than four antenatal care visits indicated a higher risk for low birth weight and preterm delivery in univariable as well as in multivariable analysis.

Most studies on the subject lack the inclusion of antenatal care into analysis. The influence of antenatal care on low birth weight might thus be highly underestimated. A case-control study from Nigeria could demonstrated, that the poorer obstetric outcome of adolescent mothers is rather due to lacking adequate antenatal care than to the age itself [58]. Absence or low quality of prenatal care could further be identified as independent risk factor for delivering a baby with low birth weight in different studies [31, 32, 54, 56, 78-80].

Number of antenatal care visits and IPTp intake are influenced by the attitude and socioeconomic possibilities concerning health behavior and the portrayed

difference may indicate a discrepancy in health behavior among adolescent mothers when compared to adults.

#### Preterm deliveries and low birth weight

Our analysis strongly suggested preterm delivery to be a main risk factor for low birth weight. A differentiation between low birth weight due to preterm delivery and due to intra uterine growth retardation was discussed before [14]. Undoubtedly, there is an importance in this differentiation since low birth weight can either depend on low growth velocity during pregnancy or a shorter duration of growth. Therefore, we aimed to identify risk factors for preterm delivery as well, finding mainly the same risk factors as for low birth weight.

#### Mode of delivery

Results of our analysis show a non-significant lower rate of caesarean sections in adolescent women when compared to adults (5.2%; 23/444 vs. 6.0%; 84/1392, respectively; OR: 0.9; 95% CI: 0.5-1.4). This difference was higher but still non-significant when only nulliparous mothers were analyzed (5.6%; 16/285 vs. 10.3%; 16/155, respectively; OR: 0.5; 95% CI: 0.3-1.1).

A lower risk for caesarean sections in younger mothers was reported before [75, 81, 82]. Nevertheless, these findings do not reveal whether younger mothers have a poorer access to caesarean section or have biological advantage, which often is considered to be the opposite due to cephalopelvic disproportion [75].

#### Birth asphyxia

Bad health condition of the newborn, in our analysis measured by low APGAR score or need of cardiopulmonary reanimation after birth was more frequent in babies with low birth weight. This reflects the suitability of LBW as surrogate marker for increased mortality and morbidity. Consistent with our findings, a large retrospective cohort study from Brazil recently showed a significant association

of APGAR score below seven with low birth weight both one and five minutes after delivery [83].

### Socioeconomic factors

Certainly, socioeconomic factors have a major impact on health behavior in general and on frequency and quality of antenatal care in particular. Anyhow, it remains difficult to measure the socioeconomic status of an individual in comparable means. Marital status [31, 78], poverty [32], low educational level [23, 31] and unemployment [56] could be identified as potential risk factors for low birth weight. They could be important confounders when analyzing adolescent pregnancies, since adolescents in many cases are more likely to be single or less educated [75]. Due to study design, none of the mentioned socioeconomic factors was reported, which surely constitutes an important limitation of this study.

### Rural vs. urban setting

As described above, our study assesses the prevalence of adolescent pregnancies and their outcome in the two towns of Fougamou and Lambaréné in Gabon. While Fougamou is considered to be a typical rural setting, Lambaréné can be classified as urban area with semi-urban surroundings.

While there were no significant differences in age distribution and prevalence of adolescent pregnancy in the study subareas, there was a difference in frequency of IPTp intake and antenatal care visits, showing lower number in the Hôpital Albert Schweitzer (HAS) in Lambaréné when compared to the Fougamou health center (CMF). However, this difference is more likely to be based on differences in health center organization than on regional varieties, since numbers of IPTp intake and antenatal care visits were similar in the second hospital in Lambaréné (Centre Hospitalier Régional Georges Rawiri, CHRGR) when compared with Fougamou.

Further, neither in univariable nor in multivariable analysis, any differences occurred in incidence of LBW when comparing the rural and the semi-urban area,

but multivariable analysis showed a significantly higher number of preterm deliveries in the rural setting of Fougamou.

Lack of differences in frequency of low birth weight were reported earlier when comparing births in different socio-economic areas [84, 85], but data concerning this subject is rather rare.

Area of living can in general be considered as determinant of socioeconomic status and could therefore influence birth outcomes indirectly. Analysis in our case could be biased due to referral of cases from Fougamou to Lambaréné and due to the partly rural surroundings of Lambaréné from which many women come to deliver in the town's hospitals.

#### Adolescent pregnancy as risk factor for low birth weight

Previous studies on adolescent pregnancy and birth outcomes showed conflicting results and available data for the study area and for sub-Saharan Africa in general remains insufficient.

Our data imply an association of young maternal age and low birth weight and preterm delivery as indicators for adverse pregnancy outcome. Further, an association of adolescence with a low frequency of antenatal care visits was demonstrated, and therefore one confounding factor concerning the influence of age on birth weight could be identified.

Nonetheless, it is misleading to analyze the influence of age on birth weight without taking the mechanisms of this influence into consideration. The question, whether the increased risk for adverse pregnancy outcome among teenage pregnant women is due to biological age itself or due to associated factors (for example low economic status, poor antenatal care, missing education) was raised before.

Literature on adolescent pregnancy and low birth weight being rare for low income countries, the following paragraph tries to summarize findings of other studies.



Similar results as in the present study were obtained by an earlier study from the study area, showing comparable prevalence of adolescent pregnancy, preterm delivery and low birth weight and identifying both adolescence and lack of antenatal care as risk factors for LBW [55].

Adolescence could be identified as significant risk factor for low birth weight when considered crude OR, but not when adjusting for other factors (preterm delivery among them) in a recent analysis from Ethiopia, which further stated lack of antenatal care as independent risk factor for LBW [85].

In a large cohort in China, maternal age less than 20 years was significantly associated with the risk of delivering a low birth weight infant [86].

Also in line with our findings, a large WHO multicountry study stated that infants of adolescent mothers are more likely to suffer preterm delivery, low birth weight and severe neonatal condition, but did not analyze quality or frequency of antenatal care as possible risk factor [75].

No prenatal care, smoking and pregnancy of adolescent unmarried women could be identified as risk factor for low birth weight in a cross-sectional study from Brazil [78].

A study from neighboring Cameroon found low birth weight, preterm delivery and early neonatal death being associated with adolescence of the mother and young maternal age, low number of antenatal care visits (<4) and unemployment as risk factors for adverse fetal outcome [56].

Adolescence was further identified as risk factor for low birth weight delivery in Nigeria [58, 87] and several studies recognized adolescence as risk factor for low birth weight, preterm delivery and birth asphyxia in India [74, 88, 89].

Adolescents are at higher risk for adverse pregnancy outcome such as low birth weight and preterm delivery not only in the study area but also in several other countries of low income.

#### MDG and indicators

Improving maternal health is one of eight UN millennium development goals and adolescent birth rates as well as antenatal care coverage are two of its indicators.

The question was raised, whether the MDGs are helpful for development or not and criticism was especially focused on ways of data assessment, in many cases being not standardized nor registered according to UN standards [90] but the effort to document progresses provides a broad and easy accessible data volume. For Gabon, as for many countries, decline in maternal mortality could be measured over the past 20 years [91].

High rates of adolescent pregnancy not only form an obstacle when trying to achieve lower rates of maternal mortality, but also when trying to reduce child mortality, since prematurity is an important risk factor for newborn mortality [92]. This linkage to the millennium development goal emphasizes the importance of analyzing teenage pregnancies.

#### Limitations

There are certainly many limitations due to the study design, which was retrospective and based of hand-entered registers from different health centers.

#### Failure to adjust for possible and known confounders

Due to study design, it was not possible to include further factors with influence on birth weight, such as wealth status, education level, information on parental height and weight, pre-pregnancy maternal weight, smoking during pregnancy and malaria infection during pregnancy.

#### Still births

While live births and stillbirths were entered in the birth registers, abortions were partly entered in separate registers and partly added to the birth registers. There was in general no differentiation of spontaneous and induced abortion, since induction of abortion is illicit in Gabon, and therefore registration of abortion might be unreliable per se.

#### Home deliveries

A further limitation was posed by the occurrence of home deliveries. For Gabon, the quantity of births attended by a skilled health worker was estimated to be 86%

in the year 2000 [62], which clearly exceeds numbers from surrounding countries. Similar figures are supplied by the ministry of economics, commerce, industry and tourism of Gabon, stating that the percentage of assisted birth being 87.1% in 2005 [70]. The remaining 13 to 14% are most likely to be home births and therefore are naturally not documented in the birth registers, although some of the newborns who were delivered at home were later brought to the clinics. Anyhow, for these cases, anthropometric measures of the newborn might be confounded, since measurement did not take place immediately after birth (WHO recommends measurement of birth weight during the first hour after birth before the onset of significant postnatal weight loss [13]). Altogether, the lack of documentation concerning home births might lead to a preselected set of births, not representing the entire population. This selection of births can bias quantitative statements on prevalence of LBW, because it is likely that children who are not born in a health center context might be of lower socioeconomic status and of lower birth weight [93].

#### Abortion rates

The lack of information on abortions and home births limit the investigation in terms of its demographic representativeness. Also, the comparison of adult and adolescent mothers might be impaired by these two factors, since there is a certain possibility, that abortion rates could be higher among teenagers in order to avoid confrontation with socioeconomic challenges due to early onset of childbearing.

#### Inaccurate reporting and misreporting

For this study, being a retrospective analyze of birth registers, there remains a risk of inaccurate reporting or misreporting concerning all data. Inaccurate reporting could be due to lack of knowledge on level of pregnant women (in example in regards of first day of last menses or date of birth, which simply might not be known) or on level of midwives (in example by mistake when copying data from the mother's maternity record booklet to the birth register).

## **5 Conclusion and perspectives**

It is uncontroversial, that the international public health community has – with its Millennium Development Goals and their indicators – set focuses on adolescent pregnancy as well as on LBW. Adolescent pregnancy and LBW are defined problems and potentially preventable, but it is necessary to identify risk factors to decide on appropriate intervention strategies.

Our data suggests that teenage pregnancy in the study area was associated with higher risks of adverse pregnancy outcomes such as preterm delivery and low birth weight. Further, low frequency of antenatal care visits could be identified as independent risk factor for low birth weight and preterm delivery.

Education among adolescents and improvement of availability of antenatal care is crucial to improve pregnancy outcomes among adolescents in the study area and comparable regions.

## 6 Literature

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## 7 Summary

### 7.1 Summary

Sub-Saharan Africa suffers high rates of maternal and neonatal mortality and morbidity. Adolescent mothers (age  $\leq 19$  years at time of delivery) are often considered to be particularly prone to adverse pregnancy outcomes, such as low birth weight (LBW, birth weight  $< 2,500$  grams) and prematurity. Various risk factors have been identified so far to contribute to adverse pregnancy outcome, but available data remains insufficient for low income countries. The considerably high rate of adolescent mothers in many regions of sub-Saharan Africa reflects the need for assessing the prevalence of adolescent pregnancies in this area as well as their influence on obstetric outcomes and the necessity of analyzing further associated risk factors.

The present study assesses the prevalence of adolescent pregnancies in a semi-urban and rural region in the Central African country Gabon. Furthermore, it analyzes maternal adolescence among other parameters as a potential risk factor for adverse pregnancy outcome, focusing on LBW.

A retrospective cohort study was performed. Data from birth registers from three different health centers in Gabon were entered in a purpose built database. A total of 1,972 births were registered in the database, the registered births took place between December 15<sup>th</sup> 2009 and August 29<sup>th</sup> 2011.

Adolescent pregnancy had a prevalence of 23.7% (N=453/1910) and 251 out of 1,915 live births (13.1%) were classified as presenting with LBW.

In univariable analysis, the percentage of newborns with LBW was significantly higher in adolescent women. 16.6% (74/445) of newborns to adolescent mothers presented with LBW, compared to 8.8% (121/1371) in mothers older than 19 years (OR: 2.1, 95% CI: 1.5-2.8). The frequency of preterm births was as well significantly higher in adolescent pregnancies with 26.1% (99/380) when compared to adult pregnancies with 15.9% (198/1244) (OR: 1.9, 95% CI: 1.4-2.5).

In multivariable analysis, young maternal age ( $\leq 19$  years) and low number of attended antenatal care visits ( $< 4$  visits during the index pregnancy) showed a significant association preterm delivery and delivery of a LBW child.

Further, an association of adolescence with a low frequency of antenatal care visits was demonstrated, and therefore one confounding factor concerning the influence of young maternal age on birth weight could be identified.

Our data suggests that teenage pregnancy in the study area is significantly associated with higher risks of adverse pregnancy outcomes such as preterm delivery and low birth weight. Besides of young maternal age, low frequency of antenatal care visits could be identified as independent risk factor for low birth weight and preterm delivery.

Education among adolescents and improvement of availability of antenatal care is crucial to improve pregnancy outcomes among adolescents in the study area and comparable regions.

## **7.2 Zusammenfassung**

Subsahara-Afrika verzeichnet hohe Raten an Mortalität und Morbidität von Müttern und Neugeborenen. Insbesondere adoleszente Mütter (im Alter von  $\leq 19$  Jahren zum Zeitpunkt der Geburt) gelten oft als besonders anfällig für unerwünschte Schwangerschaftsausgänge wie zum Beispiel Frühgeburtlichkeit und geringes Geburtsgewicht (Geburtsgewicht  $< 2500$  Gramm). Verschiedene Risikofaktoren, die zu unerwünschten Schwangerschaftsausgängen beitragen wurden bereits identifiziert, aber die Verfügbarkeit von Daten aus einkommensschwachen Ländern bleibt bisher unzulänglich. Die beträchtliche Anzahl an adoleszenten Müttern in vielen Regionen Afrikas südlich der Sahara spiegelt die Notwendigkeit wider, die Prävalenz jugendlicher Mütter in dieser Region und deren Einfluss auf Geburtsausgänge sowie weitere assoziierte Risikofaktoren zu identifizieren und zu analysieren.

Die vorliegende Studie erhebt die Prävalenz an adolescenten Müttern in einer semiurbanen und einer ländlichen Region des Staates Gabun im zentralen Afrika. Darüber hinaus wird Adoleszenz neben anderen Parametern als potentieller Risikofaktor für unerwünschte Schwangerschaftsausgänge analysiert, dieses mit einem Fokus auf geringes Geburtsgewicht.

Es wurde eine retrospektive Kohortenstudie durchgeführt. Daten wurden aus Geburtsregistern drei verschiedener Geburtszentren in Gabun gesammelt und in eine eigens dafür aufgebaute Datenbank eingegeben. 1972 Geburten aus dem Zeitraum zwischen 15. Dezember 2009 und 29. August 2011 wurden registriert.

Adoleszente Schwangerschaften hatten eine Prävalenz von 23.7% (N=453/1910) und 251 von insgesamt 1915 Lebendgeburten wiesen geringes Geburtsgewicht auf (13.1%).

Die univariate Analyse zeigte einen signifikant höheren Prozentsatz an Neugeborenen mit geringem Geburtsgewicht in der Gruppe der adolescenten Frauen. 16.6% (74/445) der Neugeborenen adolescenter Mütter wiesen geringes Geburtsgewicht auf, während in der Gruppe der Mütter im Alter über 19 Jahren 8.8% (121/1371) der Neugeborenen geringes Geburtsgewicht aufwiesen (OR: 2.1, 95% CI: 1.5-2.8). Die Häufigkeit von Frühgeburtlichkeit war ebenfalls signifikant größer in der Gruppe der adolescenten Frauen – 26.1% (99/380) im Vergleich zu 15.9% (198/1244) bei den über 19-jährigen Frauen (OR: 1.9, 95% CI: 1.4-2.5).

Die multivariate Analyse zeigte eine signifikante Assoziation von jungen mütterlichen Alter ( $\leq 19$  Jahre) sowie geringer Anzahl an pränatalen Gesundheitskontrollen ( $< 4$  Kontrollen während der Indexschwangerschaft) mit Frühgeburtlichkeit und geringen Geburtsgewicht des Neugeborenen.

Des Weiteren konnte eine Assoziation zwischen Adoleszenz der Mutter mit einer geringen Anzahl an pränatalen Gesundheitskontrollen gezeigt werden, womit eine Störvariable in Bezug auf den Einfluss jungen mütterlichen Alters auf das Geburtsgewicht identifiziert werden konnte.

Unsere Daten stützen die Annahme, dass Schwangerschaften von Teenagern in der Studienregion signifikant mit einem höheren Risiko unerwünschter Geburtsausgänge wie Frühgeburtlichkeit und geringen Geburtsgewicht assoziiert sind. Neben dem jungen mütterlichen Alter konnte eine geringe Anzahl an Gesundheitskontrollen während der Schwangerschaft als Risikofaktor für geringes Geburtsgewicht und Frühgeburtlichkeit nachgewiesen werden.

Aufklärung von adoleszenten Frauen sowie eine Verbesserung der Zugänglichkeit zu pränataler Gesundheitsvorsorge ist essentiell um Geburtsausgänge adoleszenter Mütter in der Studienregion und vergleichbaren Gegenden zu verbessern.

## **8 Erklärung zum Eigenanteil**

Die Konzeption der Studie erfolgte in Zusammenarbeit mit meinem Betreuer Assoc.-Prof. Michael Ramharter (Medizinische Universität Wien).

Die statistische Auswertung erfolgte nach Beratung durch das Institut für Biometrie durch mich.

Ich versichere, das Manuskript selbstständig verfasst zu haben und keine weiteren als die von mir angegebenen Quellen verwendet zu haben.

Esslingen, den 30.11.2014

Ulla Schipulle

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