

REPUBLIC OF CAMEROON  
*PEACE-WORK-FATHERLAND*

.....  
MINISTRY OF HIGHER  
EDUCATION

.....  
THE UNIVERSITY OF YAOUNDE I

.....  
FACULTY OF MEDICINE AND  
BIOMEDICAL SCIENCES



REPUBLIQUE DU CAMEROUN  
*PAIX-TRAVAIL-PATRIE*

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MINISTERE DE L'ENSEIGNEMENT  
SUPERIEUR

.....  
UNIVERSITE DE YAOUNDE I

.....  
FACULTE DE MEDECINE ET DES  
SCIENCES BIOMEDICALES

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

## **DELIVERY AFTER TREATMENT FOR MALARIA AT TERM: COMPARATIVE OUTCOME BETWEEN INDUCTION OF LABOUR AND EXPECTANT SPONTANEOUS LABOUR**

Thesis submitted and publicly defended in partial fulfilment of the requirements for  
the Award of Medicinae Doctor (MD) degree by:

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## TABLE OF CONTENTS

DEDICATION .....	iv
ACKNOWLEDGEMENTS .....	v
THE ADMINISTRATIVE AND TEACHING STAFF FOR 2023/2024 OF THE FACULTY OF MEDICINE AND BIOMEDICAL SCIENCES .....	vi
THE PHYSICIAN’S OATH.....	xxi
SUMMARY .....	xxii
LIST OF TABLES .....	xxv
LIST OF FIGURES .....	xxvi
LIST OF ABBREVIATIONS.....	xxvii
CHAPTER: 1 INTRODUCTION .....	1
1.1. Background .....	2
1.2. Rationale.....	2
1.3. Research Question.....	3
1.4. Research Hypothesis .....	3
1.5. Research Objectives .....	3
1.5.1. General Objective .....	3
1.5.2. Specific Objectives .....	3
CHAPTER 2: LITERATURE REVIEW .....	4
2.1. INTRODUCTION.....	4
2.1.1. Definition of Operational Terms .....	4
2.1.2 Epidemiology.....	4
2.2. RECALL .....	6
2.2.1. Anatomy .....	6
2.2.2. Physiology .....	8
2.3. At Risk Pregnancy.....	10
2.4. Malaria in Pregnancy .....	10
2.4.1. General Overview .....	10

Delivery after treatment for malaria at term: comparative outcome between induction  
of labour and expectant spontaneous labour

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2.4.2. Pathophysiology .....	11
2.4.3. Clinical Signs and Symptoms .....	15
2.4.4. Diagnosis of Malaria .....	17
2.4.5. Management of Malaria.....	18
2.5. Induction of Labor.....	21
2.5.1. General Overview .....	21
2.5.2. Indications .....	21
2.5.3. Contraindications.....	21
2.5.4. Criteria of Induction .....	22
2.5.5. Methods of Induction.....	23
2.5.6. Complications of Induction of Labour .....	25
2.6. Review of Studies.....	26
2.6.1. In the world.....	26
2.6.2. In Africa.....	31
2.6.3. In Cameroon .....	34
CHAPTER 3: METHODOLOGY .....	39
3.1. TYPE OF STUDY .....	40
3.2. SITE OF STUDY .....	40
3.3. DURATION OF STUDY .....	40
3.4. STUDY POPULATION AND SAMPLE .....	40
3.4.1. Inclusion Criteria .....	40
3.4.2 Exclusion Criteria .....	41
3.4.3. Non-Inclusion Criteria.....	41
3.4.4. Sampling Method .....	41
3.4.5. Sample size Estimation.....	41
3.5. PROCEDURE.....	42
3.5.1. Administrative Formalities .....	42
3.5.2. Recruitment and Data Collection .....	42
3.5.3. Study Variables.....	43

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3.6. STUDY RESOURCES .....	43
3.6.1. Data Collection and Management Tools .....	43
3.6.2. Human Resource.....	43
3.7. DATA ANALYSIS .....	44
3.8. ETHICAL CONSIDERATIONS .....	44
CHAPTER 4: RESULTS .....	45
4.1. Recruitment of study population .....	46
4.2. Socio-demographic profile of the study population.....	47
4.2.1. Age and marital status .....	47
4.2.2. Level of education and occupation.....	48
4.3. Clinical profile of the study population.....	49
4.3.2. Comorbidities and lifestyle during pregnancy.....	50
4.3.3. Pregnancy follow-up.....	51
4.3.4. Bishop score .....	54
4.4. Maternal outcome in the study population.....	55
4.5. Fetal and neonatal outcome of the study population.....	56
4.5.1. Fetal complications at delivery .....	56
4.5.2. Neonatal characteristics at delivery .....	57
4.5.3. Neonatal outcomes .....	58
CHAPTER 5: DISCUSSION.....	59
CONCLUSION AND RECOMMENDATIONS .....	59
REFERENCES .....	59
APPENDIX.....	59

## **DEDICATION**

**To my parents,**

***Professor NGOMO Horace MANGA***

***And***

***Mrs. NGOMO Julie ULE***

## ACKNOWLEDGEMENTS

First and foremost, praises and thanks to the Almighty God who carried me on eagle's wings throughout these seven years of medical school, showered me with unending blessings and kept me safe at all times. The outcome of this research work has been made possible, thanks to the support of many persons, some of whom deserve profound gratitude. Special thanks to;

- ❖ **Professor MBU Robinson** Director of the Yaoundé Gynaecology, Obstetrics and Pediatric Hospital (YGOPH) my supervisor. I'm deeply grateful to you for bringing the weight of your incredible experience and knowledge to this piece of work. You always made time for me, despite your numerous commitments to ensure that this piece of work is completed. Thank you for your patience, guidance and support.
- ❖ **Dr EBONG Clifford** my co-supervisor who devoted much time in continuously correcting this write-up, as well as giving orientations which permitted me to improve on the quality of this work.
- ❖ **Dr BATOUM Veronique** for accepting to co-supervise this thesis. I'm forever grateful for your tremendous support and help.
- ❖ **The Dean and the entire staff** of the Faculty of Medicine and Biomedical Sciences- University of Yaoundé I, for always leading us on the right path to success and making sure we had a grasp of everything we learned throughout medical school.
- ❖ **The honorable jury members**, for accepting to read through and evaluate my work and for your valuable input aimed at improving this work.
- ❖ **The Director** of the Yaoundé Central Hospital, for granting me authorization to carry out this research in your institution.
- ❖ The entire staff at the Obstetrics and Gynecology units of the YGOPH and YCH, for helping me throughout this work and providing the necessary assistance for it to come to fruition.
- ❖ My sincere gratitude goes to all the participants who played a crucial role in the completion of this study.
- ❖ I extend my heartfelt appreciation to my family, seniors and friends, their unwavering belief in my abilities has been a driving force in my pursuit of excellence.
- ❖ I'm extremely grateful to all those who directly or indirectly inspired and encouraged the completion of this work.



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Delivery after treatment for malaria at term: comparative outcome between induction  
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**KEY:**

-**HD**= Head of Department

-**P**= Professor

-**AP**= Associate Professor

-**SL**= Senior Lecturer

Delivery after treatment for malaria at term: comparative outcome between induction  
of labour and expectant spontaneous labour

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-**L**=Lecturer

## THE PHYSICIAN'S OATH

Declaration of Geneva adopted by the Geneva Assembly of the World Medical Association in Geneva, Switzerland, September 1948 and amended by the 22nd World Medical Assembly, Sydney, Australia (August 1968)

*On admission to the medical profession:*

*I will solemnly pledge myself to consecrate my life to the service of humanity*

*I will give my teachers the respect and gratitude which is their due*

*I will practice my profession with conscience and dignity, the health of my patients will be my first consideration*

*I will respect secrets confided in me, even after the patient has died*

*I will maintain by all the means in my power the honor and noble traditions of the medical profession*

*My colleagues will be my brothers*

*I will not permit considerations of religion, nationality, race, party politics or social standing to intervene between my duty and my patient*

*I will maintain the utmost respect for human life from the time of conception, even under threat*

*I will not use my medical knowledge contrary to the laws of humanity*

*I make these promises solemnly, freely and upon my honor.*



## SUMMARY

**BACKGROUND:** Malaria is a public health burden worldwide and especially in Sub-Saharan Africa where a significant number of individuals are affected each year. Pregnant women are part of those that are very vulnerable to this disease. In Cameroon, no study has been carried out to assess the maternal and perinatal outcome after induction of labor versus spontaneous labour following complete treatment of malaria in the third trimester of pregnancy. It is imperative to consider the most optimal delivery approach be it induction or spontaneous labor in order to minimize adverse events especially in the context of malaria.

**OBJECTIVE:** The main objective was to assess the maternal and fetal outcome of pregnancy among women diagnosed and treated for malaria at term following immediate induction compared to expectant spontaneous labor.

**METHOD:** This was a clinical trial carried out at the Yaoundé Gynaecology, Obstetrics and Pediatric Hospital (YGOPH) and the Yaoundé Central Hospital (YCH). We collected data from 170 pregnant women who were diagnosed with malaria at term and received complete treatment. We had 85 women who accepted induction of labor and 85 women who accepted to go home and await spontaneous labour.

**RESULTS:** Primigravidaes and nulliparas were the most represented in both groups. The rate of cesarean section was significantly higher in the induction group compared to the spontaneous delivery group (RR: 2.66, 95% CI [1.47-4.81],  $p < 0.001$ ). The induction group had a higher risk than the spontaneous delivery group of having labor abnormalities (RR: 3.59, 95% CI [1.75-12.02],  $p = 0.001$ ) and especially perineal tears (RR: 2.09, 95% CI [1.08-4.01],  $p = 0.01$ ) respectively. The induction group had a higher risk of non-reassuring fetal status (RR: 2.58, 95% CI [1.42-4.68],  $p = 0.001$ ) than the spontaneous delivery group. The spontaneous delivery group had more cases of intrauterine fetal demise than the induction group (RR: 0.18, 95% CI [0.04-0.79],  $p = 0.009$ ). Newborns of the induction group had a higher risk of requiring ventilation support compared to the spontaneous delivery group (RR: 2.6, 95% CI [0.96-6.97],  $p = 0.039$ ).

**CONCLUSION:** Induction of labor was more associated with adverse maternal and foetal outcomes compared to spontaneous delivery labor but foetal demise was more in the spontaneous delivery group.

**KEYWORDS:** malaria, labour, induction, spontaneous, outcome.

## RÉSUMÉ

**CONTEXTE :** Le paludisme constitue un fardeau de santé publique dans le monde entier et particulièrement en Afrique subsaharienne où un nombre important de personnes sont touchées chaque année. Les femmes enceintes font partie des personnes très vulnérables à cette maladie. Au Cameroun, aucune étude n'a été réalisée pour évaluer l'issue maternelle et périnatale après le déclenchement du travail versus le travail spontané au cours du troisième trimestre de la grossesse. Il est impératif d'envisager l'approche d'accouchement la plus optimale, qu'il s'agisse du déclenchement du travail ou du travail spontané, afin de minimiser les événements indésirables, en particulier dans le contexte du paludisme.

**OBJECTIF :** L'objectif principal était d'évaluer l'issue maternelle et fœtale de la grossesse chez les femmes diagnostiquées et traitées pour le paludisme à terme après le déclenchement immédiat par rapport au travail spontané attendu.

**MÉTHODE :** Il s'agit d'un essai clinique réalisé à l'Hôpital Gynécologie-Obstétrical et Pédiatrique de Yaoundé (YGOPH) et à l'Hôpital Central de Yaoundé (YCH). Nous avons collecté les données de 170 femmes enceintes chez qui le paludisme a été diagnostiqué à terme et qui ont reçu un traitement complet. Nous avons eu 85 femmes qui ont accepté le déclenchement du travail et 85 femmes qui ont accepté de rentrer chez elles et d'attendre un travail spontané.

**RÉSULTATS :** Les primigravides et les nullipares étaient les plus représentées dans les deux groupes. Le taux de césarienne était significativement plus élevé dans le groupe d'induction que dans le groupe d'accouchement spontané (RR : 2,66, IC 95 % [1,47-4,81],  $p < 0,001$ ). Le groupe d'induction avait un risque plus élevé que le groupe d'accouchement spontané d'avoir des anomalies du travail (RR : 3,59, IC à 95 % [1,75-12,02],  $p = 0,001$ ) et des déchirures périnéales (RR : 2,09, IC à 95 % [1,08-4,01],  $p = 0,01$ ) respectivement. Le groupe d'induction présentait un risque plus élevé d'état fœtal non rassurant (RR : 2,58, IC à 95 % [1,42-4,68],  $p = 0,001$ ) que le groupe d'accouchement spontané. Le groupe d'accouchement spontané présentait plus de cas de mort fœtale intra-utérine que le groupe d'induction (RR : 0,18, IC 95 % [0,04-0,79],  $p = 0,009$ ). Les nouveau-nés du groupe d'induction présentaient un risque plus élevé de nécessiter une assistance respiratoire par rapport au groupe d'accouchement spontané (RR : 2,6, IC à 95 % [0,96-6,97],  $p = 0,039$ ).

**CONCLUSION :** Le déclenchement du travail était davantage associé à des issues maternelles et fœtales indésirables que le travail d'accouchement spontané, mais la mort fœtale était plus fréquente dans le groupe d'accouchement spontané.

**MOTS CLÉS :** paludisme, travail, déclenchement, spontané, issue.

## LIST OF TABLES

<b>Table I:</b> Showing the Bishop's Score [47].....	23
<b>Table II:</b> Population distribution by age and marital status .....	47
<b>Table III:</b> Population distribution by level of education and occupation .....	48
<b>Table IV:</b> Population distribution according to personal and family obstetrical characteristics .....	49
<b>Table V:</b> Population distribution according to comorbidities and lifestyle .....	50
<b>Table VI:</b> Population distribution according to number of ANC's, gestational age at fist ANC and qualification of ANC provider .....	51
<b>Table VII:</b> Population distribution according to prophylactic measures during pregnancy ...	52
<b>Table VIII:</b> Population distribution according to pathologies during pregnancy .....	53
<b>Table IX:</b> Population distribution according to Bishop score.....	54
<b>Table X:</b> Population distribution according to route of delivery and maternal complications	55
<b>Table XI:</b> Population distribution according to the foetal complications at delivery .....	56
<b>Table XII:</b> Population distribution according to the neonatal characteristics at delivery.....	57
<b>Table XIII:</b> Population distribution according to the neonatal outcome .....	58

## LIST OF FIGURES

<b>Figure 1 :</b> The map shows the number of new malaria cases per 100,000 individuals across the world. The malaria incidence is highest in the central part of Africa north and south of the equator [17] .....	5
<b>Figure 2:</b> Distribution of pregnancies occurring in areas of <i>Plasmodium falciparum</i> and <i>Plasmodium vivax</i> malaria transmission in 2020 by WHO regions (proportion of global estimates) [18] .....	6
<b>Figure 3:</b> Anatomy of the uterus [22] .....	7
<b>Figure 4:</b> Fetus in utero [23] .....	8
<b>Figure 5 :</b> The figure above shows plasmodium life cycle [33] .....	12
<b>Figure 6 :</b> Placental malaria and implications [36] .....	14
<b>Figure 7:</b> Life cycle of plasmodium in pregnant woman [35] .....	15
<b>Figure 8:</b> Dilation of cervix during labor and delivery [48] .....	23
<b>Figure 9 :</b> Recruitment flow chart.....	46

## **LIST OF ABBREVIATIONS**

ACOG: American College of Obstetricians and Gynaecologists

ACT: Artemisinin-based Combination Therapy

ANC: Antenatal Care

BW: Birthweight

IOL: Induction of Labour

ITNs: Insecticide Treated Bed Nets

ITPp: Intermittent Preventive Treatment for Pregnancy

IUFD: Intrauterine Foetal Death

IUGR: Intrauterine Growth Retardation

NICU: Neonatal Intensive Care Unit

NRFS: Non-Reassuring Foetal Status

PM: Placental Malaria

LBW: Low Birthweight

WHO: World Health Organization

YCH: Yaounde Central Hospital

YGOPH: Yaounde Gynaecology, Obstetrics and Paediatrics Hospital

## **CHAPTER: 1 INTRODUCTION**

## 1.1. BACKGROUND

Malaria is a significant global health concern, particularly in regions where the disease is endemic. Pregnant women are particularly vulnerable to the adverse effects of malaria infection, with increased risks of maternal morbidity and adverse fetal outcomes [1, 2]. Globally in 2021, there were an estimated 247 million cases of malaria and specifically for the World Health Organisation (WHO) African Region, an estimated 234 million cases were recorded with 593000 deaths [3]. This region accounted for about 95% of cases and 96% of deaths globally [3]. In fact approximately 13.3 million of the 40 million pregnancies that year in that region were exposed to malaria [3]. In West Africa and in Central Africa the prevalence of malaria among pregnant women was 41% and 40% respectively in 2021, causing low birth weight in about 354000 neonates for both regions [3]. In Cameroon, precisely in the city of Yaounde the prevalence of malaria in pregnancy was 69.2% according to a recent study in 2022 [4]. Malaria is caused by parasites of the genus *plasmodium* [5]. There are various species, with *Plasmodium falciparum* being the most incriminated in Africa [6, 7]. Abnormal pregnancy outcome such as stillbirth, preterm delivery, low-birth weight neonates and anemia in pregnancy are usually associated with malaria [8]. The clinical presentation of malaria depends on the plasmodium specie involved [4, 9]. *Plasmodium falciparum*, usually attaches itself to placental villi thereby obstructing the placental blood flow [7]. Susceptibility of women to placental malaria (PM) is due to increased parasites sequestered in the placenta mediated by chondroitin sulfate A (CSA) binding to the trophoblast and pregnancy-associated suppression of inflammatory responses caused by hormonal changes [4,10]. In placental malaria, the infested red blood cells are sequestered in the intervillous space and attract mononuclear cells (mononuclear intervillous inflammatory infiltration). These cells secrete pro-inflammatory cytokines, especially tumor necrosis factor-alpha and interleukin-10. When these cytokines are released, blood flow is diminished hence there is decreased transfer of oxygen and nutrients to the fetus and conditions such as intrauterine growth restriction and intrauterine fetal demise may be observed [7, 9]. Most of these conditions occur and worsen during the third trimester especially during labor and if not properly managed have a huge impact on the pregnancy outcome which is the interest of our study.

## 1.2. RATIONALE

Malaria infection during pregnancy, particularly in the third trimester, can have detrimental effects on both the mother and the developing foetus [7]. The management of pregnant women with malaria during the third trimester poses a clinical challenge, necessitating careful

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consideration of the optimal delivery approach to minimize fetal risks [11]. Labor induction and spontaneous labor represent two distinct approaches to delivery, each with significant implications for the outcome of pregnancy in the context of malaria [12]. The impact of labor induction versus spontaneous labor on fetal outcomes in the context of malaria infection during the third trimester remains poorly understood. Existing studies have provided conflicting results, with some suggesting that labor induction may improve fetal outcomes by reducing the duration of exposure to the maternal infection while others have reported no significant differences in outcomes between the two approaches [13]. Thus there is a need for further research to elucidate the association between both methods and pregnancy outcome. Hence the interest of our study to compare the outcome in both situations in a bid to help clinicians in their quest to adopt a better approach.

### **1.3. RESEARCH QUESTION**

- What is the maternal and fetal outcome of pregnancy following induction of labor compared to expectant spontaneous labor for women treated for malaria at term?

### **1.4. RESEARCH HYPOTHESIS**

- Women who go into labor spontaneously after treatment for malaria at term may have a better pregnancy outcome compared to those whose labor is induced.

### **1.5. RESEARCH OBJECTIVES**

#### **1.5.1. General Objective**

- Assess the maternal and fetal outcome of pregnancy among women treated for malaria at term following immediate induction compared to expectant spontaneous labor.

#### **1.5.2. Specific Objectives**

1. Describe the socio-demographic and clinical profile of pregnant women diagnosed and treated for malaria at term.
2. Determine the maternal and fetal outcome following induction of labour or spontaneous labour among these women at term.
3. Compare the outcome of pregnancy in the two approaches following treatment of malaria at term.

## **CHAPTER 2: LITERATURE REVIEW**

## **2.1. INTRODUCTION**

### **2.1.1. Definition of Operational Terms**

- Stillbirth; this is the delivery of a death fetus at or after the 22<sup>nd</sup> completed week of pregnancy or with a weight greater than 1000g.
- Low birth weight: A weight at birth of a neonate less than 2,500 grams but greater than 1500 grams
- Preterm birth is defined by WHO as all births before 37 completed weeks of gestation
- Antenatal care (ANC) can be defined as the care provided by trained health-care professionals to pregnant women in order to ensure the best health conditions for both mother and baby during pregnancy.
- Primiparous: a woman's 1st delivery
- Multiparous: a woman with prior deliveries
- Labor: Labor is defined as regular uterine contractions that cause cervical dilation and effacement, leading to delivery of the fetus and the products of conception.
- Intrauterine growth retardation: this is defined as a rate of fetal growth that is less than normal for the growth potential of a fetus for that particular gestational age.
- Paroxysm: a sudden attack or increase in intensity of a symptom usually occurring in intervals.

### **2.1.2 Epidemiology**

Malaria is a mosquito borne disease of humans caused by parasitic protozoans of the genus plasmodium and the most dangerous specie is plasmodium falciparum which is responsible for most cases of malaria in Africa. It is an immense public health concern especially in pregnancy where there is a tendency towards increased severity of the disease caused by the transient depression of immunity that occurs during pregnancy.

Malaria is one of the killer diseases worldwide. Malaria is one of the most severe public health problems worldwide. It is a leading cause of death and disease in many developing countries, where young children and pregnant women are the groups most affected [14]. According to the 2021 World Malaria Report, nearly half the world's population lives in areas at risk of malaria transmission in 87 countries and territories. In 2020, malaria caused an estimated 241 million clinical episodes, and 627,000 deaths [15]. An estimated 95% of deaths in 2020 were in the WHO

African Region [15]. On average, 60%-70% of malaria cases have been due to *P. falciparum*, with the remainder caused by *P. vivax*. *Anopheles gambiae* is the main malaria vector [16]

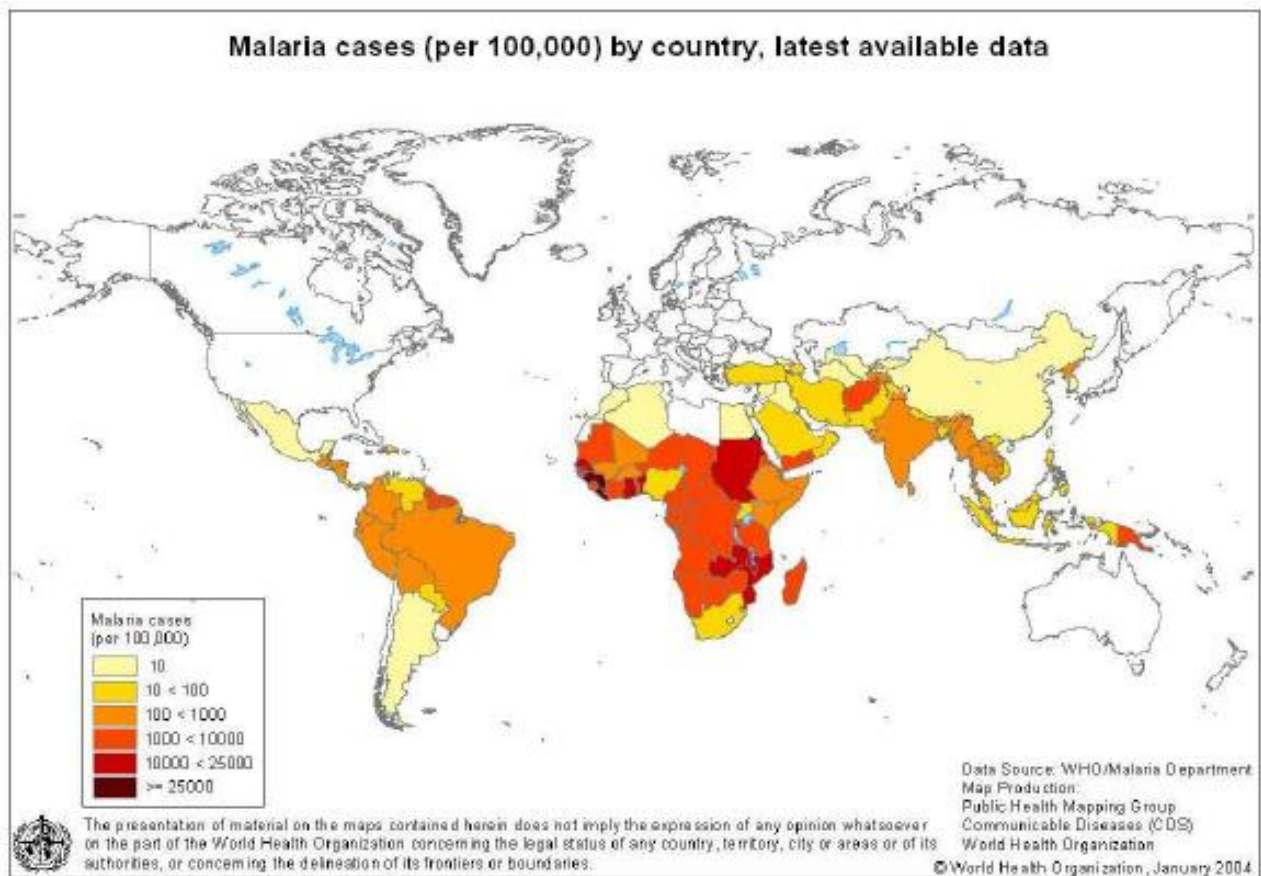


Figure 1 : The map shows the number of new malaria cases per 100,000 individuals across the world. The malaria incidence is highest in the central part of Africa north and south of the equator [17]

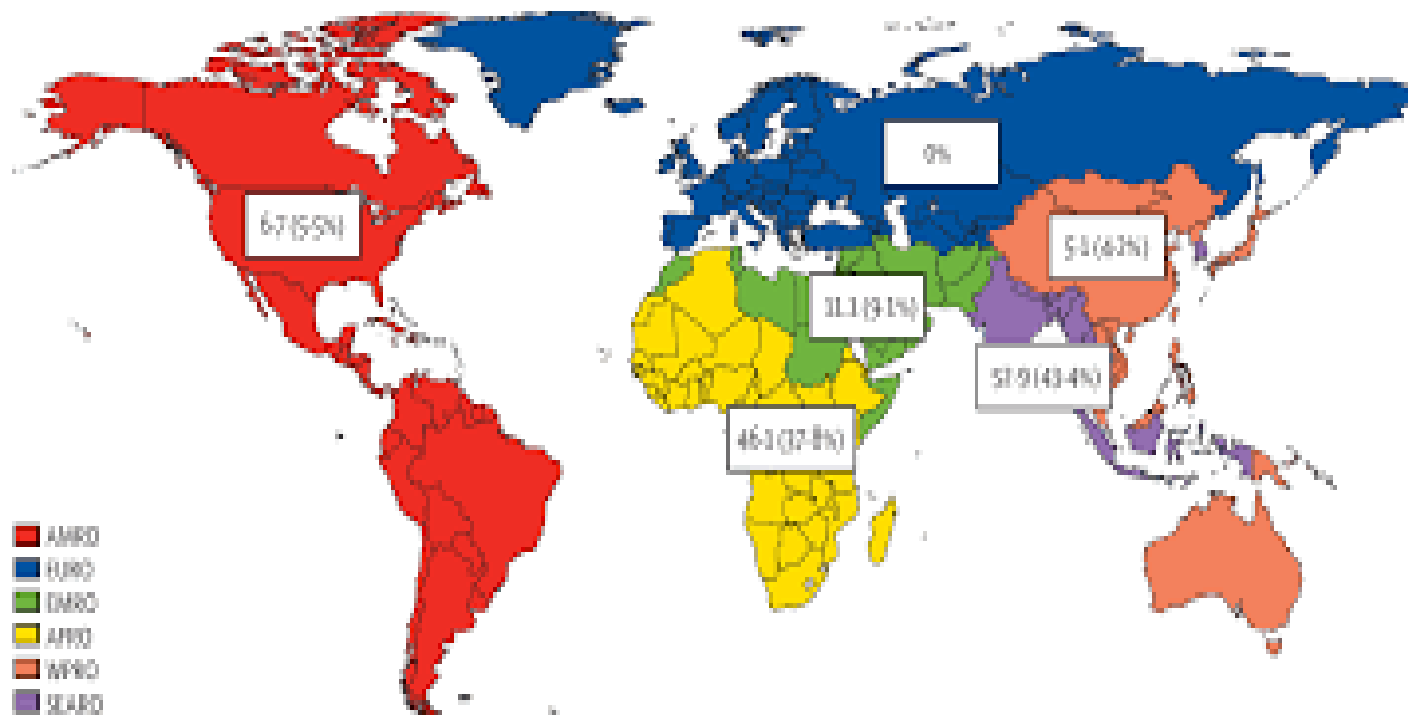


Figure 2: Distribution of pregnancies occurring in areas of *Plasmodium falciparum* and *Plasmodium vivax* malaria transmission in 2020 by WHO regions (proportion of global estimates) [18]

## 2.2. RECALL

### 2.2.1. Anatomy

#### The Uterus

The non-gravid uterus is situated in the pelvic cavity between the bladder anteriorly and the rectum posteriorly [19]. The uterus is pear shaped and consists of two major but unequal parts. The lower portion of this peritoneum forms the anterior boundary of the rectouterine cul-de-sac, or pouch of Douglas. Only the upper portion of the anterior wall of the uterus is so covered. The peritoneum in this area reflects forward onto the bladder dome to create the vesicouterine pouch. The lower portion of the anterior uterine wall is united to the posterior wall of the bladder by a well-defined loose connective tissue layer—the vesicouterine space. There is an upper triangular portion—the body or corpus, and a lower, cylindrical portion—the cervix, which projects into the vagina [20]. The isthmus is the union site of these two. It is of special obstetrical significance because it forms the lower uterine segment during pregnancy. The null gravid uterus measures 6 to 8 cm in length compared with 9 to 10 cm in multiparous women. The uterus averages 60 g and typically weighs more in parous women. In null gravidae, the fundus and cervix are approximately equal in length, but in multiparas, the cervix is only a little more than a third of the total length [21]

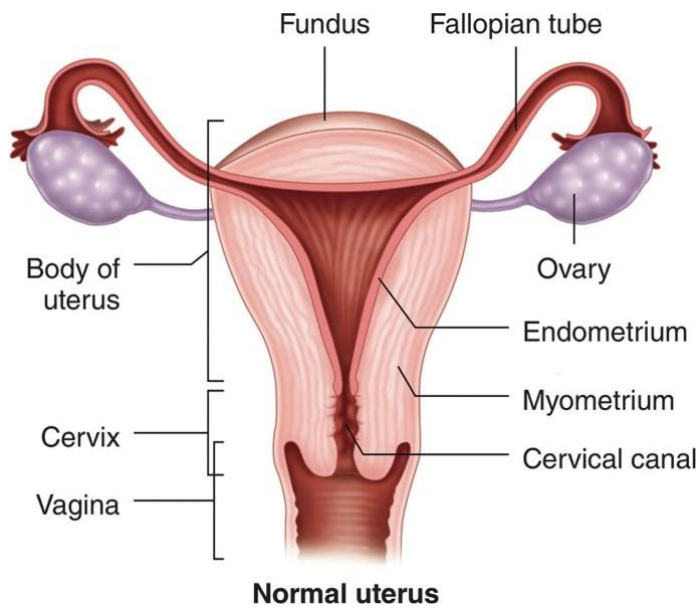


Figure 3: Anatomy of the uterus [22]

Pregnancy stimulates remarkable uterine growth due to muscle hypertrophy. The uterine fundus, a previously flattened convexity between tubal insertions, now becomes dome shaped. Moreover, the round ligaments appear to insert at the junction of the middle and upper thirds of the organ. The fallopian tubes elongate, but the ovaries appear unchanged [21]

The wall of the uterus is very thick and consists of 3 layers: serous, muscular, and mucous. The serous layer (perimetrium) is simply the peritoneal covering. It is thin and firmly adherent over the fundus and most of the body, and then thickens posteriorly and becomes separated from the muscle by the parametrium. The muscular layer (myometrium) is extremely thick at about 1.5–2.5 cm and continuous with that of the tubes and vagina. It also extends into the ovarian and round ligaments, into the cardinal ligaments at the cervix, and minimally into the uterosacral ligaments. Two principal layers of the muscular coat can be distinguished: (1) the outer layer, which is weaker and composed of longitudinal fibers; and (2) a stronger inner layer, the fibers

Of which are interlaced and run in various directions, having intermingled within them large venous plexuses. The muscle layer hypertrophies with the internal os to form a sphincter. The mucous layer (endometrium) is soft and spongy, composed of tissue resembling embryonic connective tissue. The surface consists of a single layer of ciliated columnar epithelium. The tissue is rather delicate and friable and contains many tubular glands that open into the cavity of the uterus [9]

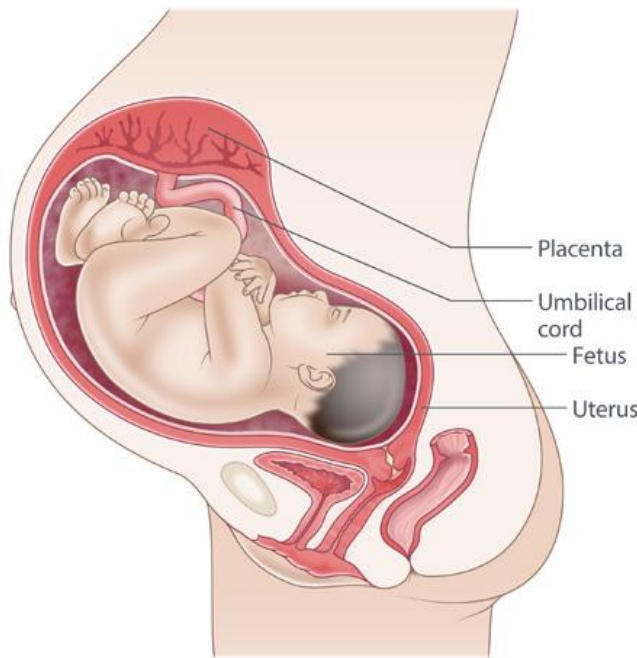


Figure 4: Fetus in utero [23]

### 2.2.2. Physiology

#### Normal Pregnancy

Pregnancy or gestation, is the physiologic process of a developing fetus within the maternal body. For obstetric purposes, the gestational age or menstrual age is the time elapsed since the first day of the last normal menstrual period (LNMP), which actually precedes the time of oocyte fertilization. The gestational age is expressed in completed weeks. The start of the gestation (based on the LNMP) is usually 2 weeks before ovulation, assuming a 28-day regular menstrual cycle. The developmental or fetal age is the age of the conception calculated from the time of implantation, which is 4 to 6 days after ovulation is completed. The menstrual gestational age of pregnancy is calculated at 280 days or 40 completed weeks. The estimated due date (EDD) may be estimated by adding 7 days to the first day of the last menstrual period and subtracting 3 months plus 1 year (Naegel's rule) [9]

Diagnosis of pregnancy is made on the basis of amenorrhea and a positive pregnancy test, added to these, are a multitude of signs and symptoms which further suggest the onset of pregnancy. Some of these signs and symptoms are;

- Amenorrhea; cessation of menses caused by hormones produced by the corpus luteum.
- Nausea and vomiting; these begin as early as the 2<sup>nd</sup> week of gestation and usually resolves between the 13<sup>th</sup> and 16<sup>th</sup> week of gestation. Hyperemesis gravidarum is an extreme form of

nausea and vomiting and is characterized by dehydration, weight loss (up to 5%), and ketonuria. This can sometimes lead to the loss of pregnancy.

- Breast changes like breast pain (mastodynia), breast engorgement and secretion of colostrum.
- Fetal movement; the initial perception of fetal movements occurs around the 18-20<sup>th</sup> week of gestation in primiparous women and as early as 14 weeks 'gestation in multiparous women. This sign will be one of the most important in our study.
- Other changes include abdominal enlargement, Braxton Hick's contractions, linea nigra, and striae gravidarum.

### **Diagnostic methods include;**

1) Pregnancy test; Sensitive, early pregnancy tests measure changes in the level of human chorionic gonadotropin (HCG). The  $\beta$  subunit of hCG is produced by the syncytiotrophoblast 8 days after fertilization and may be detected in the maternal serum 8-11 days after conception or as early as 21-22 days after the LNMP. B-hCG levels peak at 10-12 weeks' gestation and decrease afterward. Generally, serum and urine levels return to normal ( $<5\text{mIU/mL}$ ), 21-24 days after delivery or after a fetal loss [9]

2) Imaging studies; Ultrasound is one of the most useful technical aids in diagnosing and monitoring pregnancy. Cardiac activity is discernible at 5-6 weeks via transvaginal ultrasound. At the end of the embryonic period (10 weeks by LNMP), the embryo has a human appearance. The gestational age can be determined by the crown rump length between 6 and 13 weeks' gestation, with a margin of error of approximately 8% or 3-5 days [9]

3) Fetal Heart Tones; they are detectable by handheld Doppler (after 10 weeks' gestation) or by fetoscope (after 18-20 weeks' gestation). The normal heart rate is 110-160 beats per minute [9]

Uterine size/fetal palpation; uterine size can be used to diagnose pregnancy secondary to uterine enlargement. Later in pregnancy, the fetus can be palpated through the maternal abdominal wall (after 22 weeks), and the position can be determined by Leopold's manoeuvres [9]

### **Antenatal Care/Consultations**

According to the WHO, antenatal care (ANC) can be defined as the care provided by skilled health-care professionals to pregnant women and adolescent girls in order to ensure the best health conditions for both mother and baby during pregnancy. The components of ANC include: risk



identification; prevention and management of pregnancy-related or concurrent diseases; and health education and health promotion. ANC reduces maternal and perinatal morbidity and mortality both directly, through detection and treatment of pregnancy-related complications, and indirectly, through the identification of women and girls at increased risk of developing complications during labour and delivery, thus ensuring referral to an appropriate level of care [24]

### **2.3. AT RISK PREGNANCY**

At-risk pregnancy can be broadly defined as one in which the mother, foetus or new-born is or may possibly be at increased risk of morbidity or mortality before, during or after delivery. Some of the common disorders that complicate pregnancies are:

- Hyperemesis gravidarum
- Haemorrhagic disorders
- Hypertensive disorders in pregnancy
- Infections
- Gestational diabetes
- Foetal growth disorders
- Intrauterine foetal deaths
- Premature rupture of membranes
- Preterm labour

In this section, we will focus on infections in pregnancy precisely malaria.

### **2.4. MALARIA IN PREGNANCY**

#### **2.4.1. General Overview**

Malaria is a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female anopheles mosquitoes [25]. There are many species of the anopheles mosquitoes but few such as *anopheles arabiensis*, *anopheles gambiae* [26] (commonly called the African malaria mosquito), and *anopheles coluzzi* and *anopheles funestus* are classified as primary vectors for the malaria parasites [27]. Five species of the protozoan genus plasmodium usually infect humans: *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, *Plasmodium ovale*, *Plasmodium knowlesi*. *P.falciparum* and *P.vivax* and account for the vast majority of cases [26]. *P. falciparum* causes the most severe disease and is the most common specie in the African region

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[28]. Malaria infection during pregnancy has substantial risks for the pregnant woman, her fetus and the newborn child [29]. For the pregnant woman, malaria infection can lead to severe disease and death, and placental sequestration of the parasite, which can lead to maternal anaemia; it also puts the mother at increased risk of death before and after childbirth, and is an important contributor to stillbirth and preterm birth [3]. In June 2022, WHO published consolidated guidelines for malaria that contained a package of new and updated recommendations across a number of technical areas – from case management, vector control, vaccines, malaria chemoprevention and mass drug administration (MDA) to elimination [3].

#### **2.4.2. Pathophysiology**

The life cycle of the malaria parasite consists of human liver, human blood, and mosquito stages [30]. Malaria infection begins with the bite of the mosquito carrying the malaria parasite. During the bite, the infective mosquito injects the malaria parasite into the human host. After initially replicating in the liver, the parasites are released into the bloodstream. During the blood stage, parasites multiply in red blood cells, sometimes causing fever and other symptoms characteristic of malaria. Some of these parasites become a form which is infectious to mosquitoes. When the infected person is bitten again, the mosquito ingests blood containing the parasites, which then restarts the transmission cycle [31].

The malaria parasite life cycle involves 2 hosts. During a blood meal, a malaria-infected female *Anopheles* mosquito inoculates sporozoites into the human host. Sporozoites infect liver cells. There, the sporozoites mature into schizonts. The schizonts rupture and release merozoites. This initial replication in the liver is called the exoerythrocytic cycle.

Merozoites infect RBCs. There, the parasite multiplies asexually (called the erythrocytic cycle). The merozoites develop into ring-stage trophozoites. Some then mature into schizonts. The schizonts rupture, releasing merozoites. Some trophozoites differentiate into gametocytes. During a blood meal, an *Anopheles* mosquito ingests the male (microgametocytes) and female (macrogametocytes) gametocytes, beginning the sporogonic cycle. In the mosquito's stomach, the microgametes penetrate the macrogametes, producing zygotes. The zygotes become motile and elongated, developing into ookinetes. The ookinetes invade the midgut wall of the mosquito where they develop into oocysts. The oocysts grow, rupture, and release sporozoites, which travel to the mosquito's salivary glands. Inoculation of the sporozoites into a new human host perpetuates the malaria life cycle [32].

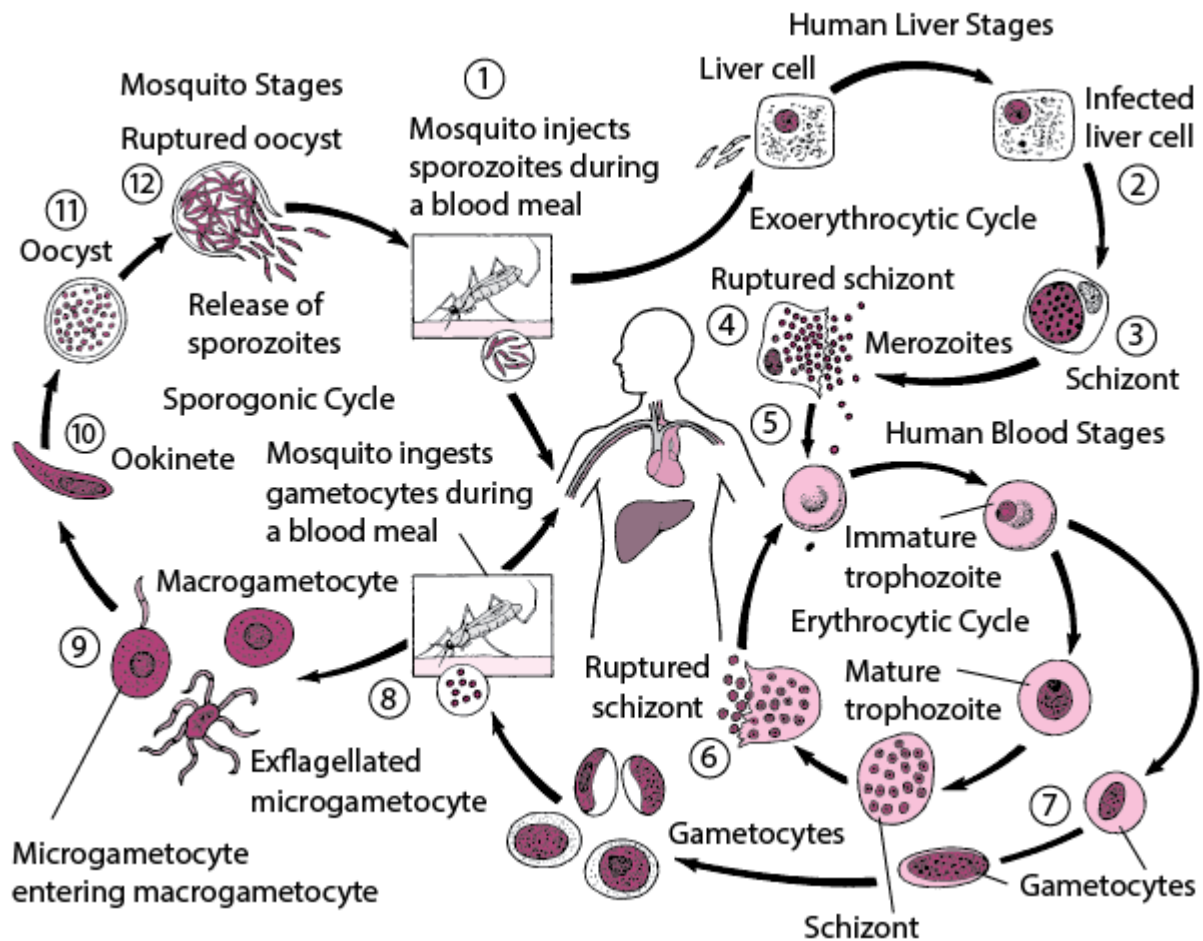


Figure 5 : the figure above shows plasmodium life cycle [33]

### The Case in Pregnancy

The general immune suppression during pregnancy makes women more susceptible to many infections, including malarial infection especially during first trimester. During pregnancy, cell-mediated immune response is very low that is required to sustain the placenta, a new organ in first pregnancy. However, low cell-mediated immune response in placenta makes it preferred site for the parasite to hide from host immune responses. Placenta, which is the interface between mother and fetus, plays an important role in good pregnancy outcome and fetal development that is intricately dependent on the placenta. There are certain pathophysiological processes that occur in the placenta due to malarial infection especially due to *P.falciparum*, making the placenta the preferred site of sequestration and development of malaria parasite in pregnancy.

## Placental Malaria

Malarial infection in placenta is characterized by sequestration of *Plasmodium falciparum*-infected erythrocytes and infiltration of immune cells within the intervillous spaces of the placenta. The placenta turns black due to deposition of the malarial pigment. The parasite densities are much higher in the placenta compared to peripheral blood. The thickening of placental basement membrane, perivillous fibrinoid deposits, and syncytial knotting results into altered exchange system between mother and fetus. The placental insufficiency to provide nutrients to the fetus causes intra-uterine growth retardation (IUGR) [34]. The enhanced susceptibility to infections during pregnancy results into high parasitemia and heavy infiltration of parasite-infected RBCs (iRBC) in placental vasculature, a privilege site where the parasite can avoid maternal immune response. The altered physiology and immunity during pregnancy and ability of *P. falciparum*-infected erythrocytes to sequester to various organs are all together responsible for severe malaria in pregnant women especially in first pregnancy and associated IUGR and LBWs in infants.

Elevated levels of pro-inflammatory cytokines, such as IFN- $\gamma$ , IL-2, and TNF- $\alpha$  in reaction to iRBC in the placenta of malaria-infected women especially in primigravidae account for the observed placental pathology and adverse pregnancy outcomes. The levels of chemokines have been observed elevated in the placental intervillous spaces, which correlate with increased monocyte density, parasite density, and malaria pigments in the placenta. Maternal macrophages are the predominant source of chemokines in the placenta, but fetus cells can also contribute. The chemokines help to recruit macrophages, cytotoxic T cells, B cells, and granulocytes in the placenta and contribute to the pathologies of placental malaria [35]. There is excessive sequestration of iRBC and leukocytes in the intervillous spaces of placenta and formation of perivillous fibrin clot during malarial infection, which interfere blood flow across the placenta thus, nutrients to the fetus. Placental pathology in malaria is caused by expression of unique *Plasmodium falciparum* erythrocyte membrane protein (Pf EMP) on iRBC which helps the parasite to sequester into the placenta. Pf EMP 1, 2 and 3 are part of a group of receptors that have been observed on the surface of plasmodium falciparum infected erythrocytes that play a major role in sequestration [5]. Women, who have malaria during pregnancy, develop Pf EMP1-specific antibodies and these antibodies protect women from malaria in subsequent pregnancies. The more complications of placental malaria in primigravidae are due to the absence of this placental parasite-specific immunity [36]

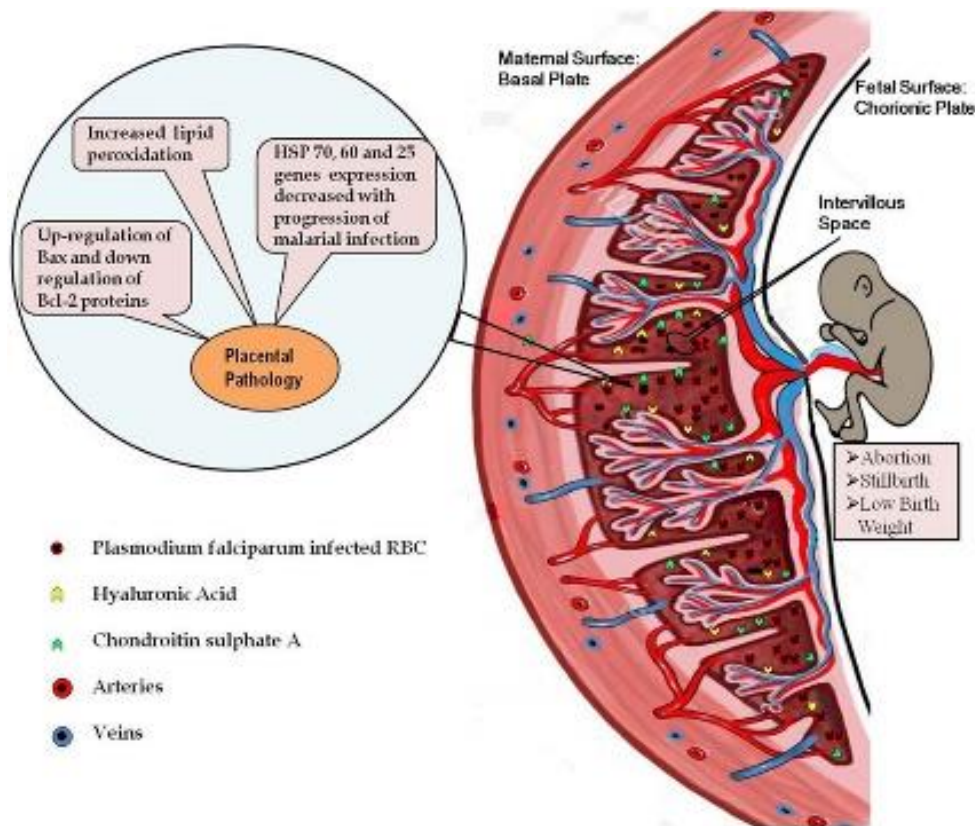


Figure 6 : placental malaria and implications [36]

Diagrammatic representation of the placental malaria and implications. Malarial infection during pregnancy results into infiltration of the parasite-infected RBCs to the intervillous space of placenta resulting into exacerbated inflammatory response. High inflammation causes oxidative stress-induced apoptotic cell death in the placenta. Decreased expressions of the heat shock protein genes (HSP 70, 60, 25) in the infected placenta further contribute to the placental pathology. All these pathological alterations in the placenta contribute to the poor pregnancy outcomes associated with malarial infection [36]



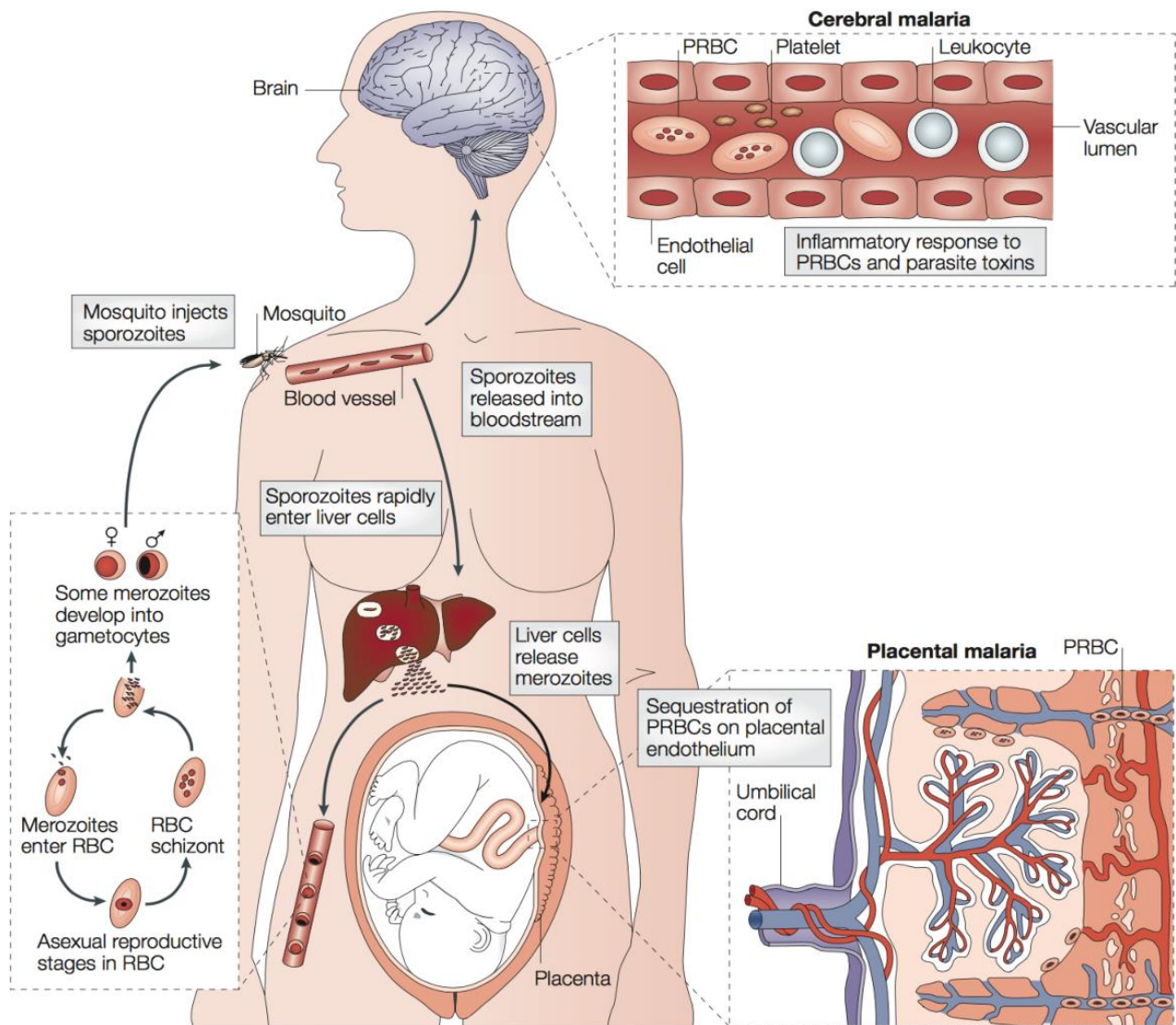


Figure 7: life cycle of plasmodium in pregnant woman [35]

### 2.4.3. Clinical Signs and Symptoms

The incubation period is usually

- 12 to 17 days for *P. vivax*
- 9 to 14 days for *P. falciparum*
- 16 to 18 days or longer for *P. ovale*
- About 1 month (18 to 40 days) or longer (years) for *P. malariae*

However, some strains of *P. vivax* in temperate climates may not cause clinical illness for months to > 1 year after infection [32]

Fever and rigors-the malaria paroxysm. Malarial paroxysm is caused by hemolysis of infected RBCs, released merozoites and other malaria antigens, and the inflammatory response they elicit. The classic paroxysm starts with malaise, abrupt chills and fever rising to 39 to 41° C, rapid and thready pulse, polyuria, headache, myalgia, and nausea. After 2 to 6 hours, fever falls, and profuse sweating occurs for 2 to 3 hours, followed by extreme fatigue. Fever is often hectic at the start of infection. In established infections, malarial paroxysms typically occur every 2 to 3 days depending on the species. Splenomegaly usually becomes palpable by the end of the first week of clinical disease but may not occur with *P. falciparum*. The enlarged spleen is soft and prone to traumatic rupture. Splenomegaly may decrease with recurrent attacks of malaria as functional immunity develops. After many bouts, the spleen may become fibrotic and firm or, in some patients, becomes massively enlarged (tropical splenomegaly) Hepatomegaly usually accompanies splenomegaly [37] In the case of severe malaria, there is an already established criteria of severity for malaria enumerated below

-Impaired consciousness: A Glasgow coma score < 11 in adults or a Blantyre coma score < 3 in children

- Prostration: Generalized weakness so that the person is unable to sit, stand or walk without assistance
- Multiple convulsions: More than two episodes within 24 h
- Acidosis: A base deficit of > 8 mEq/L or, if not available, a plasma bicarbonate level of < 15 mmol/L or venous plasma lactate  $\geq$  5 mmol/L. Severe acidosis manifests clinically as respiratory distress (rapid, deep, laboured breathing).
- Hypoglycemia: Blood or plasma glucose < 2.2 mmol/L (< 40 mg/dL)
- Severe malarial anaemia: Haemoglobin concentration  $\leq$  5 g/dL or a haematocrit of  $\leq$  15% in children < 12 years of age (< 7 g/dL and < 20%, respectively, in adults) with a parasite count > 100 000/ $\mu$ L
- Renal impairment: Plasma or serum creatinine > 265  $\mu$ mol/L (3 mg/dL) or blood urea > 20 mmol/L
- Jaundice: Plasma or serum bilirubin > 50  $\mu$ mol/L (3 mg/dL) with a parasite count > 100 000/  $\mu$ L
- Pulmonary oedema: Radiologically confirmed or oxygen saturation < 92% on room air with a respiratory rate > 30/min, often with chest indrawing and crepitations on auscultation

- Significant bleeding: Including recurrent or prolonged bleeding from the nose, gums or venepuncture sites; haematemesis or melena
- Shock: Compensated shock is defined as capillary refill  $\geq 3$  s or temperature gradient on leg (mid to proximal limb), but no hypotension. Decompensated shock is defined as systolic blood pressure  $< 70$  mm Hg in children or  $< 80$  mmHg in adults, with evidence of impaired perfusion (cool peripheries or prolonged capillary refill).
- Hyperparasitaemia: *P. falciparum* parasitaemia  $> 10\%$

#### Effects of Malaria on Pregnancy

- In the first trimester, increased risk of abortion
- Anemia in mother and baby
- Prematurity( babies born before 37 weeks of gestation)
- Intra-uterine growth retardation
- Low birth weight
- Congenital malaria(rare)
- Maternal and neonatal mortality

#### 2.4.4. Diagnosis of Malaria

Primarily in addition to clinical presentation, accurate and early diagnosis is critical for successful management [38]

Light microscopy of blood (thin and thick smears). Definitive diagnosis of malaria generally requires direct observation of malaria parasites in Giemsa-stained thick and thin blood smears. Thick blood smears are more difficult to interpret than thin blood smears but they are much more sensitive, as more blood is examined. Thick smears are more sensitive but more difficult to prepare and interpret as the RBCs are lysed before staining. Thin blood smears, in which parasites are seen within erythrocytes, are used to determine the species of the infecting parasite. The presence of diagnostic forms can vary markedly with the stage of the life cycle, especially early in disease [32, 37].

Rapid diagnostic tests that detect Plasmodium antigens or enzymes in blood [39]. Commercial rapid diagnostic tests for malaria are based on the presence of certain plasmodium antigens or enzymatic [32, 38] Assays may involve detection of a histidine-rich protein 2 (HRP-2) associated with malaria



parasites (especially *P. falciparum*) and detection of plasmodium-associated lactate dehydrogenase (pLDH). The rapid diagnostic tests are generally comparable in sensitivity to microscopy in detecting low levels of parasitemia, but they do not differentiate single infection from concurrent infection with more than one *Plasmodium* species or allow speciation except for *P. falciparum*.

Light microscopy and rapid diagnostic tests are complementary, and both should be done when available [38]. They have similar sensitivity. Negative results even in both does not exclude malaria in a patient with low parasitemia.

Polymerase chain reaction and species-specific DNA probes can be used but are not widely available at the point of care. They can help identify the infecting *Plasmodium* species after malaria is diagnosed. Because serologic tests may reflect prior exposure, they are not useful in the diagnosis of acute malaria [32]

#### **2.4.5. Management of Malaria**

Management of malaria in pregnancy involves the following three aspects

- Treatment of malaria
- Management of complications
- Management of labor

#### **Treatment of Malaria**

The artemisinin-based combination therapies are the currently recommended drugs for malaria endemic countries [38]. ACT is a combination of a rapidly acting artemisinin derivative with a longer-acting (more slowly eliminated) partner drug. The artemisinin component rapidly clears parasites from the blood (reducing parasite numbers by a factor of approximately 10 000 in each 48 h asexual cycle) and is also active against the sexual stages of the gametocytes that mediate onward transmission to mosquitos. The longer- acting partner drug clears the remaining parasites and provides protection against development of resistance to the artemisinin derivative. Partner drugs with longer elimination half-lives also provide a period of post-treatment prophylaxis.

The WHO-approved first-line ACT options are: artemether + lumefantrine, artesunate + amodiaquine, artesunate + mefloquine, dihydroartemisinin + piperaquine and artesunate + sulfadoxine–pyrimethamine. The ACTs are generally highly effective and well tolerated. This has contributed substantially to reduction in global morbidity and mortality from malaria [40]. In deciding which ACTs to adopt in national treatment policies, national policy- makers should take

into account: the pattern of resistance to antimalarial drugs in the country, the relative efficacy and safety of the combinations, their cost, the availability of pediatric formulations and the availability of co-formulated products [41].

Cameroon is one of the malaria endemic countries with established guidelines for the management of malaria as per WHO recommendations. Malaria in pregnancy is considered as severe malaria and each trimester is approached differently.

#### -First trimester

Treatment with quinine without a loading dose

Quinine bases: 8.3mg/kg of quinine bases in 4hrs infusion, every 8hrs. Relay is made with oral treatment as soon as the patient can swallow. The oral dose is 8.3mg/kg of quinine bases every 8hrs until the 7<sup>th</sup> day of treatment, starting from the beginning of the treatment. Max dose; 1,5g of quinine base per day.

#### -Second and third trimester

1<sup>st</sup> line; treatment with injectable artesunate. Dosage; 2.4mg/kg at 0, 12 and 24 hour mark followed by one administration every 24hrs until the patient is able to take oral treatment. For artesunate administration IV is preferred over IM route.

2<sup>nd</sup> line; the regimen with quinine used above in the first trimester.

Whatever regimen used, continue with oral quinine as soon as the lady can swallow. This should be at a dose of 8.3mg/kg of quinine base every 8hrs for a total of 7days from onset of treatment, otherwise administer ACTs for example Arthemether-Lumenfantrine (AL) for 3 days as from the second trimester of pregnancy. The recommended dosage regimen for AL: it is given twice a day for 3 days (total of 6 doses). First two doses should be given ideally 8h apart.

#### -Management of Complications

Severe malaria is associated with a variety of manifestations which have to be recognized and managed promptly as followed [41]

- Coma: maintain airway, place patient on his or her side, exclude other treatable causes of coma (e.g. hypoglycemia, bacterial meningitis); avoid harmful ancillary treatments, intubate if necessary.
- Hyperpyrexia: administer tepid sponging, fanning, a cooling blanket and paracetamol.
- Convulsions: maintain airways; treat promptly with intravenous or rectal diazepam, lorazepam, midazolam or intramuscular paraldehyde. Check blood glucose.

- Hypoglycemia: check blood glucose, correct hypoglycemia and maintain with glucose containing infusion. Although hypoglycemia is defined as glucose < 2.2 mmol/L, the threshold for intervention is < 3 mmol/L for children < 5 years and <2.2 mmol/L for older children and adults.
- Severe anaemia: transfuse with screened fresh whole blood.
- Acute pulmonary oedema: Prop patient up at an angle of 45 degrees, give oxygen, give a diuretic, stop intravenous fluids, intubate and add positive end expiratory pressure or continuous positive airway pressure in life-threatening hypoxemia.
- Acute kidney injury: exclude pre-renal causes, check fluid balance and urinary sodium; if in established renal failure, add hemofiltration or hemodialysis, or, if not available, peritoneal dialysis.
- Spontaneous bleeding and coagulopathy: transfuse with screened fresh whole blood (cryoprecipitate, fresh frozen plasma and platelets, if available); give vitamin K injection.
- Metabolic acidosis: exclude or treat hypoglycemia, hypovolemia and septicemia. If severe, add hemofiltration or hemodialysis
- Shock: suspect septicemia, take blood for cultures; give parenteral broad- spectrum antimicrobials, correct hemodynamic disturbances.

Not forgetting fluid therapy and fluid requirements should be assessed individually whether it be children or adults [41]

#### Prevention of Malaria

- Use of insecticide treated nets [27] and indoor residual spraying at home.
- Also the use of intermittent preventive treatment of malaria in pregnancy which is the treatment course of an antimalarial medicine at predetermined intervals, regardless of whether the pregnant woman is infected with malaria or not.

Sulfadoxine-pyrimethamine is widely used for malaria chemoprevention during pregnancy and should be started early in the 2<sup>nd</sup> trimester not before week 13 of gestation due to an increased risk of fetal malformation. Doses should be given at least one month apart at each ANC with the objective of ensuring at least three doses received.

#### -Management of Labour

The delivery approach in this women especially at term is a pertinent aspect of management for the outcome of the pregnancy [42]. Due to the potential risks of developing certain complications in these women with high-risk pregnancies, adequate obstetric interventions are carried out to

minimize this risk and ensure a safe delivery process [9]. One of such is labour induction which is usually recommended when the maternal and perinatal risks of continuing pregnancy outweigh those associated with expedited birth [43]. This intervention is equally associated with other significant complications such as uterine rupture and because of that, expectant management is also considered for these women that is allowing them to go into labor spontaneously. In both situations, childbirth is a risky event for both mother and fetus [44].

## **2.5. INDUCTION OF LABOUR**

### **2.5.1. General Overview**

Induction of labour (IOL) describes the artificial stimulation of adequate uterine contractions (after fetal viability) prior to spontaneous or natural labor initiation with the prime objective of achieving vaginal childbirth [12, 21]. Labor induction is a common and very useful intervention in contemporary obstetrics constituting about 25% of childbirths at term in developed countries, compared to approximately 4% and 12% in Africa and Asia respectively [45]. According to the World Health Organization (WHO) survey, about 9.6% of the deliveries involved labor induction. The proportion is higher in technologically advanced countries. In developed countries, induction of labor currently accounts for around one-quarter of all deliveries at term [44]. In the United States, the incidence of labor induction rose from 9.5 percent in 1991 to 27 percent in 2019 [21]. The main advantage of induction of labor lies in the facilitation of vaginal birth and avoidance of caesarean section (CS) with optimization of both maternal and fetal outcomes in carefully selected expectant mothers [12]. Generally, induction of labour may be associated with pertinent maternal and perinatal risks [44]. Therefore, the decision to prescribe the procedure to any pregnant woman must be based on accurate clinical evidence and the expected benefits should outweigh the potential harms associated with the intervention [12, 45].

### **2.5.2. Indications**

Maternal: Pre-eclampsia, eclampsia, premature rupture of membranes, oligohydramnios, post term pregnancies, abruptio placentae, chorio amnionitis, diabetes mellitus, heart diseases, kidney diseases, sickle cell disease

Fetal: intrauterine growth retardation, stillbirth, intrauterine fetal death [46].

### **2.5.3. Contraindications**

Any contraindication to vaginal delivery first of all whether it be maternal or fetal.

Maternal: contracted pelvis, cephalopelvic disproportion, vasa previa, placenta previa, cervical cancer, active genital herpes simplex virus and human papilloma virus.

Fetal: malpresentation, non-reassuring fetal status. Then specific for induction: uterine scar, grand multipara

#### **2.5.4. Criteria of Induction**

##### **Bishop's Score**

The Bishop scoring system is based on a digital cervical exam of a patient with a zero point minimum and 13 point maximum. The scoring system utilizes cervical dilation, position, effacement, consistency of the cervix, and fetal station [47].

- Cervical dilation is the measure of how dilated the cervix is in centimeters. This is performed by estimating the average diameter of the open cervix.
- Effacement is the thinning or shortening of the cervix expressed as a percentage of the whole cervix. Zero percent effacement means the cervix is a normal, pre-labor length. Fifty percent effaced means the cervix is at half of the expected length. If the cervix is 100% effaced, it is paper thin.
- The station is the position of the fetal head relative to the ischial spines of the maternal pelvis. The ischial spines are halfway between the pelvic inlet and outlet. At zero station, the fetal head is at the level of the ischial spines. Above and below this level are divided into thirds, by which station is denoted with negative numbers above and positive numbers below the zero station. As a fetal head makes its descent, the station changes from -3, -2, -1, 0, +1, +2, and 3.
- Position refers to the position of the cervix relative to the fetal head and maternal pelvis.
- The consistency of the cervix refers to the feel of the cervix on the exam. A firm cervix has a consistency similar to the tip of the nose, while a soft cervix has a consistency similar to the lips of the oral cavity.

A Bishop score of 8 or greater is considered to be favorable for induction, or the chance of a vaginal delivery with induction is similar to spontaneous labor. A score of 6 or less is considered to be unfavorable if an induction is indicated cervical ripening agents may be utilized [47]

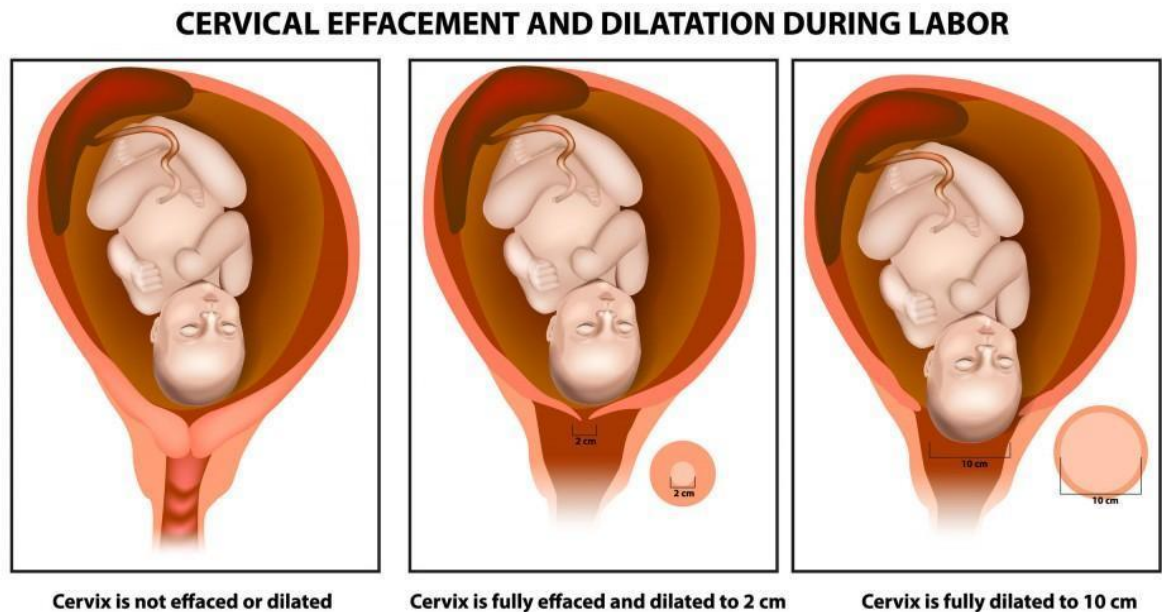


Figure 8: Dilation of cervix during labour and delivery [48]

**Table I:** showing the Bishop's Score [47]

Score	0	1	2	3
Dilatation	0	1-2	3-4	>4
Effacement	0-30%	40-50%	60-70%	>80%
Station	-3	-2	-1/0	+1, +2, +3
Consistency	Firm	Medium	Soft	-
Position	Posterior	Middle	Anterior	-

### 2.5.5. Methods of Induction

The various methods of induction are divided into,

- Mechanical: catheters and luminaria tents
- Pharmacological; oxytocin and prostaglandins
- Physical: amniotomy, membrane stripping
- Pharmacological methods
  - -Oxytocin: Oxytocin is a hormone that is produced naturally by the body, and which has a range of functions, including the stimulation of uterine contractions in the second and third stages of labor [21]. Oxytocin analogues, administered intravenously, are the commonest

induction agents used worldwide. Oxytocin is frequently administered when the cervix is dilated (or favorable) and may be combined with artificial rupture of the amniotic membranes [49]

- -Prostaglandins: Prostaglandins are hormones produced naturally by the body that are important in the onset of labor. Prostaglandins promote cervical ripening and encourage the onset of labour by acting on cervical collagen so as to encourage the cervix to soften and stretch in preparation for childbirth [49]. Prostaglandins may also stimulate uterine contractions. There are various prostaglandins preparations available for induction such as prostaglandin F<sub>2</sub> alpha (PGF<sub>2</sub>α, dinoprost), prostaglandin E<sub>2</sub> (PGE<sub>2</sub>), prostaglandin E (PGE<sub>1</sub>) and misoprostol (a synthetic analogue of PGE<sub>1</sub>).
- Physical Methods
  - Membrane sweeping; Membrane sweeping involves the clinician detaching the membranes from the lower uterine segment by a circular movement of the examining finger. Membrane sweeping is thought to lead to an increased production of prostaglandins [49].
  - Amniotomy: amniotomy refers to rupture of the membranes using a plastic hooked instrument or, occasionally, surgical forceps. It may be carried out alone or in combination with oxytocin or prostaglandins to induce labour. This procedure is risk as it can introduce infection [49]
- Mechanical Methods
  - Catheters: Foley urinary catheters have been used for the induction of labour, as have double-balloon catheters. The catheter is introduced into the extra-amniotic space, and then the balloon is inflated to keep the catheter in place. Catheters are usually left in situ until they are expelled. In some cases a saline infusion is introduced into the extra-amniotic space via the catheter.
  - Laminaria tents: Laminaria tents are made from sterile seaweed or synthetic materials. These devices are introduced into the cervical canal and expand to gradually stretch the cervix

There are other complementary methods such as sexual intercourse.

- -Labour induction is a high-risk situation, experienced medical personnel must be present and a theatre must be available for imminent cesarean section in case of failure of intervention. It must be closely monitored on all levels as enumerated below:

- Fetal: fetal heart rate, membranes, amniotic fluid, moulding
- Maternal: neurological status, temperature, blood pressure, pulse
- Progress of labor: uterine contractions, cervical dilation, descent of the fetus.

#### **2.5.6. Complications of Induction of Labour**

- Maternal: uterine rupture, tears (cervical, vaginal, perineal), postpartum hemorrhage, sepsis, chorio-amnionitis, amniotic fluid embolism, failure leading to emergency cesarean section.
- Fetal: non reassuring fetal status, fetal death, birth trauma, cord prolapse.

Induction of labour is not a risk-free procedure so it must therefore be performed only when there is a clear medical indication for it. Pregnant women must be properly prepared and counseled on the procedure before it is carried out. Close monitoring is very important during the process.



## 2.6. REVIEW OF STUDIES

### 2.6.1. In the world

Title and place of study	Author and year of study	Setting	Results
Drug treatment and prevention of malaria in pregnancy: a critical review of the guidelines	Khalid A. J. Al Khaja* and Reginald P. Sequeira 2021	Thirty-five updated national guidelines and the President's Malaria Initiative (PMI), available in English language, were reviewed. The primary outcome measures were the first-line anti-malarial treatment protocols adopted by national guidelines for uncomplicated and complicated falciparum malaria infections in early (first) and late (second and third) trimesters of pregnancy. The strategy of intermittent preventive treatment of malaria in pregnancy (IPTp) with sulfadoxine-	This review evaluated the treatment and prevention of falciparum malaria in pregnancy in 35 national guidelines/PMI-Malaria Operational Plans (MOP) reports out of 95 malaria-endemic countries. Of the 35 national guidelines, 10 (28.6%) recommend oral quinine plus clindamycin as first-line treatment for uncomplicated malaria in the first trimester. As the first-line option, artemether-lumefantrine, an artemisinin-based combination therapy, is adopted by 26 (74.3%) of the guidelines for treating uncomplicated or complicated malaria in the second and third trimesters. Intravenous artesunate is approved by 18 (51.4%) and 31 (88.6%) guidelines for treating complicated malaria during early and late pregnancy, respectively. Of the 23 national guidelines that recommend IPTp-SP strategy, 8 (34.8%) are not explicit about directly observed therapy requirements, and three-quarters,

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

		pyrimethamine (SP) was also addressed.	17 (73.9%), do not specify contra-indication of SP in human immunodeficiency virus (HIV)-infected pregnant women receiving cotrimoxazole prophylaxis. Most of the guidelines (18/23; 78.3%) state the recommended folic acid dose.
Comparison of Maternal Labor-Related Complications and Neonatal Outcomes Following Elective Induction of Labor at 39 Weeks of Gestation vs Expectant Management: a Systematic Review and Meta-analysis	James Hong, MD; Jessica Atkinson, BBiomedSc; Alexandra Roddy Mitchell, MPH; Stephen Tong, PhD; Susan P. Walker, MD; Anna Middleton, MPH; Anthea Lindquist, DPhil; Roxanne Hastie, PhD 2023	This systematic review and meta-analysis included randomized clinical trials, cohort studies, and cross-sectional studies reporting perinatal outcomes following induction of labor at 39 weeks vs expectant management.	Of the 5827 records identified in the search, 14 studies were eligible for inclusion in this review. These studies reported outcomes for 1 625 899 women birthing a singleton pregnancy. Induction of labor at 39 weeks of gestation was associated with a 37% reduced likelihood of third- or fourth-degree perineal injury (OR, 0.63 [95% CI, 0.49-0.81]), in addition to reductions in operative vaginal birth (OR, 0.87 [95% CI, 0.79-0.97]), macrosomia (OR, 0.66 [95% CI, 0.48-0.91]), and low 5-minute Apgar score (OR, 0.62 [95% CI, 0.40-0.96]). Results were similar when confined to multiparous women only, with the addition of a substantial reduction in the likelihood of emergency cesarean section (OR, 0.61 [95% CI, 0.38-0.98]) and no difference in operative vaginal birth (OR.01 [95% CI, 0.84-1.21]). However, among nulliparous women only, induction of labor was associated

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

			with an increased likelihood of shoulder dystocia (OR, 1.22 [95% CI, 1.02-1.46]) compared with expectant management,
Maternal and newborn outcomes with elective induction of labor at term	Vivienne Souter MD, Ian Painter PhD, Kristin Sitcov BS, Aaron B Caughey MD PhD	We conducted a retrospective cohort study using chart-abstracted data on births from January 1, 2012, to December 31, 2017, at 21 hospitals in the Northwest United States. The study was restricted to singleton cephalic hospital births at 39+0–42+6 week's gestation. Exclusions included previous cesarean birth, missing data for delivery type or gestational week at birth, antepartum stillbirth, and cesarean birth without any attempt at vaginal birth, fetal anomaly, gestational diabetes mellitus, prepregnancy diabetes mellitus,	A total of 55,694 births were included in the study cohort: 4002 elective inductions at $\geq 39+0$ weeks gestation and 51,692 births at 39+0–42+6 week's gestation that were not electively induced. In nulliparous women, elective induction at 39 weeks gestation was associated with a decreased likelihood of cesarean birth (14.7% vs 23.2%; adjusted odds ratio, 0.61; 95% confidence interval, 0.41–0.89) and an increased rate of operative vaginal birth (18.5% vs 10.8%; adjusted odds ratio, 1.8; 95% confidence interval, 1.28–2.54) compared with on-going pregnancies. In multiparous women, cesarean birth rates were similar in the elective inductions and on-going pregnancies. Elective induction at 39 weeks gestation was associated with a decreased likelihood of pregnancy-related hypertension in nulliparous (2.2% vs 7.3%; adjusted odds ratio, 0.28; 95% confidence interval, 0.11–0.68) and multiparous women (0.9% vs 3.5%; adjusted odds ratio,

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

		<p>and prepregnancy hypertension. The rate of cesarean birth for elective inductions at both 39 and 40 weeks gestation was compared with the rate in all other on-going pregnancies in the same gestational week. Maternal outcomes (operative vaginal birth, shoulder dystocia, 3rd- or 4th-degree perineal laceration, pregnancy-related hypertension, and postpartum hemorrhage) and newborn infant outcomes (macrosomia, 5-minute Apgar &lt;7, resuscitation at delivery, intubation, respiratory complications, and neonatal intensive care unit admission) were also compared between elective</p>	<p>0.24; 95% confidence interval, 0.15–0.38). Term elective induction was not associated with any statistically significant increase in adverse newborn infant outcomes. Elective induction of labor at 39 weeks gestation was associated with increased time from admission to delivery for both nulliparous (1.3 hours; 95% confidence interval, 0.2–2.3) and multiparous women (3.4 hours; 95% confidence interval, 3.2–3.6).</p>
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Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

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		<p>inductions and on-going pregnancies at 39 and 40 weeks gestation. Logistic regression modeling was used to produce odds ratios for outcomes with adjustment for maternal age and body mass index. Results were stratified by parity and gestational week at birth. Duration of hospital stay (admission to delivery, delivery to discharge, and total stay) were compared between elective inductions and on-going pregnancies.</p>	
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## 2.6.2. In Africa

Title and place of study	Author and year of study	Setting	Results
The Prevalence of Malaria among Pregnant Women in Ethiopia: A Systematic Review and Meta-Analysis	Yalewayker Tegegne , Daniel Asmelash ,Sintayehu Ambachew ,Setegn Eshetie ,Ayenew Addisu ,and Ayalew Jejaw Zeleke 2019	Six authors (YT, SA, SE, DA, AA, and AJZ) independently conducted a search in PubMed, Google Scholar, HINARI, and Science Direct literature, using the key words, for including researches which were published up to August 2018. Then searched articles were screened by the title and abstract to consider the articles in the full-text review. Following exclusion of duplicates, abstracts and titles of 125 papers were screened for eligibility criteria, and seven were chosen for full-text evaluation. Differences in the selection of articles being included in the review were resolved by the third reviewer decision, though there was a very low degree	Among a total of 10207 studies, seven studies were included in this analysis. The estimated pooled prevalence of malaria among pregnant women in Ethiopia was 12.72% (95% CI: 7.45, 17.98). In subgroup analysis, the prevalence of malaria showed a significant variation between asymptomatic and symptomatic cases, which was 7.83% (95% CI: 2.23, 13.43) and 17.97% (95% CI: 7.31, 28.92), respectively

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

		of discrepancy between the authors in the choice of articles for the review. The quality of articles was assessed using Joana Briggs Institute (JBI) critical appraisal checklist for simple prevalence	
Factors associated with adverse obstetric events following induction of labor: a retrospective study in a tertiary hospital in Ghana	Kwame Adu-Bonsaffoh, Joseph Seffah 2022	Retrospective study involving women with singleton gestations, conducted at the Korle Teaching Hospital in Ghana. Multivariable logistic regression was used to explore the factors associated with adverse outcomes of IOL	A total of 195 women who had IOL were analysed with 161 (82.6%) and 34 (17.4%) undergoing vaginal and caesarean deliveries respectively. The main IOL methods used included Misoprostol (91.3%), Oxytocin (5.1%) and Foley's catheter (3.6%). Composite adverse perinatal outcomes occurred in 46 neonates (23.6%) comprising perinatal deaths (7.2%) and or NICU admission (21.0%). Caesarean delivery following IOL was significantly associated with

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

			<p>nulliparity, gestational age &lt;41 weeks, hypertensive disorders in pregnancy and birth weight <math>\geq 3.5</math>kg. Gestational age &lt;41 weeks and birth weight &lt;2.5kg were significantly associated with adverse perinatal outcome. Five women (2.6%) had uterine rupture all of which occurred in the misoprostol group.</p>
<p>Adverse neonatal outcomes and associated factors among mothers who gave birth through induced and spontaneous labor in public hospitals of Awi zone, Northwest Ethiopia: a comparative cross-sectional study</p>	<p>Melaku Laikemariam Almaz Aklilu Fikadu Waltengus Melkamu Addis, Wubishet Gezimu, Fekadu Baye and Temesgen Getaneh 2023</p>	<p>A comparative cross-sectional study was conducted at Awi Zone public hospitals from May 1 to June 30, 2022. A simple random sampling technique was employed to select 788 (260 induced and 528 spontaneous) women. The collected data were analyzed using statistical package for social science (SPSS) software version 26. The Chi-square test and an independent t-</p>	<p>The adverse neonatal outcomes among women who gave birth through induced labor were 41.1%, whereas spontaneous labor was 10.3%. The odds of adverse neonatal outcomes in induced labor were nearly two times higher than in spontaneous labor (AOR = 1.89, 95% CI: 1.11–3.22). No education (AOR= 2.00, 95% CI: 1.56, 6.44), chronic disease (AOR = 3.99, 95% CI: 1.87,</p>



Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

		test were used for categorical and continuous variables, respectively. A binary logistic regression was used to assess the association between the outcome and explanatory variables. In the bivariate analysis, a p-value $\leq 0.2$ at a 95% confidence interval was used to consider the variables in the multivariate analysis. Finally, statistical significance was stated at a p-value of less than 0.05.	8.52), male involvement (AOR= 2.23, 95% CI: 1.23, 4.06), preterm birth (AOR= 9.83, 95% CI: 8.74, 76.37), operative delivery (AOR = 8.60, 95% CI: 4.63, 15.90), cesarean section (AOR= 4.17, 95% CI: 1.94, 8.95), and labor complications (AOR = 5.16, 95% CI: 2.90, 9.18) were significantly associated factors with adverse neonatal outcomes.
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### 2.6.3. In Cameroon

Title and place of study	Author and year of study	Setting	Results
Chemokine modulation in microscopic and submicroscopic Plasmodium falciparum malaria infection in women at delivery in Yaoundé ,Cameroon	Rosette Megnekou,Chris Marco Mbianda Nana ,Jean Claude Djontu ,Bernard Marie Zambo Bitye ,Benderli Christine Nana ,Berenice Kenfack Tekougang Zangue, Christiane	This was a retrospective case-control study (1:3 ratio) involving samples from 134 women (34 PM+ and 100 PM-) enrolled at delivery at the Marie Reine Health Center in Yaoundé , Cameroon	Overall, PM was associated with increased plasma levels ofCXCL-13 and CXCL-16 and low levels ofCXCL-4 and CCL-24 in both peripheral and placental blood

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

	<p>Josiane Donkeu ,Estelle Essangui ,Rodrigue Mbea Salawiss ,Reine Ndeumou Medouen Seumko'o Lawrence Ayong ,Rose Gana Fomban Leke</p> <p>2023</p>	<p>between June 2013 and October 2018. Samples were collected just after delivery and used to diagnose microscopic and submicroscopic Plasmodium falciparum infections. Submicroscopic infections were detected by reverse transcription LAMP whereas chemokine levels were determined by Magnetic Luminex Screening Assay.</p>	<p>(0.0002 <math>\diamond</math> p <math>\diamond</math> 0.042). Similarly, CCL-24 levels in peripheral and placental blood samples were significantly lower insubmicroscopically infected women compared to healthy controls (p=0.04 and 0.02, respectively). Maternal hemoglobin levels increased with peripheral plasma levels ofCXCL-4 (p=0.005), CXCL-16 (p=0.03), and CCL-24 (p=0.002) while birth weight was lower for babies born from women with high levels of peripheral CXCL-13 (p=0.0006) and low levels of cord CXCL-4 and CCL-24 (p=0.02 and 0.08, respectively). Together the data suggest that low levels of CXCL-4 and CCL-24 coupled with high plasma levels ofCXCL-13 and for a lesser extend</p>
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Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

			CXCL-16 represent signatures of PM in the study population. These findings are relevant for understanding the immune pathogenesis of PM and developing new therapeutic or preventive strategies against severe PM outcomes
Malaria in the third trimester and maternal-perinatal outcome	Elie Nkwabong Diane N. Mayane Esther Meka Felix Essiben 2020	A parity-matched comparative cohort study was carried out between December 1, 2018, and April 30, 2019, in three university teaching hospitals in Yaoundé (Cameroon). Women with and without TTM were followed up till delivery. The variables analyzed included maternal and gestational ages at delivery, the regimen of intermittent preventive treatment, usage of insecticide-treated net, history of malaria recorded during	Of 3063 pregnant women, 130 (4.2%) had TTM. Adverse outcomes associated with TTM were maternal anemia (relative risk [RR] 10, 95% confidence interval [CI] 4.91–20.34), intrauterine fetal demise (RR 7.50, 95% CI 1.47–38.06), preterm delivery (RR 4.50, 95% CI 2.37–8.51), low birth weight (adjusted RR 2.88, 95% CI 1.34–6.19), neonatal asphyxia especially if delivery occurred during parenteral treatment

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

		pregnancy, birth and placenta weights, Apgar score, and early neonatal outcomes. Fisher exact test, t-test, and logistic regression were used for comparison. $P < 0.05$ was considered statistically significant.	(RR 5.18, 95% CI 2.56–10.48), transfer of the newborn to the neonatal intensive care unit (RR 4.38, 95% CI 2.59–7.42), and intrapartum or early neonatal death (RR 4.18, 95% CI 1.48–11.74). Third Trimester Malaria was associated with adverse perinatal outcome especially if labor started during parenteral treatment.
Impact of long lasting insecticidal nets on asymptomatic malaria during pregnancy, in a rural and urban setting in Cameroon	Nfor Omarine Nlinwe *, Fundoh Golory Nchefor, Negesa Bright Takwi 2022	This study was therefore designed to assess the impact of long lasting insecticidal nets (LLINs) on asymptomatic malaria in the pregnant women attending the Foubot District Hospital (rural setting) and the Bamenda Regional Hospital (urban setting). This was a hospital based cross-sectional study done within three months.	The prevalence of asymptomatic malaria was 10.14% (63/621), with a higher prevalence among the pregnant women in the rural setting (12.21%; 37/303), than the urban setting (8.18%; 26/318). As indicated by the attributable risk, 21% of malaria incidence was attributed to absence of LLINs distribution in neighborhoods of the rural setting

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

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			meanwhile 10% of malaria incidence is attributed to absence of LLINs distribution in neighborhoods of the urban setting.
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## **CHAPTER 3: METHODOLOGY**

### **3.1. TYPE OF STUDY**

We conducted a non-randomized clinical trial.

### **3.2. SITE OF STUDY**

The study was carried out at the obstetrics and gynecology units of two reference hospitals in Yaoundé. These hospitals were chosen because of their great patient influx and adequate follow up of patients.

#### The Yaoundé Gynecology-Obstetrics and Pediatrics Hospital (YGOPH).

It is a reference health facility created in 2002 and specializes in mother and child health care. It's Obstetrics and Gynecology department has a capacity of 34 inpatient beds, 3 delivery tables, and 4 operating theatres with two laparoscopy columns. The service carries out an average of 3015 deliveries per annum with a staff of 14 specialists in obstetrics and gynaecology.

#### The Yaoundé Central Hospital

This reference hospital located at the heart of Yaoundé has one of the biggest and most specialized maternity units with over 72 in-patient beds, 6 delivery tables, 2 operating theatres and a large highly trained staff. It records about 219 deliveries per month.

### **3.3. DURATION OF STUDY**

The study was carried out during a seven month period precisely from November 2023 to May 2024. During this period the following was accomplished; writing of protocol, obtention of ethical clearance and other authorization documents, data collection and analysis, thesis writing, proofreading and publishing of the results. Recruitment of participants began in January 2023 up to May 2024.

### **3.4. STUDY POPULATION AND SAMPLE**

The study population comprised of pregnant women who were diagnosed with malaria at term and who had received full treatment.

#### **3.4.1. Inclusion Criteria**

- Gestational age at term (37weeks- 42weeks).
- Diagnosis of malaria infection during pregnancy and complete treatment.
- Accepted to participate in study by signing the informed consent form.

### 3.4.2 Exclusion Criteria

- Contraindications for induction of labour
- Women who entered into labour before the end of treatment

### 3.4.3. Non-Inclusion Criteria

- Gestational age < 37weeks
- Pregnant women at term with fevers other than malaria

### 3.4.4. Sampling Method

Patients were consecutively recruited until the desired sample size was obtained.

### 3.4.5. Sample size Estimation

To estimate the sample size, we used the sample size formula for a randomized clinical trial where

$$n = 1/(1 - f) \left\{ 2(Z_{\alpha} + Z_{\beta})^2 p(1 - p) / (p_0 - p_1)^2 \right\}$$

n= sample size

f= the proportion of study subjects expected to leave the study for reasons other than the outcome under investigation. There was no loss to follow up, thus f=0.

$p_0$ = The proportion of the participants in the control treatment group who are expected to exhibit the outcome of interest

$p_1$ = The proportion of the participants in the treatment group that are expected to exhibit the outcome of interest. This proportion is usually set relative to  $p_0$

$$p = \{p_0 + p_1/2\}$$

$Z_{\alpha}$ = 1.96 when confidence level is 95%

$Z_{\beta}$ = 1.28 When confidence level is 80%

$$\text{Therefore } n = 1/1-0 \{ 2(1.96 + 1.28)^2 0.375(1-0.375) / (0.25 - 0.50)^2 \}$$

n=79 participants

With a ratio of 1:1 that is 79 participants for induction of labour and 79 participants for spontaneous labour.



### **3.5. PROCEDURE**

#### **3.5.1. Administrative Formalities**

The research proposal was approved by the supervisors before we requested for ethical clearance from the Institutional Review Board of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I. We requested for authorizations and obtained them from the administrations of the Yaounde Gynaecology, Obstetrics and Pediatrics Hospital and the Yaoundé Central Hospital.

#### **3.5.2. Recruitment and Data Collection**

On a daily basis, we followed up in the various services, women who were admitted for malaria and at the end of complete treatment. We selected women at term who conformed to the selection criteria. The women were divided into two groups, those who accepted to deliver immediately by induction before discharge and those who accepted discharge and wait for spontaneous labour and delivery. The choice to be induced or wait for spontaneous labour was that of the women themselves and in collaboration with the treating doctor.

Induction was done using the standard protocol of the services and the uterotonic mostly used was misoprostol. Delivery was monitored using the partogram based on the norms and standard of the services. For those who opted to be discharged and wait for spontaneous labour, we made phone calls daily to monitor the beginning of spontaneous contractions and they were then asked to come to the respective hospitals and to the delivery rooms directly to meet with us and labour was managed using the partogram as well. In both case, labour was managed by experienced midwives who have long records of managing deliveries.

For specific objective 1: Baseline data were collected on enrolment including demographic information like age, marital status, profession, religion, level of education, past medical history and that of current pregnancy, gestational age, gravidity and parity.

For specific objective 2: Data sheets were used to monitor labour and variables collected included birthweight, Apgar score, neonatal intensive care unit admission, perinatal mortality as well as maternal complications. They were also used to monitor labour such as number and duration of contractions, foetal heart rate, cervical dilation, descent of the representing part, mode of delivery.

For specific objective 3: The information obtained by method of delivery was compared between the induction and spontaneous delivery groups. All these were recorded in the questionnaire which was designed, internally validated by supervisors, tested and then adapted for the study.

### **3.5.3. Variables studied**

- Sociodemographic data: these included age, gestational age, parity, marital status, religion, profession, level of education of the pregnant women.
- Medical and Obstetric profile: we checked for presence or past histories of comorbidities such as diabetes, hypertension.
- History of current pregnancy: we obtained information on the number of ANC, gestational age at first ANC, serology, prophylaxis received, morphology, lifestyle during pregnancy.
- Clinical presentation; fetal presentation, Bishop's score
- Perinatal data: mode of delivery (cesarean section or vaginal birth), Apgar score at birth, birthweight, coloration, neurological status, febrile illness, admission to NICU, early neonatal death
- Delivery complications: postpartum hemorrhage, perineal tears

## **3.6. STUDY RESOURCES**

### **3.6.1. Data Collection and Management Tools**

Pre-established data collection worksheets

- Patient medical records
- A4 reams of paper
- Writing material (pens, pencils, and eraser)
- Computer
- Microsoft Suite Package
- USB flash drives

### **3.6.2. Human Resource**

- Main Investigator

MBELE CHELSEA NGOMO

-Supervisor

-Co-Supervisors

-Statistician

### **3.7. DATA ANALYSIS**

Data collected was entered and analyzed using the IBM SPSS (Statistical Package for Social Sciences). Pearson's chi-square test was used for comparison between categorical data and Student's T-test for numerical data. All p values less than 0.05 will be considered statistically significant. Results were represented in tables and presented using relative risks, 95% confidence intervals and p-values.

### **3.8. ETHICAL CONSIDERATIONS**

Ethical considerations were followed in accordance with the Helsinki Declaration which goes as thus- "It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, and right to self-determination, privacy, and confidentiality of personal information of research subjects". Prior to data collection for this study, Ethical clearance was obtained from the Institutional Review Board at the Faculty of Medicine and Biomedical Sciences, University of Yaoundé I.

## **CHAPTER 4: RESULTS**

#### 4.1. RECRUITMENT OF STUDY POPULATION

For this study, we actively recruited participants who came to the Obstetrics and Gynecology services of the YGOPH and the YCH from January 1<sup>st</sup> 2024 to May 30th 2024.

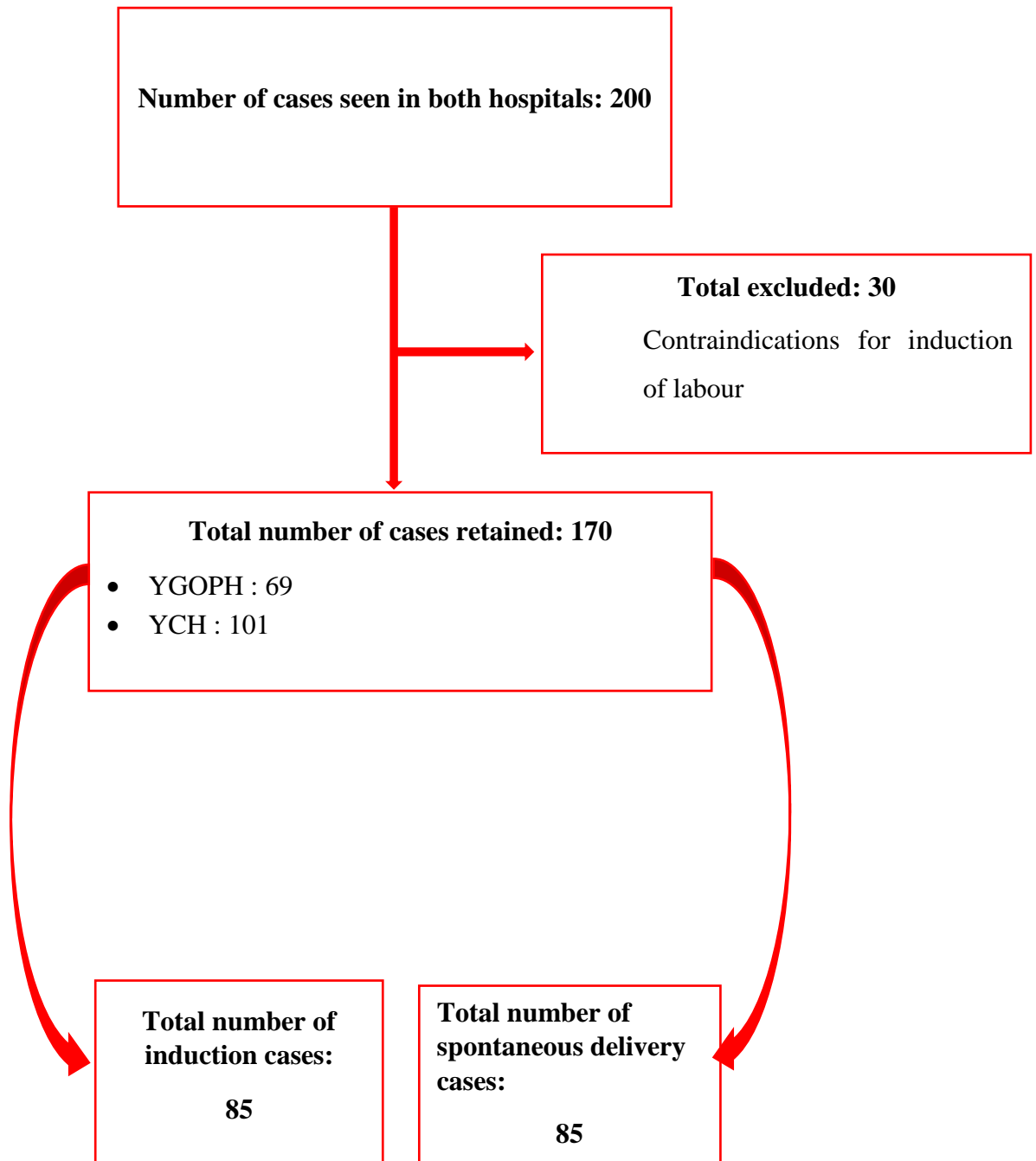


Figure 9 : Recruitment flow chart

## 4.2. SOCIO-DEMOGRAPHIC PROFILE OF THE STUDY POPULATION

### 4.2.1. Age and marital status

**Table II:** Population distribution by age and marital status

Variables	Induction group	Spontaneous group	RR (CI at 95%)	p-value
	N=85; n(%)	N=85; n(%)		
Age groups (in years)				
[15-19[	9 (10.6)	10 (11.8)	0.88 (0.34-2.30)	0.500
[20-24[	19 (22.4)	26 (30.6)	0.65 (0.32-1.30)	0.148
[25-29[	27 (31.8)	28 (32.9)	0.94 (0.49-1.80)	0.500
[30-34[	17 (20.0)	15 (17.6)	1.16 (0.54-2.52)	0.422
[35-39[	10 (11.8)	4 (4.7)	2.70 (0.81-8.97)	0.081
[40-45[	3 (3.5)	2 (2.4)	1.51 (0.24-9.32)	0.500
Marital status				
Married/Concubine	34 (40.0)	19 (22.4)	2.31 (1.18-4.52)	0.010
Single	51 (60.0)	66 (77.6)	1	

The age group most represented was 25-29 years with 31.8% and 32.8% respectively as shown in the table above.

#### 4.2.2. Level of education and occupation

**Table III:** Population distribution by level of education and occupation

Variables	Induction group N=85; n(%)	Spontaneous group N=85; n(%)	RR (CI at 95%)	p-value
<b>Level of education</b>				
Primary	7 (8.2)	9 (10.6)	0.75 (0.26-2.13)	0.397
College	24 (28.2)	22 (25.9)	1.12 (0.57-2.21)	0.432
High school	17 (20.0)	15 (17.6)	1.16 (0.54-2.52)	0.422
University	37 (43.5)	39 (45.9)	0.90 (0.49-1.66)	0.439
<b>Occupation</b>				
Informal sector	17 (20.0)	18 (21.2)	0.93 (0.44-1.95)	0.500
Student	28 (32.9)	23 (27.1)	1.32 (0.68-2.55)	0.252
Civil servant	11 (12.9)	18 (21.2)	0.55 (0.24-1.25)	0.110
Private servant	15 (17.6)	14 (16.5)	1.08 (0.48-2.41)	0.500
Unemployed	14 (16.5)	12 (14.1)	1.20 (0.51-2.77)	0.416

The groups were comparable for the level of study and occupation. The majority had secondary level of education and were mostly students as shown in Table II above.

### 4.3. CLINICAL PROFILE OF THE STUDY POPULATION

#### 4.3.1. Obstetrical characteristics

**Table IV:** Population distribution according to personal and family obstetrical characteristics

Variables	Induction group N=85; n(%)	Spontaneous group N=85; n(%)	RR (CI at 95%)	P
<b>Gravidity</b>				
Primigravida	34 (40.0)	37 (43.5)	0.86 (0.47-1.59)	0.378
Paucigravida	26 (30.6)	25 (29.4)	1.05 (0.54-2.03)	0.500
Multigravida	15 (17.6)	11 (12.9)	1.44 (0.62-3.35)	0.262
Grand multigravida	10 (11.8)	12 (14.1)	0.81 (0.33-1.99)	0.410
<b>Parity</b>				
Nulliparous	42 (49.4)	43 (50.6)	0.95 (0.52-1.74)	0.500
Primiparous	18 (21.2)	15 (17.6)	1.25 (0.58-2.68)	0.349
Pauciparous	10 (11.8)	16 (18.8)	0.57 (0.24-1.35)	0.143
Multiparous	12 (14.1)	8 (9.4)	1.58 (0.61-4.09)	0.238
Grand multiparous	3 (3.5)	3 (3.5)	1.00 (0.19-5.10)	0.659

The population was mainly primigravida (40.0% vs 43.5% ;  $p = 0.378$ ) and nulliparas (49.4% vs 50.6% ;  $p = 0.500$ ) as shown in Table III above.



#### 4.3.2. Comorbidities and lifestyle during pregnancy

**Table V:** Population distribution according to comorbidities and lifestyle

Variables	Induction group	Spontaneous group	RR (CI at 95%)	P
	N=85; n(%)	N=85; n(%)		
<b>Comorbidities</b>				
HIV infection	2 (2.4)	2 (2.4)	1.00 (0.13-7.26)	0.690
Hepatitis B/C	0 (0.0)	1 (1.2)	/	0.500
Hypertension	2 (2.4)	2 (2.4)	1.00 (0.13-7.26)	0.690
Diabetes	0 (0.0)	2 (2.4)	/	0.249
<b>Lifestyle</b>				
Alcohol consumption	3 (3.5)	7 (8.2)	0.40 (0.10-1.63)	0.164
Tobacco consumption	1 (1.2)	2 (2.4)	0.49 (0.04-5.55)	0.500
Traditional medication	7 (8.3)	13 (15.3)	0.50 (0.19-1.33)	0.122

Regarding comorbidities during pregnancy, HIV infection was 2.4% in each of the groups ( $p = 0.690$ ). As for lifestyle, no difference was found in the consumption of tobacco or traditional medications ( $p \geq 0.05$ ). (Table IV).

### 4.3.3. Pregnancy follow-up

**Table VI:** Population distribution according to number of ANC visits, gestational age at first ANC and qualification of ANC provider

Variables	Induction group	Spontaneous group	RR (CI at 95%)	p-value
	N=85; n(%)	N=85; n(%)		
Number of ANC				
1-3	20 (23.5)	29 (34.1)	0.59 (0.30-1.16)	0.088
4	22 (25.9)	17 (20.0)	1.39 (0.68-2.86)	0.233
5-7	35 (41.2)	26 (30.6)	1.58 (0.84-2.98)	0.100
≥ 8	8 (9.4)	13 (15.3)	0.57 (0.22-1.46)	0.176
Gestational age at first ANC (WA)				
< 12	23 (27.1)	26 (30.6)	0.84 (0.43-1.63)	0.368
[12-16[	27 (31.8)	25 (29.4)	1.11 (0.58-2.14)	0.434
[16-20[	18 (21.2)	18 (21.2)	1.00 (0.47-2.08)	0.574
[20-24[	9 (10.6)	6 (7.1)	1.55 (0.53-4.59)	0.295
≥ 8	8 (9.4)	10 (11.8)	0.77 (0.29-2.08)	0.402
ANC provider				
Gynaecologist	36 (42.4)	32 (37.6)	1.21 (0.65-2.25)	0.319
General practitioner	36 (42.4)	27 (31.8)	1.57 (0.84-2.95)	0.102
Others	13 (15.3)	26 (30.6)	0.41 (0.19-0.86)	0.014

No difference was found between the groups in the number of antenatal care visits, nor in the gestational age at the first ANC visit, with respective mean values of  $4.81 \pm 1.97$  ANC versus  $4.78 \pm 2.32$  ANC ( $p = 0.915$ ) and  $15.15 \pm 5.54$  weeks of gestation versus  $14.84 \pm 6.49$  weeks of gestation ( $p = 0.732$ ) as shown in (Table V)

**Table VII:** Population distribution according to prophylactic measures during pregnancy

Variables	Induction	Spontaneous	RR	p-value
	group	group		
	N=85; n(%)	N=85; n(%)	(CI at 95%)	
<b>TPI</b>				
0	1 (1.2)	8 (9.4)	<b>0.11 (0.01-0.93)</b>	<b>0.017</b>
1-2	31 (36.5)	32 (37.6)	0.95 (0.51-1.77)	0.500
3-4	40 (47.1)	35 (41.2)	1.27 (0.69-2.32)	0.268
≥ 5	13 (15.3)	10 (11.8)	1.35 (0.55-3.28)	0.327
<b>Slept under treated mosquito net</b>				
Yes	71 (83.5)	61 (71.8)	1.99 (0.94-4.19)	0.048
No	14 (16.5)	24 (28.2)	1	
<b>Iron / folic acid consumption</b>				
Yes	78 (91.8)	78 (91.8)	1.00 (0.33-2.98)	0.609
No	7 (8.2)	7 (8.2)	1	

Table VI showed that most women had received 3 to 4 doses of IMP during pregnancy that is 47.1% against 41.2% ( $p = 0.268$ ). Most of them slept under a mosquito bed net impregnated with insecticide (83.5% vs 71.8%) and had taken iron alongside folic acid (91.8% vs 91.8%).

**Table VIII:** Population distribution according to pathologies during pregnancy

Pathologies during pregnancy	Induction group	Spontaneous group	RR	P
	N=85; n(%)	N=85; n(%)	(CI at 95%)	
<b>Malaria in 1<sup>st</sup> or 2<sup>nd</sup> semester</b>				
Yes	28 (32.9)	41 (48.2)	<b>0.52 (0.28-0.98)</b>	<b>0.030</b>
No	57 (67.1)	44 (51.8)	1	
<b>Anaemia</b>				
Yes	16 (18.8)	24 (28.2)	0.58 (0.28-1.21)	0.103
No	69 (81.2)	61 (71.8)	1	
<b>Bleeding</b>				
Yes	3 (3.5)	4 (4.7)	0.74 (0.16-3.41)	0.500
No	82 (96.5)	81 (95.3)	1	

Women whose labor had been induced had less frequent malaria in the first and second trimester of pregnancy, at 32.9% versus 48.2% of cases (**p = 0.030**). As for anemia or bleeding during pregnancy, the frequencies were comparable in the two groups ( $p \geq 0.05$ ) as shown above in (Table VII).

#### 4.3.4. Bishop score

**Table IX:** Population distribution according to Bishop score

Variables	Induction	Spontaneous	RR	p-value
	group	group		
	N=85; n(%)	N=85; n(%)	(CI at 95%)	
<b>Bishop score</b>				
< 7	24 (28.2)	14 (16.5)	1.99 (0.84-4.19)	0.048
≥ 7	61 (71.8)	71 (83.5)	0.50 (0.23-1.05)	0.048

Women in the induction of labour group had a higher frequency of a poor Bishop's score compared to women in the spontaneous labour group, at 28.2% and 16.5% respectively (RR : 1.99 (0.84-4.19) ; p = 0.048) as shown in (Table VIII)

#### 4.4. MATERNAL OUTCOME IN THE STUDY POPULATION

**Table X:** Population distribution according to route of delivery and maternal complications

Variables	Induction	Spontaneous	RR	p-value
	group	group	(CI at 95%)	
	N=85; n(%)	N=85; n(%)		
<b>Mode of delivery</b>				
Cesarian section	32 (37.6)	12 (14.1)	<b>2.66 (1.47-4.81)</b>	<b>&lt; 0.001</b>
Vaginal delivery	53 (62.4)	73 (85.9)	<b>0.72 (0.60-0.87)</b>	<b>&lt; 0.001</b>
<b>Complications</b>				
Labour abnormalities	22 (25.9)	6 (7.1)	<b>3.59 (1.75-12.02)</b>	<b>0.001</b>
Perineal tears	23 (27.1)	11 (12.9)	<b>2.09 (1.08-4.01)</b>	<b>0.017</b>
Post partum hemorrhage	10 (11.8)	4 (4.7)	2.50 (0.81-7.66)	0.081

The caesarean section rate was higher in women who had induction of labour compared to those who had spontaneous labour, at 37.6% and 14.1% respectively (**RR: 2.66: p < 0.001**). Regarding maternal complications, women who had been induced had 3.5 times and 2 times more risk than those who entered labor spontaneously of having labour abnormalities such as precipitated labour and prolonged labour(**p = 0.001**) or perineal tears (**p = 0.017**), respectively as illustrated in (Table IX)

#### 4.5. FETAL AND NEONATAL OUTCOME OF THE STUDY POPULATION

##### 4.5.1. Fetal complications at delivery

**Table XI:** Population distribution according to the foetal complications at delivery

Variables	Induction group	Spontaneous group	RR (CI at 95%)	p-value
<b>Fetal complications</b>				
Non reassuring fetal status(NRFS)	31 (36.5)	12 (14.1)	<b>2.58 (1.42-4.68)</b>	<b>0.001</b>
Intrauterine fetal demise(IUFD)	2 (2.4)	11 (12.9)	<b>0.18 (0.04-0.79)</b>	<b>0.009</b>

The study of foetal complications during labour was characterized by a risk multiplied by 2.5 for fetuses in the induction group, of having a non-reassuring foetal status (**p = 0.001**). More cases of intrauterine foetal death were found in the spontaneous delivery group as shown in (Table X) above.

#### 4.5.2. Neonatal characteristics at delivery

**Table XII:** Population distribution according to the neonatal characteristics at delivery

Variables	Induction group N=85; n(%)	Spontaneous group N=85; n(%)	RR (CI at 95%)	p-value
<b>Sex</b>				
Male	49 (57.6)	36 (42.4)	1.36 (1.01-1.85)	0.033
Female	36 (42.4)	49 (57.6)	0.73 (0.54-0.99)	0.033
<b>Birth weight (in grams)</b>				
[2000-2499[	6 (7.1)	7 (8.2)	0.85 (0.30-2.44)	0.500
[2500-4000[	77 (90.6)	74 (87.1)	1.43 (0.54-3.75)	0.314
≥ 4000	2 (2.4)	4 (4.7)	0.50 (0.09-2.65)	0.341
<b>Hypotrophy</b>				
Yes	0 (0.0)	0 (0.0)	/	/
No	85 (100.0)	85 (100.0)	/	/
<b>Macrosomia</b>				
Yes	2 (2.4)	4 (4.7)	0.50 (0.09-2.65)	0.341
No	83 (97.6)	81 (95.3)	1	
<b>Apgar score</b>				
0	2 (2.4)	11 (12.9)	<b>0.16 (0.03-0.75)</b>	<b>0.009</b>
1-6	2 (2.4)	2 (2.4)	1.00 (0.14-6.93)	0.690
≥ 7	81 (95.3)	72 (84.7)	<b>1.12 (1.01-1.24)</b>	<b>0.019</b>

The birth weight was comparable in both groups, with a normal birth weight predominating in 90.6% vs 87.1% ( $p = 0.314$ ) respectively. As for the Apgar score, it was good in most cases for both groups, but more frequently so in the newborns of the induction group, at 95.3% vs 84.7% ( $p = 0.019$ ) as shown in Table XI above.



#### 4.5.3. Neonatal outcomes

**Table XIII:** Population distribution according to the neonatal outcomes

Variables	Induction group	Spontaneous group	RR (CI at 95%)	p-value
	N=85; n(%)	N=85; n(%)		
Neonatal ressuscitation				
Yes	8(9.4)	3 (3.5)	2.66 (0.73-9.71)	0.106
No	77(90.6)	82 (96.5)	1	
Need for ventilation				
Yes	13(15.3)	5(5.9)	2.60 (0.96-6.97)	0.039
No	72 (84.7)	80(94.1)	1	
Neonatal intensive care unit admission				
Yes	21 (24.7)	14 (16.5)	1.50 (0.81-2.74)	0.127
No	64 (75.3)	71 (83.5)	1	

Regarding neonatal outcomes, the frequency of neonatal resuscitation was 9.4% in the induction group and 3.5% in the spontaneous delivery group with no statistical significance (p=0.106). Newborns in the induction group had 2.6 times higher risk of requiring ventilatory support compared to the spontaneous delivery group. There was no early neonatal death in our study. However, the observed difference was statistically significant (RR : 2.60 (0.96-6.97);p=0.039). as shown in Table XII above.

## **CHAPTER 5: DISCUSSION**

### **Malaria and Pregnancy**

Malaria is known to have deleterious effects on pregnancy and perinatal outcomes as it is a major public health concern in our country [50]. Therefore it is important to use the optimal delivery approach to minimize the occurrence of adverse events [29]. This was an experimental study with the aim of assessing the maternal and foetal outcome of pregnancy among women diagnosed and treated for malaria at term following induction of labour compared to expectant spontaneous labour. The study tested the hypothesis that pregnant women who enter into labour spontaneously after treatment of malaria at term may have a better pregnancy outcome compared to those whose labour was induced.

To achieve this, we collected data from 170 pregnant women who were diagnosed with malaria at term and received treatment over a period of five months running from Jan 1<sup>st</sup> 2024 through May 1<sup>st</sup> 2024. Half of these women were induced and the other half went into spontaneous labour after discharge. We then compared the maternal and foetal outcome among these groups of women.

### **Sociodemographic profile of pregnant women**

The study population was comparable in terms of age between the induction of labour and spontaneous delivery groups. The mean ages for both groups were similar as well and most of the women fell in the age group of 25-30 years. This is slightly higher than the less than 21 years reported by a study conducted in Cameroon in 2018 for most age group affected by malaria [51]. Conversely very few women were found in the older age groups. This suggests that there is some decrease in susceptibility to malaria infection with increasing maternal age and emphasizes on the idea of possible existence of maternal-age dependent immunity that can be significant for the protection against malaria infection among pregnant women living in stable malaria transmission zones [51]. However with respect to the marital status, a significant difference ( $p=0.010$ ) was observed in the participants with a higher proportion of women in the induced group married compared to those of the spontaneous labour group. Marital status has been previously associated with certain maternal and perinatal outcomes, with married women generally experiencing better outcomes compared to single women due to various social, economic and psychological factors that can impact the labour and delivery process, as well as postpartum outcomes[52].

The distribution of educational levels and occupation was similar for the two groups. The largest proportion in both groups had a university-level education (43.5% in the induced group vs 45.9% in the spontaneous labour group,  $p=0.439$ ) and the most common occupation in both groups was

being a student (32.9% in the induction group vs 27.1% in the spontaneous delivery group,  $p=0.252$ ).

### **Clinical profile of pregnant women**

In our study, we found that the largest proportion of the women in both groups infested with malaria were primigravidae and nulliparous women compared to their multigravidae and multiparous counterparts. This has been observed in previous research [8, 25]. The explanation is that nulliparous and primigravidae women have not developed placenta parasite specific immunity compared to multiparous and multigravidae women who due to their successive pregnancy have acquired these antibodies against parasitized red blood cells that bind chondroitin sulphate A in the placenta [36].

Concerning lifestyle and comorbidities in our study, it was quite similar for both groups. The prevalence of HIV infection was 2.4% in our study population which is lower compared to the 6.0% prevalence reported in a study done in 2013 in Cameroon, HIV infected women have a higher susceptibility to pathologies like malaria that influence evolution of pregnancy[50]. The prevalence of hypertension in this study was 2.4%. There were two cases of diabetes and one case of Hepatitis B all in the spontaneous delivery group and none in the induction group. HIV infection adds to the deleterious effects of malaria in pregnancy due to diminished immunity [50]. The proportion of women who consumed alcohol during pregnancy was (3.5% vs 8.2%) for induction and spontaneous delivery groups respectively. In the same line, that of women who consumed tobacco (1.2% vs 2.4%) and then those who consumed traditional medication (8.3% vs 15.3%) respectively.

With respect to the antenatal care, there was no difference for both groups when considering the number of antenatal contacts and gestational age at first antenatal contact. Many of these pregnant women had taken more than 4 ANC contacts in both groups and a smaller proportion had less than 4 contacts that was 23.5% for the induction group and 34.1% for the spontaneous delivery group. The timing of the first ANC contact was similar with most women beginning ANC contacts at less than 20 weeks of gestation. Also we realized that most of the women of both groups had some significant level of follow up by an antenatal care provider, in many cases gynaecologists and general practitioners. The only statistically significant difference was that fewer women in the induction group saw other types of providers compared to the spontaneous delivery group. Overall the antenatal care received by the two groups during pregnancy appeared to have been well balanced.

The majority of women in both the induction (47.1%) and spontaneous delivery (41.2%) groups received 3-4 doses of intermittent preventive treatment for malaria during pregnancy. This finding is in line with the 42.1% in a study done in 2019 in Cameroon. The lack of any significant difference in the higher doses of IPTp suggests that they received comparable malaria prevention during pregnancy and this is essential because IPTp is one of the main interventions recommended by WHO to help curb the number of poor outcomes associated with the disease [25, 53]. Furthermore, malaria is one of the most common pathologies women suffer from during pregnancy [52]. The small but significantly lower proportion of women in the induction group who received no IPTp at all (1.2% vs 9.4%) may indicate slightly better adherence to malaria prevention guidelines in this group.

In this study, most of the women slept under insecticide-treated mosquito bed nets with a higher frequency in the induction group as compared to those of the spontaneous delivery group (83.5% vs 71.8%). This finding is also in line with the 81.13% reported in a study conducted in 2022 in Cameroon for the urban setting [14]. ITNs are a necessary intervention for preventing malaria in pregnancy [11, 26]. Consistent and proper use of ITNs helps mitigate the risk of malaria-related complications [14]. As for iron and folic acid supplementation, over 91% of the women in both groups received it throughout their pregnancy. This is very essential in combating pregnancy-related anemia and supporting foetal development [21].

Regarding malaria in the first and second trimesters, we noticed a significantly lower rate of malaria for the induction group compared to the spontaneous delivery group (32.9% vs 48.2%,  $p=0.030$ ). This suggested that the induction group perhaps had better management of malaria during early pregnancy relative to the spontaneous delivery group. Malaria especially in the critical first trimester of pregnancy can have serious consequences for the mother and foetus [5]. The rates of pregnancy-related anaemia and bleeding during pregnancy was comparable for the two groups.

For the Bishop's score, our findings indicated that women in the induction group had a significantly higher frequency of Bishop's scores less than 7 compared to those of the spontaneous delivery group ( $p=0.048$ ). This finding is comparable to studies conducted in Ethiopia [54–56]. This suggested that women who belonged to the induction group presented with a less favourable cervical condition compared to those who went into spontaneous labour at onset. The increased frequency of low Bishop's scores in the induction group is consistent with the fact that induction of labour is often performed in the setting of an unripe cervix and may contribute to the adverse outcomes associated with the procedure [12, 57].

### **Maternal outcome in the study population**

For the mode of delivery, the frequency of caesarean section was significantly higher in the induction group compared to the spontaneous delivery group (37.6% vs 14.1%) respectively. This is similar to the findings of a study conducted in 2020 which reported a frequency of (33% vs 12%) for the induction group and spontaneous delivery group in a study conducted in South Africa [58]. Furthermore, a higher frequency of caesarean section in the induction group compared to spontaneous delivery group at (85.7% vs 14.3%) was reported in a study carried out in 2023 in Ethiopia and this large discrepancy is accounted for by the larger study population they investigated [44]. Conversely the rate of vaginal delivery was significantly lower in the induction group (62.4% vs 85.9%). This equally indicates that women whose labour was induced were 2.66 times more likely to have a caesarean delivery than those in the spontaneous delivery group. This finding suggests that induction of labour definitely led to more dysfunctional labour progressions ultimately resulting in more caesarean sections to ensure safe delivery of the babies [59].

Labour abnormalities such as precipitated labour, prolonged labour were more common in the induction group compared to the spontaneous delivery group and the difference was statistically significant (25.9% vs 7.1%,  $p=0.001$ ) and a 3.5 higher risk than their spontaneous counterparts. This finding is consistent with a study conducted in 2021 that reported a value of 24.2% in Ethiopia for the induction group [55]. This finding points to potential challenges in labour progression and foetal descent with induction of labour.

Perineal tears were also more frequent in the induction group and the difference in both groups was statistically significant ( $p=0.017$ ) with about a 2.1 times higher risk for women who were induced. This finding is contrary to what was reported in a study carried out in 2019 which showed no difference between the two groups carried out in Greece. Perineal trauma is often associated with more difficult second stages of labour, which may be more common when labour is induced [60].

The difference in postpartum haemorrhage rates between the two groups was not significant (11.4% vs 4.7%  $p=0.08$ ) although the induction group had a higher risk. This finding is similar to what was reported in 2020 in South Africa where postpartum haemorrhage was found to be more prevalent in the induction group compared with the spontaneous delivery group (6.3% vs 4.7%) respectively [58].

### **Foetal and Neonatal Outcome of the Study Population**

The rate of non-reassuring foetal status was significantly higher in the induction group compared to the spontaneous delivery group (31.6% vs 14.1%,  $p=0.001$ ). New-borns of the induction group had

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a 2.58 risk of having a non-reassuring foetal status during labour compared to those of the spontaneous delivery group. This finding is similar to what was reported in studies carried out in Somalia and Ghana in 2023(23.6%) and in 2022 (35.3%) respectively [12, 61]. This finding suggests that induction of labour may have increased the stress and strain on the foetus, potentially due to factors like stronger or more frequent uterine contractions and longer labour duration.

Intrauterine foetal death was significantly less common in the induction group compared to the spontaneous delivery group ( $p=0.009$ ). Intrauterine foetal death is a major complication associated with malaria in pregnancy. The infested red blood cells sequestered into the intervillous space attract mononuclear cells. These cells secrete proinflammatory cytokines, these changes reduce placental blood flow and subsequently there is decreased transfer of nutrients and oxygen to the foetus and intrauterine foetal demise may occur.

As for the neonatal characteristics, the induction group had a significantly higher proportion of male infants compared to the spontaneous delivery group (57.6% vs 42.4%,  $p=0.033$ ). Sex differences in labour and delivery outcomes have been reported before, however the underlying mechanisms driving these sex-based differences are not fully understood and may involve a complex interplay of hormonal, genetic and physiological factors.

The birth weight distribution was similar between the two groups, with the majority of infants in both groups having a normal birth weight between 2500-4000g. Only a small proportion of infants in each group had low birth weights (less than 2500g) or macrosomia (more than 4000g) and the differences were not statistically significant. This suggested that neither labour induction nor expectant spontaneous labour had a significant impact on overall birth weight in our study population.

As for Apgar scores, a higher proportion of infants in the induction group had Apgar scores greater than 7 at 1 minute compared to the spontaneous delivery group (95.3% vs 84.7%,  $p=0.019$ ). This finding is in agreement with findings reported in a study carried out in the USA in 2023[43]. A similar finding is also reported in a study in India done in 2018, though in the study the difference is not statistically significant. This suggests better initial adaptation and wellbeing. It may be related to a factor like timely delivery. However, it is important to note that Apgar scores alone do not fully capture the complexity of neonatal status and longer-term outcomes should be considered. Moreover, different induction procedures may have some influence as well [62].

For neonatal resuscitation, the rate in the induction group was higher than that of the spontaneous delivery group (9.4% vs 3.5%). The 2.6 fold higher rate in the induction group was not significant

( $p=0.106$ ). This finding correlates with that reported in a study done in India with a rate of (4.9% vs 0.6%) in the induction group and spontaneous delivery group respectively and the difference was not significant as well ( $p=0.097$ ) [63].

As for the need for ventilation, infants in the induction group had a 2.6-fold higher risk of requiring ventilatory support compared to the spontaneous delivery group (15.3% vs 5.9%). This difference was statistically significant ( $p=0.039$ ). This finding indicates a potentially meaningful increase in respiratory distress or compromise among the new-borns of the induction group. This finding is similar to what was reported in a study carried out in Ethiopia in 2023, however it was contrary to what was reported in a study done in Greece in 2019 where induction of labour was associated with a significant reduction in the need for neonatal respiratory support [44, 60].

Regarding neonatal intensive care unit admission, a higher proportion of new-borns in the induction group were admitted to the neonatal intensive care unit compared to the spontaneous labour group (24.7% vs 16.5%). However this difference was not statistically significant ( $p=0.127$ ). This finding is in line with studies in Sri Lanka and Ethiopia carried out in 2022 with a rate at (15.8% vs 8.6%,  $p<0.001$ ) and in 2023 with a rate at (15.4% vs 5.7%  $p<0.001$ ) for the induction group and spontaneous delivery group respectively [44, 64]. This finding in our study though not statistically significant suggests that new-borns of the induction group are more prone to neonatal complications requiring intensive care. This finding could be due to the fact that induction of labour results in early neonatal complications that need special care in the NICU [55].

### **Limitations of the study**

This study was carried out in just two hospitals among the about 8000 hospitals in the country and with a small sample size which therefore limits its generalizability to the broader population of pregnant women who undergo induction of labour and those who go into spontaneous labour after diagnosis and treatment for malaria at term in the country and therefore cannot be utilized as a national statistics,



## **CONCLUSION AND RECOMMENDATIONS**

## CONCLUSION

At the end of this study we can draw the following conclusion,

- ❖ Most women in both groups were in their late 20s, married, students and had a secondary level education. They were mostly primigravidae and nulliparous women.
- ❖ Induction of labour as compared to spontaneous labour was significantly associated with increased risk of caesarean deliveries, labour abnormalities such as prolonged labour, precipitated labour and perineal tears.
- ❖ Higher rates of postpartum hemorrhage were observed with the induction group.
- ❖ Adverse neonatal outcome such as of non-reassuring fetal status was more in the women who delivered through induction.
- ❖ Infants delivered through induction had increased need for reanimation and admission into neonatal intensive unit.
- ❖ Women who went into spontaneous labour had a higher risk of foetal demise.

## RECOMMENDATIONS

### ❖ **To pregnant women,**

- To be cautious and seek medical attention as soon as they notice any irregularities especially in temperature.
- Adhere to all preventive measures put in place to reduce the burden of malaria infection in pregnancy including IPTp and sleeping under mosquito treated bed nets.

### ❖ **To health personnel**

- To propose induction of labor as against discharge for anticipation of spontaneous labor because the latter is associated with foetal demise.
- To include malaria prevention education during health promotion

### ❖ **To the Faculty of Medicine and Biomedical Sciences**

- To encourage further studies on the comparative outcome between induction of labour and spontaneous labour after complete treatment of malaria at term.

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**APPENDIX**

## APPENDIX I

### Informed Consent Form

**Title: Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour**

I, Mrs/Ms: \_\_\_\_\_, the undersigned, acknowledge that I have been informed and fully briefed by the final year medical student, **Mbele Chelsea Ngomo**, on the study entitled “Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour”, in view of her M.D. Thesis under the supervision of Prof. MBU ROBINSON ENOW, Dr. EBONG CLIFORD and Dr MBOUA BATOUM

She precised that I am free to accept or deny to participate in the research.

- I have received and understood information pertaining to the aim of this study, the procedure and possible constraints.
- I have been given adequate time to ask questions about the study.
- I accept that my medical records be consulted by the research personnel for research purposes only and all data concerning me will be strictly confidential.
- My participation can be interrupted at any time if the principal investigator deems it necessary or if I so wish.
- The research proposal has been reviewed and validated by the Ethics and Research Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I.
- At any time, I can ask for additional information from the investigator Mbele Chelsea Ngomo using number +237 678194360
- I hereby accept to participate in the study under the aforementioned conditions.

Date : \_\_\_\_/\_\_\_\_/\_\_\_\_

Investigator's signature

Participant's signature

Fiche de consentement éclairée.

Mme/Mlle \_\_\_\_\_

**Titre : « Accouchement après traitement du paludisme a terme : resultat comparatif entre le déclenchement du travail et le travail spontané attendu »**

L'étudiante **Mbele Chelsea Ngomo**, étudiante en 7ème année de formation médicale à la FMSB, m'a proposé de participer à une étude qu'ils mènent à l'Hôpital Central de Yaoundé et l'Hôpital Gyneco-Obstetrique et Pédiatrie de Yaoundé, pour sa thèse en fin de formation.

Cette étude a pour but principal d'évaluer le devenir des grossesses après traitement du paludisme a terme : déclenchement du travail vs travail spontané.

- Elle m'a précisé que je suis libre d'accepter ou de refuser sa proposition. J'ai reçu des informations concernant : le but de l'étude, la procédure et les analyses réalisées, les possibles risques et les contraintes liés à l'étude et les avantages liés à l'étude.
- J'accepte que mon dossier médical soit consulté par les membres de l'équipe de recherche et les informations utilisées dans le but de la recherche seulement. Toutes les informations personnelles seront confidentielles.
- Le protocole de recherche relatif à cette étude a été revu et validé par le comité institutionnel d'éthique et de la recherche de la faculté de médecine et des sciences biomédicales.
- À tout moment, je pourrai demander des informations supplémentaires à l'étudiante à travers le contact : +237 678194360
- J'accepte donc de participer à cette étude sous les termes susmentionnés.

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Signature de l'investigateur

Signature de la participante

Mbele Chelsea Ngomo  
19M001  
7<sup>TH</sup> year General Medicine  
Faculty of Medicine and  
Biomedical Sciences  
University of Yaounde I  
P.O.Box 1364 Yaounde

The president,  
Institutional Ethical Review Board,  
Faculty of Medicine and Biomedical Sciences,  
University of Yaoundé 1.

Dear Professor,

**Subject: An application for ethical clearance**

I am a seventh year medical student at the Faculty of Medicine and Biomedical Sciences, and it is with great honour that we write you to apply for authorization to carry out our research study. We wish to carry out a research entitled; **delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour**, under the supervision of Professor MBU ROBINSON ENOW, Dr. EBONG CLIFORD and Dr MBOUA BATOUM.

Attached to this demand is a copy of the research proposal. While hoping for a positive response, do accept our profound gratitude.

Yours sincerely,

MBELE CHELSEA NGOMO

Attachment: Copy of research proposal

### APPENDIX III: RESEARCH AUTHORIZATION I

REPUBLIQUE DU CAMEROUN  
Pays-Trouvill-Patrie  
MINISTÈRE DE LA SANTÉ PUBLIQUE  
HOPITAL GYNÉCO-OBSTÉTRIQUE  
ET PÉDIATRIQUE DE YAOUNDE  
HUMILITÉ - INTEGRITÉ - VÉRITÉ - SERVICE

HGOPY  
YGOPY

REPUBLIC OF CAMEROON  
Pays-Trouvill-Patrie  
MINISTRY OF PUBLIC HEALTH  
YAOUNDE GYNÆCO-OBSTETRIC  
AND PEDIATRIC HOSPITAL  
HUMILITY - INTEGRITY - TRUTH - SERVICE

COMITE INSTITUTIONNEL D'ETHIQUE DE LA RECHERCHE  
POUR LA SANTE HUMAINE (CIERSH)

Arrêté n° 0977 du MINISANTE du 18 avril 2012 portant création et organisation des  
Comités d'Éthiques de la Recherche pour la santé Humaines. (CERSH).

AUTORISATION N° 624 /CIERSH/DM/2024

CLAIRANCE ETHIQUE

Le Comité Institutionnel d'Éthique de la Recherche pour la Santé Humaine (CIERSH) a examiné le 21 février 2024, la demande d'autorisation et le Protocole de recherche intitulé « pregnancy outcome following treatment for malaria at term : immediate induction versus expectant spontaneous labour » soumis par l'étudiant MBELE CHELSEA NGOMO.

Le sujet est digne d'intérêt. Les objectifs sont bien définis. La procédure de recherche proposée ne comporte aucune méthode invasive préjudiciable aux participants. Le formulaire de consentement éclairé est présent et la confidentialité des données est préservée. Pour les raisons qui précèdent, le CIERSH de HGOPY donne son accord pour la mise en œuvre de la présente recherche.

MBELE CHELSEA NGOMO devra se conformer au règlement en vigueur à HGOPY et déposer obligatoirement une copie de ses travaux à la Direction Médicale de ladite formation sanitaire.

Yaoundé, le 28 FEV 2024

LE PRESIDENT

Prof MBU Robinson  
Directeur Général  
HGOPY

N°1827 ; Rue 1564 ; Ngoussou ; Yaoundé 5<sup>ème</sup>  
BP : 4362 Tél. : 242 05 92 94 / 222 21 24 33 / 222 21 24 31 Fax : 222 21 24 30  
E-mail : hgopy@hotmail.com / hgopy@hgopy.cm

### APPENDIX III: RESEARCH AUTHORIZATION II

REPUBLIC OF CAMEROON  
Foua-Foua-Patle  
MINISTRE DE LA SANTE PUBLIQUE  
SECRETAIRAT GENERAL  
DIRECTION DE L'HOPITAL CENTRAL DE YAOUNDE  
SECRETAIRAT MEDICAL  
N° 0121 Dp / AP/MINSANTE/SG/DHCY/CM/SM

REPUBLIC OF CAMEROON  
Foua-Foua-Patle  
MINISTRE DE LA SANTE PUBLIQUE  
GENERAL SECRETARY  
DIRECTORATE OF CENTRAL HOSPITAL OF YAOUNDE  
MEDICAL SECRETARY  
Yaoundé, le 10<sup>th</sup> FEB 2024

**ACCORD DE PRINCIPE**

Je soussigné Professeur FOUDA Pierre Joseph, Directeur de l'Hôpital Central de Yaoundé, marque mon Accord de Principe à Madame MBELE Chelsea NGOMO, étudiante en 7<sup>ème</sup> année de Médecine Générale à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I, sous le thème « PREGNANCY OUTCOME FOLLOWING TREATMENT FOR MALARIA AT TERM : IMMEDIATE INDUCTION VERSUS EXPECTANT SPONTANEOUS LABOUR » dans le service de Gynécologie et Obstétrique à l'Hôpital Central de Yaoundé, sous la codirection du docteur EBONG Cliford EBONTANE.

Ampliations :

- Conseiller Medical ;
- Chef service concerné ;
- Intéressée;
- Chrono/Archives.

Pour le Directeur et par ordre  
Le Conseiller Médical.

Le Conseiller Médical

Pr. Dr. Pierre Ngolo Logo





<b>3. HISTORY OF PREGNANCY</b>		
19.	Gestational age at time of diagnosis(in weeks):	
20.	Number of antenatal consultations done:	
21.	Gestational age at first antenatal consultation( in weeks):	
22.	Antenatal consultations done by: Gynaecologist = 1; Resident/Intern= 2; General Practitioner =3; Midwife = 4; Nurse = 5	
23.	HIV done? Yes = 1; No = 2	
24.	Hepatitis B done? Yes = 1; No = 2	
25.	Hepatitis C done? Yes = 1; No = 2	
26.	Syphilis done? Yes = 1; No = 2	
27.	Toxoplasmosis done? Yes = 1; No = 2	
28.	Anaemia in pregnancy? Yes = 1; No = 2	
29.	Did you take daily iron and folic acid? Yes = 1; No = 2	
30.	Number of VAT(anti-tetanus vaccine) doses:	
31.	Sleeping under insecticide treated long lasting mosquito nets? Yes = 1; No = 2	
32.	Number of doses intermittent preventive treatment (TPI):	
33.	How many ultrasounds done:	
<b>Confirmed Cases of Malaria in Pregnancy</b>		
34.	Treatment completed? Yes=1; No=2	
35.	Bishop's Score:	
<b>4. DELIVERY OPTION</b>		
36.	Immediate Induction=1; Discharge and wait for spontanoous labour=2	
<b>Complications due to Induction</b>		
37.	Failure of induction=1; Prolonged labour=2; Perineal tears=3; Postpartum hemorrhage=4; Uterine rupture=5; Nonreassuring fetal status=6; Intrauterine fetal death=7; Cord Prolapse=8; Infection=9, Birth trauma=10	
<b>Complications following Spontaneous labour</b>		

Delivery after treatment for malaria at term: comparative outcome between induction of labour and expectant spontaneous labour

38.	Prolonged labour=2; Perineal tears=3; Postpartum hemorrhage=4; Uterine rupture=5; Nonreassuring fetal status=6; intrauterine fetal death=7; Cord Prolapse=8; Infection=9, Birth trauma=10	
<b>Mode of Delivery</b>		
39.	Vaginal birth=1; Cesarean section=2	
<b>Characteristics of Newborn</b>		
40.	Early neonatal death? Yes=1, No=2	
41.	If alive sex? Male=1, Female=2	
42.	Apgar score at 1 <sup>st</sup> minute:	
43.	Apgar score at 5 <sup>th</sup> minute:	
44.	Newborn birthweight:	
45.	Fetal length in cm:	
46.	Fetal head circumference in cm:	
47.	Fetal mid upper arm circumference in cm:	
48.	Need for resuscitation? Yes=1; No=2	
49.	Need for ventilation? Yes=1; No=2	
50.	Neonatal intensive care unit(NICU) admission? Yes=1; No=2	
51.	Reason for NICU admission? Asphyxia=1; Intrauterine growth restriction=2; Low birth weight=3; neonatal infection=4	