### REPUBLIC OF CAMEROON PEACE-WORK-FATHERLAND

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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

# IMMEDIATE NEONATAL OUTCOME FOLLOWING MULTIFETAL PREGNANCIES IN TWO HOSPITALS IN YAOUNDE

Thesis written and defended publicly in partial fulfilment of the requirements for the award of the *Medicinae Doctor* (MD) degree by:

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Academic year 2023-2024

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### **DEDICATION**

To my lovely parents,

Mr Batebe-Agbor Boniface

and

Mrs Fotabong Magdaline Epse Batebe

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# THE ADMINISTRATIVE AND TEACHING STAFF FOR 2023/2024 OF THE FACULTY OF MEDICINE AND BIOMEDICAL SCIENCES

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### KEY:

**HD**= Head of Department

**P**= Professor

**AP**= Associate Professor

**SL**= Senior Lecturer

**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)

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 honour 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

**SUMMARY** 

Background: Multifetal pregnancies are considered high risk because they have an increased

incidence of perinatal mortality and morbidity worldwide. This is quite common in our setting

occurring in about 2.8% of pregnancies. These pregnancies can imply an increased risk for

women and children because of higher rates of obstetrical complications. It is therefore

important to understand the relationship between these pregnancies and their outcomes.

Objective: The main objective was to evaluate immediate neonatal outcome following

multifetal pregnancies.

**Methods:** We conducted a retrospective cohort study at the Yaoundé Gynaecology, Obstetrics

and Paediatrics Hospital and the Yaoundé Central Hospital. All files of pregnant women who

delivered in the selected hospitals from January 2018 to December 2022 were included. The

exposed group consisted of files of pregnant women with multifetal pregancies who were

admitted in labor and delivered in these hospitals. The unexposed group were files of women

with singleton pregnancies who were admitted in labor and delivered just after the cases of the

multifetal pregnancy.

**Results:** We had a total of 150 exposed and 150 unexposed cases. The highest number of

multifetal pregnancies occurred among women aged between 30-35 years (26.7%) with a mean

maternal age of  $27.9 \pm 6.2$  years. The highest level of education among women in the exposed

group was high school (40.0% vs. 28.0%) in contrast to women in the unexposed group who

were mostly university graduates (46.7% vs. 30.7%) ( $\mathbf{p} < 0.05$ ). Grand multigravidity and

grand multiparity were associated with multifetal pregnancies (p<0.001). Women in the

exposed group had a 1.7-fold higher risk of caesarean delivery than women in the unexposed

group (p = 0.002). After multivariate analysis using the binary logistic regression method,

neonates in the exposed group were significantly less likely to fall within the birth weight range

of 2500-4000 (aRR: 0.27, 95% CI 0.16-0.47; adjusted p < 0.001).

**Conclusion:** Multifetal pregnancies were associated with adverse neonatal outcomes such as

low birth weight.

**Keywords:** Multifetal, neonatal, outcome, pregnancy.

**RESUME** 

Contexte: Les grossesses multifœtales sont considérées comme étant à haut risque car elles

présentent une incidence accrue de mortalité et de morbidité périnatale dans le monde entier.

Dans notre pays, ce type de grossesse est assez courant, puisqu'il concerne environ 2,8 % des

grossesses. Ces grossesses peuvent impliquer un risque accru pour les femmes et les enfants en

raison des taux plus élevés de complications obstétricales. Il est donc important de comprendre

la relation entre ces grossesses et leurs devenir.

**Objectif**: L'objectif principal était d'évaluer l'issue néonatale immédiate après les grossesses

multifœtales.

Méthodes: Nous avons mené une étude de cohorte rétrospective à l'hôpital de gynéco-

obstétrique et pédiatrique de Yaoundé et à l'hôpital centrale de Yaoundé. Tous les dossiers des

femmes enceintes ayant accouché dans les hôpitaux sélectionnés de janvier 2018 à décembre

2022 ont été inclus. Le groupe exposé était constitué des dossiers de femmes enceintes

présentant des grossesses multifœtales qui ont été admises en travail et ont accouché dans ces

hôpitaux. Le groupe non exposé était constitué de dossiers de femmes avec des grossesses

monofœtales qui ont été admises en travail et ont accouché juste après les cas de grossesse

multifætale.

Résultats: Nous avons eu un total de 150 cas exposés et 150 cas non exposés. Le plus grand

nombre de grossesses multifœtales a été enregistré chez les femmes âgées de 30 à 35 ans (26,7

%), avec un âge maternel moyen de  $27.9 \pm 6.2$  ans. Le niveau d'éducation le plus élevé parmi

les femmes du groupe exposé était le lycée (40,0 % contre 28,0 %), contrairement aux femmes

du groupe non exposé qui étaient pour la plupart à l'université (46,7 % contre 30,7 %) (p <

0,05). La grande multigravité et la grande multiparité ont été associées à des grossesses

multifœtales (p<0,001). Les femmes du groupe exposé présentaient un risque d'accouchement

par césarienne 1,7 fois plus élevé que les femmes du groupe non exposé (p = 0,002). Après une

analyse multivariée utilisant la méthode de régression logistique binaire, les nouveau-nés du

groupe exposé étaient significativement moins susceptibles de se situer dans la fourchette de

poids de naissance de 2500-4000 (RR : 0,27, 95% CI 0,16-0,47 ; p ajusté < 0,001).

Conclusion: Les grossesses multifœtales sont associées au faible poids de naissance.

Mots-clés: Multifœtale, néonatale, issue, grossesse.

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### LIST OF ABBREVIATIONS

**ANC:** Antenatal Consultations

**ART:** Assisted Reproductive Technologies

ACOG: American College of Obstetrics and Gynaecology

**β-hCG:** beta-human Chorionic Gonadotropin

**FSH:** Follicle Stimulating Hormone

**IVF:** In Vitro Fertilization

**PPROM:** Preterm Premature Rupture of Membranes

**TRAP:** Twin Reversed Arterial Perfusion

**WHO:** World Health Organization

YCH: Yaoundé Central Hospital

YGOPH: Yaoundé Gynaecology, Obstetrics and Paediatrics Hospital

**CHAPTER 1: INTRODUCTION** 

#### 1 INTRODUCTION

#### 1.1 BACKGROUND

The simultaneous development of two or more fetuses in the uterus is referred to as multifetal pregnancy or multiple gestation [1]. It presents unique challenges, both maternal and fetal, due to increased risk of pregnancy-related deaths [2]. Multifetal pregnancies are regarded as high risk pregnancies in the whole world with a twin birth rate of 31.2 per 1000 live births and a triplet or higher order birth rate of 78.9 per 100,000 live births according to the United States' National Centre for Health Statistics[3].

Studies have shown that, the highest incidence of multiple pregnancies has been found in low and middle-income countries particularly in Sub-Saharan Africa with an average twinning rate of 20 per 1000 births compared to 10 per 1000 deliveries in Europe and 5-6 per 1000 deliveries in Asia[4].

Globally, there is extensive evidence that multifetal births are associated with a substantially higher risk of perinatal mortality and morbidity with a mortality rate being six times higher compared to that with singleton births [1,5,6]. The complications include prematurity, low birth weight, intrauterine growth restriction and fetal demise [7]. These pregnancies are responsible for 17% of all preterm births (before 37 weeks of gestation), 23% of early preterm births (before 32 weeks of gestation), and 24% of low birth weight infants(a weight at birth of a neonate less than 2,500 grams but greater than 1500 grams) [8,9].

In Cameroon, studies have been done to determine the prevalence and outcomes of multifetal pregnancies, one of which revealed a prevalence of 2.8% in Bamenda, in 2022 [1]. This study evaluated the neonates at birth and found adverse fetal outcomes such as prematurity, low birth weight and birth asphyxia, however little is known about the outcomes in the early neonatal period following multiple gestations in the public hospitals in Yaounde.

Due to the increased risks associated with multifetal pregnancies, it is necessary to assess the early neonatal outcomes in our setting in order to propose preventive measures in a bid to improve these outcomes.

#### 1.2 RATIONALE

The occurrence of multifetal pregnancies has significantly increased over the past years, most likely due to advancements in assisted reproductive technologies such as in vitro fertilization and induction of ovulation [5,10]. As stated in the introduction the highest incidence of multifetal pregnancies has been found in low and middle-income countries particularly in Sub-

Saharan Africa [4]. This implies an increased risk for women and children because of higher rates of obstetrical complications and lower access to adequate management skills in these countries [11].

A better understanding of the relationship between multifetal pregnancies and the immediate neonatal outcome in our setting is imperative due to the distinct anatomical and physiological characteristics of multifetal gestations as well as the difficulties faced by healthcare workers in managing these pregnancies.

We therefore proposed to carry out this study to evaluate the immediate neonatal outcome following multifetal pregnancies in two hospitals in Yaoundé.

#### 1.3 RESEARCH QUESTION

What is the immediate neonatal outcome following multifetal pregnancies at the Yaoundé Gynaecology, Obstetrics and Paediatrics Hospital and in the Yaoundé Central Hospital?

#### 1.4 RESEARCH HYPOTHESIS

Multifetal pregnancies are most likely to be associated with a poorer neonatal outcome compared to singleton pregnancies.

#### 1.5 OBJECTIVES

#### 1.5.1 Main Objective

The main objective was to evaluate the immediate neonatal outcome following multiple gestations in 2 hospitals in Yaoundé.

#### 1.5.2 Specific Objectives

Our specific objectives were to:

- 1. Describe the sociodemographic and obstetrical profiles of women with multifetal pregnancies who gave birth during the study period.
- 2. Describe the clinical profiles of neonates born following multifetal pregnancies.
- 3. Determine the immediate neonatal outcome associated with multifetal pregnancies.
- 4. Compare the immediate neonatal outcome of multifetal pregnancies with those of singleton pregnancies.

#### 1.6 DEFINITION OF OPERATIONAL TERMS

- Antenatal care (ANC): It 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 [12].
- Assisted reproductive technology: These are techniques that involve manipulation of oocytes outside the body and other medical procedures used primarily to address infertility. [13].
- In vitro Fertilization (IVF): It is medical procedure whereby an oocyte is fertilized by sperm in a petri dish or elsewhere outside the body [13].
- Singleton birth: It refers to the birth of only one child during a single delivery with a gestation of 20 weeks or more [14].
- Preterm birth: It is defined by WHO as all live births before 37 completed weeks of gestation [15].

LITERATURE REVIEW

#### 2 LITERATURE REVIEW

#### 2.1 INTRODUCTION

The incidence of multifetal pregnancies has increased dramatically, and this is mainly due to assisted reproductive techniques such as in vitro fertilization and ovulation induction drugs [16,17].

Multifetal pregnancies may result from two or more fertilization events, from a single fertilization followed by a splitting of the zygote, or both.

Multifetal gestations remain problematic for both the mother and her foetuses as it accounts for about 15% of all infant deaths[18].

A good understanding of the early neonatal outcomes following multiple gestations is warranted by health care providers in order to propose preventive measures for better outcomes.

#### 2.1.1 Definition

According to the American College of Obstetricians and Gynaecologists, a multifetal pregnancy is defined as a pregnancy with more than one fetus [19].

#### 2.1.2 Epidemiology

Births from multifetal pregnancies account for 4-5% of all births [20]. In the United States there was a reported twin birth rate of 31.2 per 1000 live births [1,3]. Higher rates are found in low and middle-income countries particularly in Sub-Saharan Africa with an average twinning rate of 20 per 1000 births.

In Cameroon, studies have been done to evaluate the prevalence of multiple pregnancies, one of which revealed a prevalence 2.8% in Bamenda, in 2022.

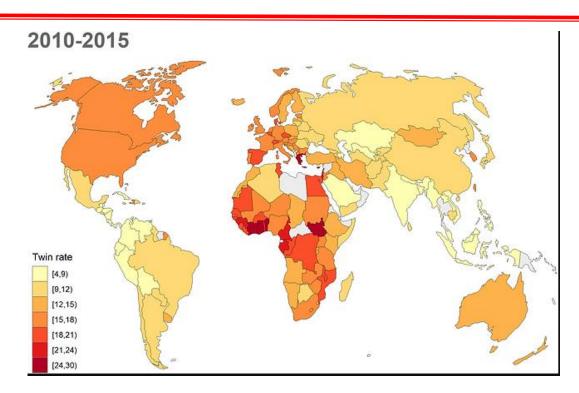


Figure 1: Twinning rates per country in 2015.

Moving from the yellow to brown areas, the twinning rate increases in the countries. We note the highest incidence in Ivory Coast, Ghana and South Sudan [21].

#### 2.2 RECALL

#### **2.2.1 Anatomy**

#### **2.2.1.1** The uterus

The nongravid uterus is situated in the pelvis between the bladder anteriorly and the rectum posteriorly. 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. The isthmus is the union site of these two. It is of special obstetrical significance because it forms the lower uterine segment during pregnancy [18]. The nulligravid uterus measures 7 to 8 cm in length and 4-5cm in width but these values are higher in multiparous women. The uterus averages 30-40g and typically weighs more in

parous women. In nulligravidae, 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 [22].

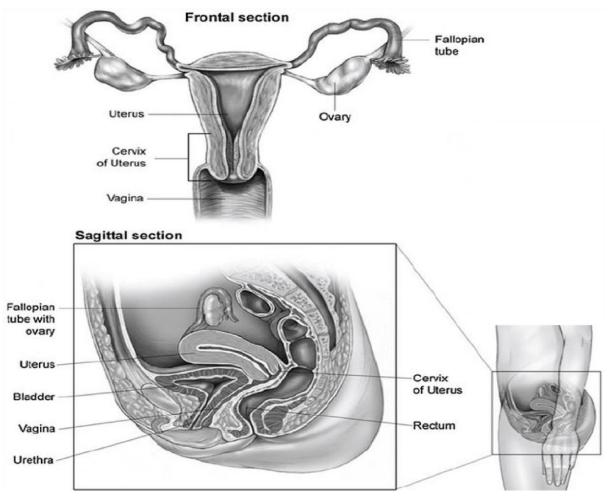


Figure 2: Anatomy and location of the uterus [18].

Pregnancy stimulates remarkable uterine growth owing 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.

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 [22].

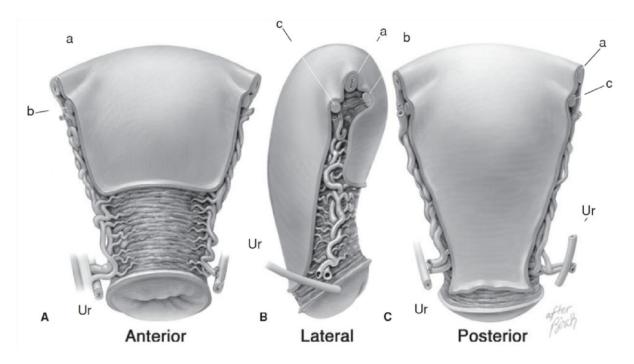


Figure 3: Overview of the uterus.

A=anterior, B=right lateral, C=posterior views. a=fallopian tube, b=round ligament, c=uteroovarian ligament, Ur=ureter [18].

### 2.2.2 Reproductive Physiology

#### 2.2.2.1 Physiology of the menstrual cycle

The menstrual cycle is a coordinated cyclical change that occurs under hormonal influences resulting in anatomic and physiological changes to the ovary and uterus. It occurs as a result of the joint action of the hypothalamus, pituitary gland, ovaries and the endometrium [23].

These changes enable normal pregnancy or shedding during menstruation. The average age of menarche and menopause is 12yrs old and 51 years respectively [24].

The menstrual cycle can be divided into 03 different phases;

- ❖ The follicular phase: the release of GnRh from the hypothalamus triggers the release of follicle stimulating hormone from the anterior pituitary gland. FSH promotes ovarian follicles to grow to develop causing the dominant follicle containing oocyte to grow. Follicular granulosa cells produce estrogen which in turn promotes endometrial proliferation. The rise in the levels of estrogen results in a negative feedback mechanism on the hypothalamus-pituitary axis through follicular inhibin and stops further FSH production.
- ❖ The ovulatory phase: Increasing follicular estrogen causes an alteration in the pituitary GnRH pulsatility resulting in production of LH and later ovulation.
- ❖ The luteal phase: It starts from the end of ovulation to the first day of the menstrual flow [25]. The follicle degenerates after release of oocyte to become the corpus luteum which produces estrogen and progesterone (from the theca cells) these hormones act on the endometrium to induce secretory changes such a thickening of the endometrial lining and increase vascularity. After 14 days, the corpus luteum undergoes involution to produce the corpus albicans. If implantation occurs, beta HCG allows the continued production of progesterone by preservation of the corpus luteum. In the absence of pregnancy, the corpus luteum degenerates leading to a rapid fall in progesterone and estrogen, initiating menstruation.

#### **\*** Menstruation

The rapid drop in progesterone levels result in shedding of the unused endometrium. This process is enabled by the release of inflammatory mediators such as prostaglandins, interleukin, TNF leading to vasospasm in the spiral arteries, hypoxia and endometrial devitalization leading to the loss of the endometrial layer and bleeding. At the end of menstruation, all steroid hormones would return to basal levels, restarting the negative feedback mechanism and GnRH FSH production will begin the new cycle.

#### The menstrual cycle

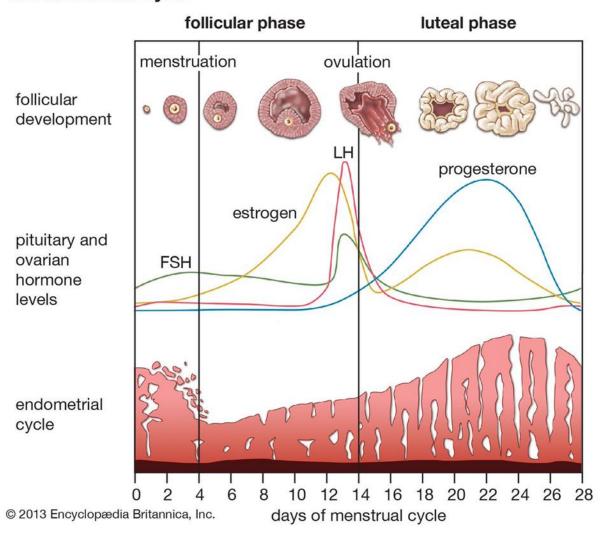


Figure 4: The menstrual cycle [26].

#### 2.2.2.2 Fertilization

This is the fusion of male and female gamete, usually occurring at the ampulla of the fallopian tube resulting in the formation of the ovum which later travels to the uterus for implantation.

If the oocyte is not fertilized here, it slowly passes to the uterus, where it becomes degenerated and is absorbed [27].

During ovulation, the secondary oocyte is released from the ovary into the Fallopian tube. Transport through the tube is accomplished by the directional movement of cilia and tubal peristalsis.

For fertilization to occur successfully the spermatozoa need to be present in the Fallopian tube at the time of arrival of the oocyte, this usually takes place 2 days preceding or on the day of ovulation.

The process of fertilization involves at the molecular level, the passage of spermatozoa between follicular cells, through the zona pellucida into the oocyte cytoplasm. The fusion 02 nuclei and intermingling of maternal and paternal chromosomes leads to the formation of the zygote.

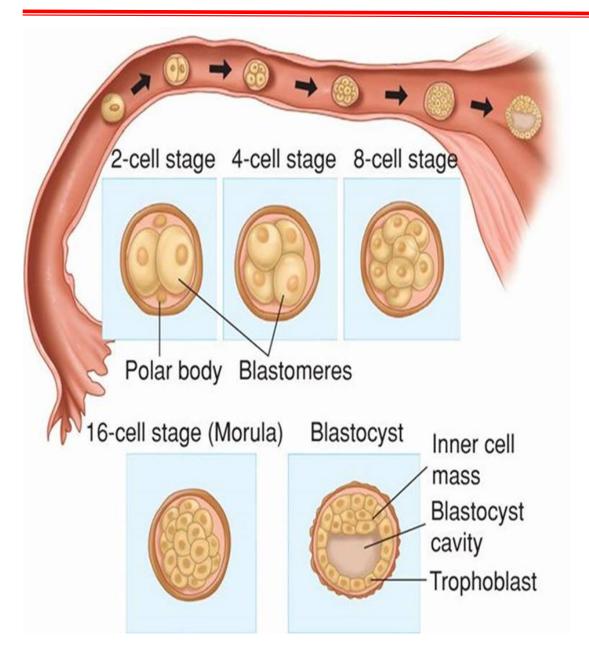


Figure 5: Zygote cleavage and blastocyst formation.

The morula period begins at the 12- to 16-cell stage and ends when the blastocyst forms, which occurs when there are 50 to 60 blastomeres present. The polar bodies, shown in the 2-cell stage, are small nonfunctional cells that degenerate [18].

#### 2.2.2.3 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 (Naegele's rule) [22].

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  $\beta$  submit 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.  $\beta$ -hCG levels peak at 10-12 weeks' gestation and decrease afterward. Generally, serum and urine levels return to normal (<5mIU/mL), 21–24 days after delivery or after a fetal loss [22].

- 2. <u>Imaging studies</u>; 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 [22].
- 3. <u>Fetal Heart Tones</u>; 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 [22].
- 4. <u>Uterine size/fetal palpation</u>; 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 [22].

#### 2.2.2.4 Antenatal Care

According to the WHO, antenatal care (ANC) can be defined as the care provided by skilled healthcare 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 REFERENCE WHO.

The figure below shows how often ANC visits should be done and what should be done at each visit;

First Visit	11-13 <b>W</b> EEKS	16-20 WEEKS	26-28 WEEKS
1. History and physical (H&P) 2. Labs:  Hct/Hgb Rh factor Blood type Antibody screen Pap smear Gonorrhea and Chlamydia cultures Urine analysis (protein, glucose, ketones) Urine culture Infection screen: Rubella, syphilis, hepatitis B, human immunodeficiency virus (HIV), tuberculosis (TB) Cystic fibrosis screen Urine drug screen Hemoglobin	<ol> <li>Fetal exam:         <ul> <li>Fetal heart tones</li> </ul> </li> <li>Urine dip: Protein, gleukocytes</li> <li>First-trimester screen</li> </ol>	3. Urine dip: Protein, glucose,	1. H&P 2. Fetal exam:  Fetal heart  Fundal height 3. Labs:  Complete blood count  Ab screen  Gonorrhea and Chlamydia cultures (optional)  Diabetes screen  Urine dip: Protein, glucose, leukocytes  Syphilis screen (optional)  Give anti D immunoglobulin if indicated (28 weeks)
1. H&P 1 2. Fetal exam: 2 = Fetal heart = Fundal height 3. Urine dip: protein, glucose, leukocytes 3	. H&P	Week 38  Week 39  1. H&P 2. Fetal exam: Fetal heart Fundal height Fetal	Week 40  1. H&P 2. Fetal exam:  = Fetal heart  = Fundal height  = Fetal presentation 3. Urine dip: Protein, glucose, leukocytes

Figure 6: Content and frequency of antenatal consultations [28].

#### 2.3 AT-RISK PREGNANCY

At-risk pregnancy can be referred to as one in which the mother, fetus or newborn is or may possibly be at increased risk of morbidity or mortality before, during or after delivery. The presence of the following can increase risk during pregnancy:

- Hyperemesis gravidarum
- Hemorrhagic disorders
- Hypertensive disorders in pregnancy

- Multifetal pregnancies
- Infections
- Gestational diabetes
- Fetal growth disorders
- Intrauterine fetal deaths
- Premature rupture of membranes
- Preterm labor
- Etc

In this study, we will focus on multifetal pregnancies.

#### 2.3.1 Multifetal pregnancy

#### 2.3.1.1 Mechanisms of multifetal pregnancies

Multifetal pregnancies are often described by zygosity, amnionicity, and chorionicity, which are the number of zygotes, amnions, and chorions, respectively. Twin fetuses most often result from fertilization of two separate ova, which yields dizygotic or fraternal twins. Less often, twins arise from a single fertilized ovum that then divides to create monozygotic or identical twins [18].

#### **2.3.1.1.1** Monozygotic

The rate of monozygotic twinning is 1 in 250 pregnancies, and 30% of all twins are monozygotic. Monozygotic twins are the result of cleavage of a fertilized single ovum by a single sperm. The process remains uninfluenced by race, age, and parity, but is affected by infertility treatment interventions thought to occur due to injury to the zona pellucida that influences splitting. Timing of division of the embryo dictates placentation.

- **Dichorionic Diamniotic**: If the zygote divides within 72 hours of fertilization prior to the morula phase and trophoblast differentiation, a dichorionic diamniotic twin pregnancy occurs with separate or fused placentas, 2 chorions, and 2 amnions. This accounts for one-third of monozygotic twinning. Dichorionic gestations have the lowest rate of overall complications [22].
- Monochorionic Diamniotic: Monochorionic diamniotic pregnancy results from division on day 4-8, after differentiation of the trophoblast has occurred but prior to the formation of the amnion. A single placenta is found with a common chorion and 2 amnions. This accounts for two-thirds of monozygotic twinning. Monochorionic pregnancies have an increased risk of adverse outcomes including fetal structural

- malformations, intrauterine growth restriction, and spontaneous premature birth. They are also associated with an increased risk of twin-twin transfusion syndrome.
- Monochorionic Monoamniotic: Monoamniotic twins are among the rarest form of twins with an incidence of 1 in 10,000 pregnancies. This occurs with division after differentiation of the amnion on day 8-13 after fertilization. There is a single placenta, 1 chorion, and I amnion. Congenital anomaly rates are as high as 25%, and fetal weights are most often discordant. Perinatal mortality rates as high as 80% have been recorded, primarily due to cord entanglement due to the absence of a dividing membrane between the fetuses.
- Conjoined Twins: Conjoined twins may occur due to incomplete splitting of an embryo or late splitting on day 13 or beyond; incidence is 1 in 50,000-100,000 births. Conjoined twins are described by site of union: thoracopagus (chest), omphalopagus (abdominal wall), craniopagus (head), and pyopagus (sacrum) [22].

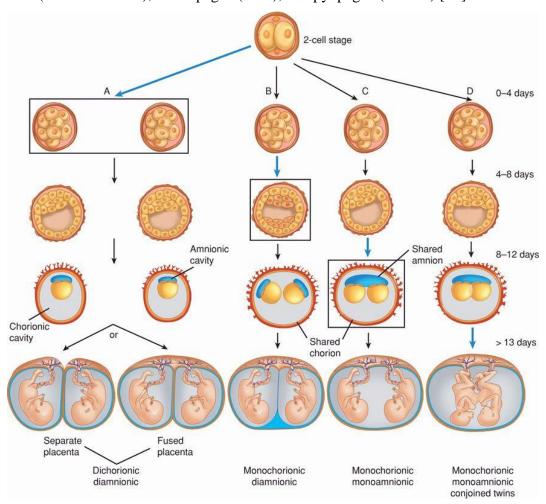


Figure 7: Mechanism of monozygotic twinning.

Black boxing and blue arrows in columns A, B, and C indicate timing of division. **A.** At 0 to 4 days postfertilization, an early conceptus may divide into two. Division at this early stage creates two chorions and two amnions (dichorionic, diamnionic). Placentas may be separate or fused. **B.** Division between 4 and 8 days leads to formation of a blastocyst with two separate embryoblasts (inner cell masses). Each embryoblast will form its own amnion within a shared chorion (monochorionic, diamnionic). **C.** Between 8 and 12 days, the amnion and amnionic cavity form above the germinal disc. Embryonic division leads to two embryos with a shared amnion and shared chorion (monochorionic, monoamnionic). **D.** Differing theories explain conjoined twin development. One describes an incomplete splitting of one embryo into two. The other describes fusion of a portion of one embryo from a monozygotic pair onto the other [18].

#### **2.3.1.1.2** Dizygotic

Although rates vary globally, in the United States, dizygotic twinning occurs in 1 in 80 births. A traditional formula approximates triplets to occur in 1 in 6400 births and quadruplets to occur in 1 in 512,000 births. Overall, 70% of all twins are dizygotic. Dizygotic twins occur when 2 separate ova are fertilized by 2 separate sperm.

• **Dichorionic Diamniotic:** As each pregnancy will have its own placenta, every dizygotic pair will be dichorionic and diamniotic. Incidence is affected by age, race, heredity, nutrition, parity, and fertility therapies. Superfecundation refers to fertilization of 2 ova during separate episodes of coitus, not necessarily from sperm of the same individual [22].

#### 2.3.1.1.3 Superfecundation and superfetation

Superfecundation is fertilization of two ova within the same menstrual cycle but not at the same coitus nor necessarily by sperm from the same male. The latter leads to heteropaternity. This is an extremely rare phenomenon with a reported frequency of 2.4% heteropaternal superfecundation among dizygotic twins whose parents were involved in paternity disputes [29].

In superfetation, an interval as long as or longer than a menstrual cycle intervenes between fertilizations. Superfetation is not known to occur spontaneously and is likely due to ART. It is a rare event that involves getting pregnant a second time while already pregnant [30]. Pseudo-superfetation often results from markedly unequal growth of twins with the same gestational age.

#### 2.3.1.2 Risk Factors

#### 1. **Dizygotic**:

- Race and ethnicity greatly influence twinning rates. Multiple gestations occur
  most commonly among African-Americans and least frequently among
  Asians, with an intermediate occurrence among whites. One theory relates to
  varying levels of follicle-stimulating hormone (FSH) across peoples. Maternal
  heredity of twinning increased rates up to 1 in 60 births.
- Maternal age is an independent risk in twinning. Women greater than 30 have a greater chance of multiple conception [31]. Multifetal gestations naturally occur in 16.3 of 1000 births in women < 20 years old, but 71 of 1000 births in women> 40 years old. The peak age is 37 years, when FSH levels reach maximum levels. Greater parity is an independent risk factor for twinning.
- Increased gonadotropin levels, namely FSH, are related to an increase in twinning. This occurs as a rebound effect of increased release of pituitary gonadotropin after the discontinuation of long-term oral-hormonal contraceptives in the first spontaneous cycle.
- Ovulation induction increases the chances of multifetal gestations due to the recruitment of multiple follicles. The estrogen analogue clomiphene citrate increases the incidence of dizygotic gestations to 5-10%. The ART of in vitro fertilization (IVF) was responsible for a massive increase in multifetal gestation rates directly related to the number of embryos transferred during each cycle. Rates have decreased with a concurrent decrease in the number of transferred embryos. In 2010, 26% of ART gestations were twin pregnancies, and 1.3% were of a higher order.

#### 2. Monozygotic:

 Monozygotic twinning rates are not influenced by factors such as race, age and parity. This type of twinning is affected by ART (Assisted Reproductive Tecnologies) including IVF (In Vitro Fertilization) and intra-cytoplasmic sperm injection due to disruption of the pellucida.

#### 2.3.1.3 Diagnosis of multifetal pregnancies

#### 2.3.1.3.1 Clinical Evaluation

Women carrying multiple gestations may be initially asymptomatic or may have normal signs and symptoms of pregnancy (eg, breast tenderness, fatigue, nausea, vomiting)[32]. Multiple gestations may be suspected in the setting of hyperemesis gravidarum or in a patient who has undergone assisted reproductive technology. A complete history, including a family history, should be taken in every woman suspected to have multiples. Early diagnosis can help with management of the associated risks posed by twins. Accurate fundal height measurement can be an initial tool. With multiples, uterine size is typically larger during the second trimester than that expected for a singleton.

Palpation of fetal parts to diagnose twins before the third trimester is difficult. Even then, obesity or hydramnios can hinder assessment. Palpating two fetal heads strongly supports the diagnosis. Moreover, a hand-held Doppler ultrasonic unit may isolate two fetal heartbeats if their rates are clearly distinct from each other and from the mother. Overall, however, clinical criteria alone to diagnose multifetal gestations is unreliable. In the Routine Antenatal Diagnostic Imaging with Ultrasound (RADIUS) trial, for 37 percent of women who did not have a screening ultrasound examination, their twin pregnancy was not diagnosed until 26 weeks' gestation. In 13 percent of unscanned women, their multifetal gestation was identified only during their admission for delivery [18]

#### 2.3.1.3.2 Imaging Studies

Sonographic examination should detect practically all sets of twins. Further, it should aim to determine fetal number, estimated gestational age, chorionicity, and amnionicity. Importantly, the risk for many twin-specific complications varies in relation to these

Table I: Incidence of some complications related to twin characteristics [18].

Type of twinning	Rates of Tw	Rates of Twin-Specific complications in percent			
	Twins	Fetal-	Preterm	Placental	Perinatal
		growth	Delivery	Vascular	Mortality
		Restriction		Anastomosis	
Dizygotic	80	25	40	0	10-12
Monozygotic	20	40	50	-	15-18
Diamniotic/dichorionic	6-7	30	40	0	18-20
Diamniotic/monochorionic	13-14	50	60	100	30-40
Monoamniotic/monochorionic	<1	40	60-70	80-90	58-60
Conjoined	0.002- 0.008	-	70-80	100	70-90

With sonography, separate gestational sacs, if present, can be identified early in twin pregnancy

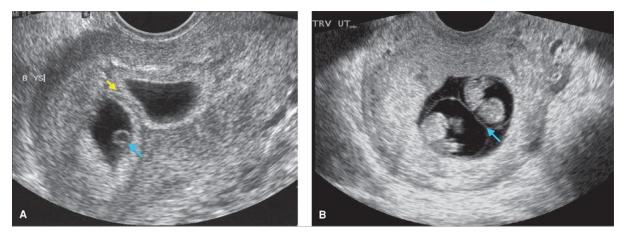


Figure 8: Sonograms of first-trimester twins.

A. Dichorionic diamnionic twin pregnancy at 6 weeks' gestation. Note the thick dividing chorion (yellow arrow). One of the yolk sacs is indicated (blue arrow). B. Monochorionic diamnionic twin pregnancy at 8 weeks' gestation. Note the thin amnion encircling each embryo, resulting in a thin dividing membrane (blue arrow) [18].

Subsequently, each fetal head should be seen in two perpendicular planes to avoid mistaking a fetal trunk for a second fetal head. Ideally, two fetal heads or two abdomens are seen in the same image plane to avoid scanning the same fetus twice and interpreting it as twins. Higher-order multifetal gestations are more challenging to evaluate. Even in the first trimester, identifying the actual number of fetuses and their position can be diffcult.

Ultrasonography is a vital tool in diagnosis of multiple gestation and chorionicity. Transvaginal approach allows detection as early as 5 weeks. Identification of chorionicity is essential to patient counselling for the remainder of the pregnancy. Counting the number of gestational sacs, yolk sacs, and fetal poles, and measuring the thickness of a dividing membrane are the first steps. Later in pregnancy, precise determination of chorionicity poses more difficulty. Interrogation involves identification of the number of placentas relative to the number of fetuses and attempted visualization of the dividing membrane for 2 versus 4 layers of the fused amnion-chorion and for the thickness of the membrane;

#### 2.3.1.3.2.1 Dichorionic diamniotic

A membrane > 2 mm is generally indicative of dichorionicity. In the latter part of the first trimester, the base of the intertwine membrane should be inspected. It appears as the "twin peak" or "lambda" sign, which is a triangular projection of tissue extending beyond the chorionic placental surface and is indicative of a dichorionic gestation. Two placentas are most commonly noted; however, they may be fused, which may make it difficult to identify 2 separate entities

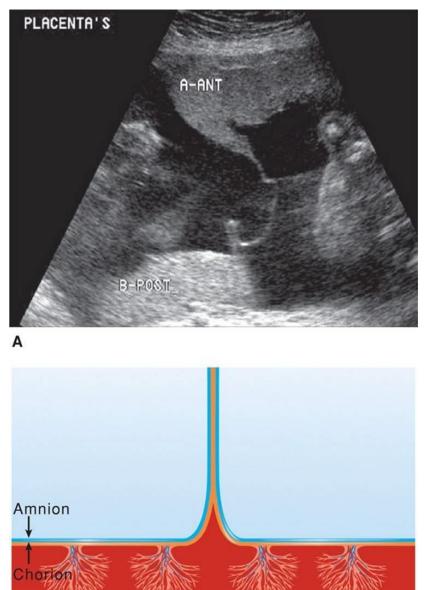


Figure 9:Twin-peak or lambda sign

В

A. Sonographic image of the "twin-peak" sign, also termed the "lambda sign" in a 24-week gestation. At the top of this sonogram, tissue from the anterior placenta is seen extending

downward between the amnion layers. This sign confirms dichorionic twinning. B. The "twin-peak" sign is seen at the bottom of this schematic diagram. The triangular portion of placenta insinuates between the amniochorion layers [18].

#### 2.3.1.3.2.2 Monochorionic diamniotic

In contrast to dichorionic pregnancies, monochorionic pregnancies will have a right angle "T" sign at the base of the intertwine membrane, without any extension of placenta into the membrane (Figure 17-2). An intertwine membrane will be noted separating the fetuses; however, it will be noted to be very thin and hair-like, measuring < 2 mm. After the first trimester, monochorionic diamniotic pregnancies can be mistaken for monoamniotic pregnancies. A "stuck twin" appearance can occur in monochorionic diamniotic pregnancies where oligohydramnios of 1 twin causes the fetus to be held against the uterine wall. In this situation, it is often difficult to identify the dividing membrane, as it is mutually abutting the stuck twin, and it may give the illusion of a monoamniotic pregnancy. One way to differentiate between a "stuck twin" and a monoamniotic pregnancy is to perform ultrasound with the patient in different positions: supine, on her left side, and on her right side. If there indeed is a "stuck twin," that fetus will remain adherent to the same position on the uterine wall regardless of the maternal position, whereas with monoamniotic pregnancies, both fetuses will shift in accordance with gravity.

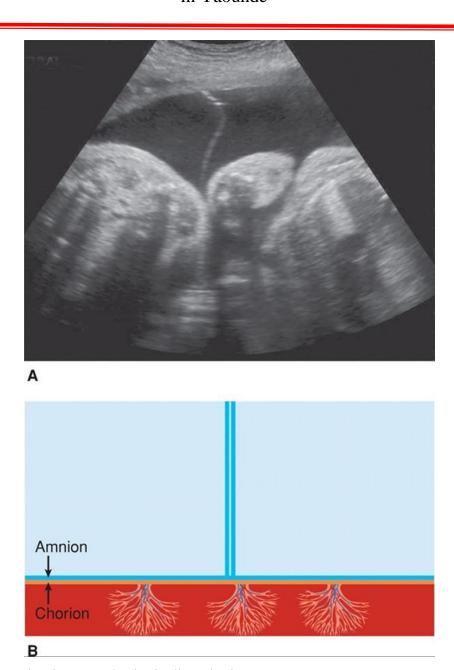


Figure 10: "T" sign in monochorionic diamnionic gestation.

A. Sonographic image of the "T" sign in a monochorionic diamnionic gestation at 30 weeks. At the top of this sonogram, the two apposed amnion layers are seen as the thin line extending downward. B. Schematic diagram of the "T" sign. Twins are separated only by a membrane created by the juxtaposed amnion of each twin. A "T" is formed at the point at which amnions meet the placenta [18].

#### 2.3.1.3.2.3 Monochorionic monoamniotic

In a monoamniotic gestation, there will be no identifiable membrane between fetuses. A single placenta will be identified with multiple origin sites of umbilical cord. It is common to detect

tangling of the cords between the fetuses, often including knotting of the cords, as early as the first trimester.

#### 2.3.1.3.2.4 Conjoined

When 2 separate fetuses are noted in a gestational sac, with a single placenta, and without an intertwine membrane, but with a connection at a particular body site, conjoined twins may be diagnosed. The most common points at which conjoined twins are united include the head, lower abdomen, and sacrum.

#### 2.3.1.3.3 Laboratory Findings

Although no biochemical test reliably identifies multifetal gestation, levels of human chorionic gonadotropin in maternal plasma are higher than those found in singletons. Elevated maternal serum a fetoprotein levels are also commonly seen. Maternal hypochromic microcytic anemia is near universal due to fetal demands for iron that are beyond maternal ability to compensate. There are no known discernible laboratory differences between monozygotic and dizygotic gestations.

#### 2.3.1.3.3.1 Screening in multiple gestations

In twin pregnancies not complicated by neural tube defects, the median maternal serum a fetoprotein level will be 2.5-fold that of the median level for a singleton gestation at 14-20 weeks. A value greater than 4.5 times the median is considered abnormal for twins. A targeted ultrasound should be performed with consideration for amniotic fluid collection for a fetoprotein and acetylcholinesterase measurement.

Routine aneuploidy screening should be offered regardless of maternal age. The mathematical likelihood of trisomy is higher due to presence of multiple fetuses. The age-related risk of Down syndrome is similar for a 33-year-old woman carrying twins and a 35-year-old woman with a singleton pregnancy. Second-trimester serum screening is less sensitive in multifetal gestation due to an average measure in the mother's serum, with a 63% detection rate for trisomy 21 in twins. Nuchal translucency screening with first-trimester serum analytes can detect 75-85% of trisomy 21 cases and 66.7% of trisomy 18 cases in twin pregnancies with minimal added benefit of second-trimester serum analyte screening. Nuchal translucency measurements are similar for a given gestational age regardless of fetal count.

At present, data remain limited on the use of cell-free DNA aneuploidy screening in multifetal pregnancies. Failure rates of the test are higher and detection rates are lower than in singletons.

Results are especially nonreliable with a vanishing twin or empty sac. Therefore, non-invasive prenatal testing is not routinely recommended in multifetal gestations.

Both amniocentesis and chorionic villus sampling may be safely performed in multifetal pregnancies for definitive diagnostic testing within the limits of today's genetic technologies. Both procedures are associated with a 1% risk of pregnancy loss when used in twin gestations. Detailed ultra-sonographic mapping of both fetal and placental location is essential. To avoid sampling error during amniocentesis, indigo carmine may be injected into the sampled sac prior to needle removal. When the subsequent sac is sampled, fluid should be clear. However, there is a 1% risk of sampling error in women who undergo chorionic villus sampling.

#### 2.3.1.3.4 Other diagnostic aids

#### 2.3.1.3.4.1 Placental examination

Careful visual examination of the placenta and membranes alter delivery can establish zygosity and chorionicity in many cases. First, the placenta is gently delivered to preserve the attachment of the amnion and chorion. With one common amnionic sac or with juxtaposed amnions not separated by chorion, the fetuses are monozygotic (see Fig. 48-1). If adjacent amnions are separated by chorion, the fetuses could be either dizygotic or monozygotic, but dizygosity is more common (Fig. 48-5). If the neonates are of the same sex, blood typing of cord blood samples may be helpful. Different genders or blood types reflects dizygosity, although the same gender or blood type in each fetus does not confirm monozygosity. Postnatal zygosity genetic testing is available, and the benefits and ethics have been debated.



Figure 11: Dichorionic diamnionic twin placenta.

The membrane partition that separated twin fetuses is elevated and consists of chorion (c) between two amnions (a) [18].

#### 2.3.1.4 Differential Diagnosis

The following conditions may be considered when a uterus appears large for gestation:

- Multifetal gestation
- Inaccurate dating
- Hydramnios
- Hydatiform mole with or without concurrent fetal gestation
- Abdominal tumors (leiomyoma, adnexal mass)

#### 2.3.1.5 Maternal physiological adaptations

The physiological burdens of pregnancy and likelihood of serious maternal complications are typically greater with multifetal gestations than with singleton ones. In the first trimester and with its higher serum  $\beta$ -hCG levels, multifetal gestations often cause nausea and vomiting. In women carrying more than one fetus, blood volume expansion is greater and averages 50 to 60 percent compared with 40 to 50 percent in those with a singleton. This augmented hypervolemia offsets blood loss with vaginal delivery of twins, which is twice that with a single fetus. Although red cell mass also accrues, it does so proportionately less in twin pregnancies.

Combined with greater iron and folate requirements, this predisposes to anaemia. Women carrying twins also have a typical pattern of blood pressure change. One study assessed serial blood pressures in more than 13,000 singleton and twin pregnancies. As early as 8 weeks' gestation, the diastolic blood pressure in women with twins was lower than that with singleton pregnancies. It generally rose by a greater degree at term. An earlier study demonstrated that this later rise was at least 15 mm Hg in 95 percent of women with twins compared with only 54 percent of women with a singleton. Hypervolemia along with decreased vascular resistance has an impressive effect on cardiac function. In one study of 119 women with twins, cardiac output rose another 20 percent above that in women with a singleton. Similarly, a study of serial maternal echocardiography examinations found a greater elevation in cardiac output in 20 women with uncomplicated twin pregnancies. Both studies found that the augmented cardiac output was predominantly due to greater stroke volume rather than higher heart rate. Vascular resistance was significantly lower in twin gestations throughout pregnancy compared with singleton ones. In a study of 30 uncomplicated twin pregnancies, this same group of investigators identified progressive diastolic dysfunction from the first to third trimester. The dysfunction subsequently normalized after delivery. Uterine growth in a multifetal gestation is substantively greater than in a singleton one. The uterus and its nonfetal contents may achieve a volume of 10 L or more and weigh in excess of 20 pounds. Especially with monozygotic twins, excessive amounts of amniotic fluid may rapidly accumulate. In these circumstances, maternal abdominal viscera and lungs can be appreciably compressed and displaced by the expanding uterus. As a result, the size and weight of the large uterus may preclude more than a sedentary existence for these women. Rarely, maternal renal function can become seriously. Rarely, maternal renal function can become seriously impaired, most likely as the consequence of obstructive uropathy. Hydramnios is a common associate, and therapeutic amniocentesis may provide relief for the mother, may improve obstructive uropathy, and possibly may lower rates of preterm labor or rupture of membranes. Unfortunately, hydramnios often develops remote from term and rapidly reaccumulates.

#### 2.3.1.6 Complications

Multiple gestations are high risk pregnancies which may have many complications. These complications increase with each additional fetus in a multiple pregnancy and include many medical issues that will be discussed below. In addition to these, the incidence of severe nausea and vomiting, cesarean section, or forceps delivery is higher.

#### 2.3.1.6.1 Maternal Complications

All potential maternal complications of pregnancy are more common in multifetal gestation as the maternal systems undergo greater stress with higher maternal-fetal nutritional requirements. Women are more likely to be anemic; have urinary tract infections, velamentous cord insertion, vasa previa, or placenta previa; experience vaginal hemorrhage before, during, and after delivery; undergo cesarean section; and experience postpartum depression. They experience greater rates of hyperemesis gravidarum due to elevated β-human chorionic gonadotropin. Women are more likely to be diagnosed with gestational diabetes mellitus due to a greater presence of pregnancy-associated hormones such human placental lactogen.

Hypertensive disorders of pregnancy are more common and occur in proportion to the total number of foetuses present [33]. This leads to greater incidence of placental abruption and iatrogenic preterm delivery. Singletons have a 6.5% total rate of hypertensive pregnancies. Preeclampsia occurs more frequently in women with multiples. It is one of the most frequent complications in these pregnancies [34]. Women with twin gestations have a 2.6-fold greater relative risk of developing preeclampsia, which also tends to occur earlier in gestation. Higher order multiples have a propensity toward atypical presentations of preeclampsia. Of note, fetal reduction reduces the risks of hypertensive complications down toward the relative number of living fetuses. Twin pregnancy is also known to be a risk factor for pulmonary embolism due to increased demand from both foetuses [35].

#### 2.3.1.6.2 Fetal Complications

The average gestational age at delivery is 36-37 weeks in twins, 33 weeks in triplets, and 31 weeks in quadruplets.

#### **2.3.1.6.2.1** Prematurity

Perinatal morbidity and mortality rates are significantly higher in multifetal gestation mainly due to preterm delivery and consequences of neonatal prematurity. The gestational age decreases with an increase in the number of foetuses[8]. Preterm premature rupture of membranes (PPROM) occurs more frequently in multifetal gestations: 25% in twin pregnancies, 50% in triplet pregnancies, and 75% in quadruplet pregnancies. Twins have a 6-fold increased rate of preterm delivery, a 5-fold higher rate of stillbirth, and 7-fold increased rate of neonatal death. Intracranial injury including intraventricular hemorrhage,

periventricular leukomalacia, and cerebral palsy is more common in infants born from a multifetal gestation at matched gestational ages in singleton pregnancies [7].

#### 2.3.1.6.2.2 Fetal and New-born Complications

Preterm delivery place increases the risk for severe complications or early death. A baby's lungs, brain, circulatory system, intestinal system, and eyes may be not completely developed. Of the premature babies who die, 50% succumb to respiratory distress syndrome, caused by immaturity of the lungs. Brain damage is responsible for almost 10% of premature new born deaths. Birth defects and stillbirths account for about 30% of the deaths in twins and multiple pregnancies. Neonatal intensive care unit admission is required for one-fourth of twin and three-fourths of triplet deliveries [7]. There is a 10-fold increase in the risk of perinatal mortality following multiple gestations than singleton gestations [36].

#### 2.3.1.6.2.3 Twin-twin transfusion syndrome

Twin-twin transfusion syndrome (TTTS) is a complication of mono-chorionic diamniotic gestation. It affects 15% of such pregnancies and occurs most commonly due to arteriovenous anastomoses, which lead to unequal fetal-placental sharing and transfusion between twins. The donor twin is typically affected by hypovolemia and anemia, which may lead to hydrops and oligohydramnios. The recipient twin will have evidence of polyhydramnios, hypervolemia, multiorgan enlargement, and frequently heart failure that may lead to death. Ultrasonography should be used every 2 weeks starting at 16 weeks in monochorionic gestations to screen for the development of TTTS. Laser therapy is available for advanced-stage TTTS (Table 17-1) with improved neurodevelopmental outcomes.

Table II: Quitero staging for twin-twin transfusion syndrome [22].

Stage 1	Monochorionic diamniotic gestation with oilgohydramnios and
	polyhydramnios
Stage 2	Donor twin with absent bladder
Stage 3	Abnormal Doppler findings
Stage 4	Hydrops fetalis
Stage 5	Death of 1 or both twins

#### 2.3.1.6.2.4 Abnormal fetal growth

Discordant fetal growth occurs when there is a 20% or more difference in the estimated fetal weight as determined by ultrasound between fetuses. When discordance in size occurs but both fetuses remain appropriate for gestational age, they are not at increased risk for morbidity or mortality. In cases of selective growth restriction of a single fetus or of multiple fetuses, however, there is a significantly increased risk of neonatal morbidity and mortality when compared to gestational age-matched singleton controls.

#### 2.3.1.6.2.5 Fetal demise

The spontaneous reduction of a fetus, known as "vanishing twin," may occur in 20-60% of spontaneous twin pregnancies. Rates are higher with increasing maternal age, greater number of gestational sacs, and earlier detection of multifetal gestation via ultrasound. A vanishing twin may affect not only maternal serum analyte results, but also chorionic villus sampling karyotype results.

In the second and third trimesters, the fetal loss rate reaches 5% and 15% in twin and triplet gestations, respectively. The loss of 1 foetus poses a greater risk of demise of the remaining gestations.

- **Dichorionic Diamniotic**: Demise of a single twin in a dichorionic pregnancy is less common than in monochorionic pregnancies. In the event of a twin demise, the surviving co-twin is at minimal risk of subsequent morbidity due to housing in a separate sac and separate placentation. Delivery is not recommended in the event of demise of a co-twin; however, it may be considered in the early term period.
- Monochorionic Diamniotic: Monochorionic diamniotic gestations are at increased risk compared to dichorionic gestations. The risk of neurologic morbidity is greatest in the surviving twin of a monochorionic gestation, reaching nearly 20%. Unfortunately, there appears to be no benefit to immediate delivery of the surviving twin once demise has occurred in a co-twin during the late second or third trimester. In the event of co-twin demise, delivery is not routinely recommended prior to 34 weeks due to compounded risks of prematurity.

#### 2.3.1.6.3 Unusual Presentations

#### **2.3.1.6.3.1** Conjoined twins

A rare event, conjoined twins occur as a result of incomplete separation of co-twins during early development. Although most commonly, 30% of conjoined twins are fused at the chest

to lower abdomen regions, or thoraco-omphalopagus, body site fusion may occur at any location. There is a 3:1 female gender preference in conjoined twin pregnancies. Although 50% of conjoined twin pregnancies will culminate with intrauterine fetal demise, a majority of those who survive to birth have anomalies that are not compatible with life. Rare cases of conjoined twins surviving into child and adulthood exist and procedures to separate conjoined twins may be attempted at specialized centres when organs are duplicated and organized to support survival of 2 individuals.

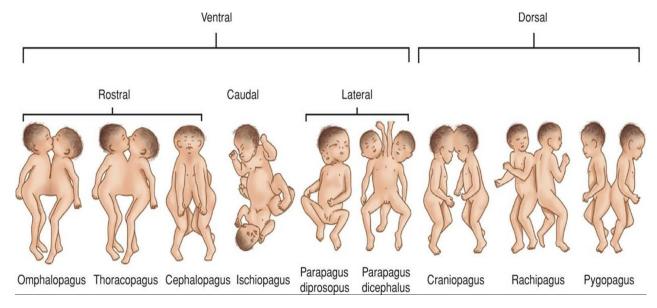


Figure 12: Types of conjoined twins [18].

#### 2.3.1.6.3.2 Twin reversed arterial perfusion (TRAP) sequence

TRAP sequence, also known as acardiac twin pregnancy, occurs in 1% of monochorionic gestations. In this condition, 1 fetus lacks normal heart and head development and is perfused by placental anastomoses from the donor twin. This may occur as part of the TRAP sequence, in which a normal donor twin feeds the recipient twin. The donor, or pump twin, develops high-output cardiac failure resulting in demise in 50% of such cases.

#### 2.3.1.7 Management

#### 2.3.1.7.1 Antepartum Interventions

#### **2.3.1.7.1.1** Fetal reduction

Fetal reduction is a procedure that may be considered in multifetal gestations with clearly separate chorionicity (ie, trichorionic triamniotic pregnancies).

Multifetal pregnancy reduction decreases the risks inherent to multifetal gestations such as hypertensive disorders and spontaneous preterm delivery. A Cochrane review found that

women who reduced a triplet pregnancy to twins observed lower rates of loss, preterm birth, low-birth-wag infants, operative delivery, neonatal death, and maternal complications during the antepartum period. The fetus to be reduced is selected based on fetal health when predetermined by definitive invasive prenatal diagnosis, technical issues such as positioning and accessibility, and chorionicity.

Monochorionic gestations complicate reduction procedures due to potential morbid consequences to the surviving twin. It is recommended that both fetuses of a monochorionic pair be reduced when applicable.

Selective reduction is a specific term that refers to fetal reduction of an abnormal fetus in a multifetal gestation the risks are greater than in multiferal reduction largely duet later gestational age of diagnosis. It can be performed under ultrasound guidance with intracardiac potassium chlonide injection.

#### 2.3.1.7.1.2 Preterm birth prediction and prevention

Serial cervical length assessment. fetal fibronectin screening, and uterine home monitoring have all been considered as methods to reducing spontaneous preterm birth in twins. No interventions have been proven to be effective for screening asymptomatic women with multifetal gestation and are not recommended. Although the positive predictive value of fetal fibronectin testing and a short cervical length is poor, they may be used for the acute management of symptomatic women. Prophylactic cerclage has shown no benefit and has even been shown to be harmful when placed in women with twin gestations and a short cervix; thus, it should be avoided.

Progesterone treatment is not recommended for use with intent to reduce spontaneous preterm birth in asymptomatic women with multifetal gestation. It has even resulted in higher rates of early loss in higher order gestations Although data to recommend progesterone in women with a twin gestation and a short cervical length < 25 mm are insufficient, the use of either 17-hydroxyprogesterone caproate or vaginal progesterone capsules has not been shows to prolong pregnancy.

There is no role for prophylactic tocolysis in mutile gestations. Calcium channel blockers (nifedipine) or nonsteroidal anti-inflammatory drugs (indomethacin) may be used for short-term pregnancy prolongation during corticosteroid administration and to allow transfer to a tertiary care centre. Maternal complication of pulmonary edema is more profound in multifetal pregnancy with use of tocolytics.

Primarily, extracted from benefits seen in singleton pregnancies, it is recommended to administer antenatal corticosteroids (dexamethasone or betamethasone) to women with multifetal gestations between 23 and 34 weeks at risk of delivery within 1 week. A single repeat course may be considered if a woman remains at risk of preterm delivery least 1 week from the completion of the prior course and before 34 weeks of gestation. No data exist to support any added benefit of an additional corticosteroid course in the setting of PPROM.

Administration of magnesium sulphate prior to preterm delivery at < 32 weeks has been shown to decrease the severity and risk of cerebral palsy in surviving infants regardless of fetal number.

#### **2.3.1.7.1.3** Fetal well-being

- **Dichorionic Diamniotic**: Ultrasonography is essential to monitor fetal growth throughout gestation. Scans should be performed every 4-6 weeks in otherwise uncomplicated pregnancies. More frequent monitoring is required for pregnancies complicated by growth restriction.
- Monochorionic Diamniotic: Monochorionic placentation requires more frequent ultrasonography in order to monitor closely for development of TTTS. Ultrasound should be performed every 2 weeks to monitor for changes in amniotic fluid index in both sacs and to monitor fetal growth.

Antepartum testing via external electronic fetal monitoring is not routinely recommended in uncomplicated, normally grown pregnancies. This is rare, however, and most women will undergo weekly testing in the late third trimester for gestations complicated by growth restriction or discordance between fetuses. Bed rest is not recommended due to lack of benefit and risk of thrombosis and deconditioning, even during a prolonged admission.

#### 2.3.1.7.2 Intrapartum Interventions

#### 2.3.1.7.2.1 Indicated Timing of Delivery

- **Dichorionic Diamniotic:** Timing of delivery is balanced between risks of prematurity and rising perinatal mortality rates after 38 weeks in dichorionic twin gestations. Therefore, dichorionic diamniotic twin gestations should be delivered at 38 weeks.
- Monochorionic Diamniotic: Monochorionic diamniotic gestations should be delivered between 34 and 38 weeks with timing dependent on the given gestation's associated complications or maternal morbidities. For example, a gestation

- complicated by TTTS may be considered for delivery at 34 weeks, while a gestation that has 2 normally grown fetuses could be maintained until 38 weeks.
- Monochorionic Monoamniotic: Management of monochorionic monoamniotic gestations remains controversial. Most commonly, patients are admitted at 24-28 weeks for daily fetal surveillance, serial growth assessments and delivery between 32-34 weeks via cesarean section.

#### **2.3.1.7.2.2** Mode of delivery

Multifetal gestation is not itself an indication for cesarean delivery. A history of a previous low transverse cesarean delivery is not a contraindication for a twin vaginal delivery. However, fetal malpresentation is 10 times more common in multiple gestations. Fifty percent of twins will both be cephalic at time of birth. In 33% of cases, twin A will present cephalic and twin B will present breech. Both fetuses will be breech in 10% of cases, and just < 10% will be dually transverse [7].

Delivery should be performed in the operating suite due to potential need for emergent cesarean delivery of twin B. Regional anesthesia is recommended, and pediatricians should be in attendance at the birth. Vaginal delivery may be attempted when both twins are cephalic and when twin A is cephalic but twin B is not. Both external cephalic version and internal podalic version of twin B may be considered by experienced providers. There is no definitive recommended time interval between infant deliveries, as long as the in-utero twin shows reassuring testing with fetal monitoring.

When twin A is breech and twin B is cephalic, they are at risk of becoming "locked twins." Their heads become impacted against one another and impacted in the pelvis. This is an obstetrical emergency and may require cesarean delivery of both twins.

#### 2.3.1.8 Prognosis

Maternal and fetal complications are more frequent in multifetal gestations. Although infants of multifetal pregnancies have an increased risk of neurologic sequelae, the most important prognostic factor for developmental outcome is gestational age at delivery. Although women are at increased risk of hypertensive crisis, uterine atony, hemorrhage, and hysterectomy, the maternal mortality rate for women with a multifetal gestation is only slightly above that for singleton gestations in the United States.

### 2.4 REVIEW OF STUDIES

### 2.4.1 In the World

Title and Place of study	Authors and year of study	Setting	Results
Maternal and	Na Sua, Wei-Wei	Data concerning	The rate of
neonatal outcomes	Zhub, Yu-Mei Weia,	maternal and	caesarean deliveries
in multiple	Chen Wanga, Hui	neonatal adverse	was much higher in women with
pregnancy: A	Fenga, Li Lina,Hui-	outcomes in multiple	multiple pregnancies
multicentre study in	Xia Yang	and singleton	(85.8%) than that in
the Beijing	2015.	pregnancies were	women with
population, China.		collected from 15	singleton pregnancies (42.6%,
		hospitals in Beijing	$\chi^2 = 190.8, P <$
		by a systemic cluster	0.001). The
			incidences of anemia
		sampling survey	$(\chi^2 = 40.023, P <$
		conducted from 20	0.001), preterm
		June to 30	labor ( $\chi^2 = 1021.172, P <$
		November 2013.	0.001), gestational
		The SPSS	diabetes mellitus
		software(version	$(\chi^2 = 9.311, P <$
		20.0) was used for	0.01), hypertensive disorders ( $\chi^2$ =
		data analysis.	122.708, P < 0.001
		Thec2test was used	and post-partum
		for statistical	hemorrhage ( $\chi^2$ =
		analyses	48.550, <i>P</i> < 0.001)
		anaryses	was significantly increased with
			multiple pregnancy.
			In addition, multiple
			pregnancy was
			associated with a
			significantly higher
			rate of small-for-
			gestational-age
			infants ( $\chi^2 =$

			92.602, $P < 0.001$ ), low birth weight ( $\chi^2 = 1141.713$ , $P < 0.001$ ), and neonatal intensive care unit (NICU) admission ( $\chi^2 = 340.129$ , $P < 0.001$ ).
Perinatal outcomes	Danielly S.	Secondary analysis	
in twin pregnancies	Santana1, Carla	of the WHO	
complicated by	Silveira1, Maria L.	Multicountry Survey	
maternal morbidity:	Costa1, Renato T.	on Maternal and	
evidence from the	Souza1, Fernanda G.	Newborn Health	
WHO Multicountry	Surita1, João P.	(WHOMCS), a	
Survey on Maternal	Souza2, Syeda	cross-sectional study	
and Newborn Health	Batool Mazhar3,	implemented in 29	
	Kapila Jayaratne,	countries. Data from	
	Zahida Qureshi,	8568 twin deliveries	
	Maria H. Sousa,	were compared with	
	Joshua P. Vogel,	308,127 singleton	
	José G. Cecatti,	deliveries. The	
	2018.	occurrence of	
		adverse perinatal	
		outcomes and	
		maternal	
		complications were	
		assessed. Factors	
		independently	
		associated with	
		adverse perinatal	
		outcomes were	
		reported with	
		adjusted PR	

		(Prevalence Ratio)	
		and 95%CI.	
Maternal and Perinatal Outcome	Mahendra Raj Pandey, Bikash Jang	The prospective observational study	The total number of deliveries between
		The prospective	
		delivery was taken in the cohort.	ovulation induction. The main maternal adverse outcomes were preterm delivery (62.58%), anemia (8.6%), pregnancy induced hypertension (5%), and antepartum hemorrhage (2.2%), respectively. Postpartum hemorrhage occurred in 12 cases whereas eclampsia,

Complications of multiple pregnancies. Overwiew Stara zagora, Bulgaria.	S. Lazarov, L. Lazarov, N. Lazarov. 2016	Department of Obstetrics and Gynecology, Medical Faculty, Trakia University, Stara Zagora, Bulgaria	postpartum cardiomyopathy, vulval hematoma, and puerperal pyrexia occurred in 2 cases each, the cause of puerperal pyrexia was urinary tract infection. The average birth weight of first twin was 2100 grams and of second twin was 2040 grams. The average birth weight of the 1st, 2nd, and 3rd triplets was 1300 grams, 1630 grams, and 1460 grams, respectively etc.  Preterm labor and birth represent the greatest risk to a multiple pregnancy. Sixty percent of multiples are born prematurely (<37 weeks) compared to about 10% of singleton pregnancies. Placental function is more likely to be abnormal in a multiple pregnancy. Another placental problem is twintwin transfusion, a life- threatening condition in identical twins. Preeclampsia, also
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	known as toxemia,
	occurs 2 to 5 times
	more often in
	multiple
	pregnancies. Fifteen
	percent to 20% of
	women with twin
	pregnancies will
	experience
	preeclampsia, and an
	even higher
	percentage is
	preeclamptic in
	triplet or high-order
	pregnancies. Preterm
	labor and birth pose
	the greatest risk to a
	multiple pregnancy.
	Sixty percent of
	multiples are born
	prematurely (<37
	weeks) compared to
	about 10% of
	singleton
	pregnancies. Fetal
	and Newborn
	complications such
	as preterm delivery,
	respiratory distress
	syndrome, brain
	damage are
	responsible for
	almost 10% of
	premature newborn
	deaths. Birth defects
	and stillbirths
	account for about
	30% of the deaths in
	twins and multiple
	pregnancies. Low
	birth weight of less
	than 5.5 pounds (lb.)
	man 3.3 pounds (10.)

	[2,500 grams] occurs
	in over half of
	twins

### 2.4.2 In Africa

Title and place of study	Authors and year of study	Setting	Results
Perinatal Outcomes	Bolajoko O.	This cross-sectional	Of the 4,573 deliveries,
of Multiple Births	Olusanya, 2007.	study was conducted	there were 4,416
in Southwest		at the Island	(96.6%) singletons and 157 (3.4%) multiples,
Nigeria		Maternity Hospital	comprising 296 twins
		(IMH) in Lagos,	and six triplets together
		southwest Nigeria,	(6.4% of all live 4,718 infants). After
		from May 2005 to	adjusting for maternal
		December 2007.	age, ethnicity,
			occupation, parity, and antenatal care, multiple
			gestations were
			associated with
			increased risks of
			hypertensive disorders
			and caesarean delivery.
			Similarly, after
			adjusting for potential
			maternal confounders,
			multiple births were
			associated with low
			five-minute Apgar
			score (OR: 1.47, 95%
			CI 1.13-1.93), neonatal
			sepsis (OR: 2.16, 95%
			CI 1.28-3.65), severe
			hyperbilirubinaemia
			(OR: 1.60, 95% CI
			1.00-2.56), and
			admission to a special-
			care baby unit (OR:
			1.56, 95% CI 1.12-
			2.17) underpinned by
			2.17) underprinted by

			preterm delivery before 34 weeks (OR: 1.91, 95% CI 1.14-3.19), birthweight of less than 2,500 g (OR: 6.45, 95% CI 4.80-8.66), and intrauterine growth restriction (OR: 9.04, 95% CI 6.62-12.34). Overall, the results suggest that, in resourcepoor settings, infants of multiple gestations are associated with a significantly-elevated risk of adverse perinatal outcomes. Since these perinatal outcomes. Since these perinatal outcomes are related to the increased risk of later neurodevelopmental disabilities, multiple-birth infants merit close developmental
			surveillance for timely
Darinatal Outcomes	Inona Manata	The Global Network	intervention.
Perinatal Outcomes	Irene Marete,		A total of 69,706 women were enrolled.
of Multiple-	Constance Tenge et	for Women and	Multiple gestations
Gestation	al. 2014.	Children's Health	accounted for 0.9% of
Pregnancies in		Research Maternal	all births (twins 0.9%,
Kenya, Zambia,		Newborn Health	triplets 0.01%). Kenya and Pakistan had the
Pakistan, India,		registry study is a	highest rates of
Guatemala, and		prospective	multiple gestation
Argentina: A		multicenter study	deliveries with
Global Network		conducted in Kenya,	14.6/1000 and 10.7/1000 live births
Study		Zambia Pakistan,	respectively. The
		Guatemala,	mothers with a
	<u> </u>	<u> </u>	

		Argentina and India (8). The registry includes 106 geographically defined study clusters across the sites	multiple gestation were more likely to deliver in a health care facility compared to singleton pregnancy mothers (70% and 66% respectively, p<0.001), to be attended by skilled health personnel (71% and 67%, p<0.001) and to be delivered by Cesarean section (18% vs. 9%, p<0.001). Multiple gestation fetuses had a relative risk (RR) for stillbirth of 2.65 (2.06, 3.41) and for perinatal mortality rate (PMR) a RR of 3.98 (3.40, 4.65) relative to singletons (both p<0.0001). Neither delivery in a health facility nor the Cesarean section rate was associated with decreased PMR. Among multiple gestation deliveries, physician attended delivery relative to
			Among multiple gestation deliveries, physician attended
			providers was associated with a decreased risk of perinatal mortality.
Early neonatal	Saverio Bellizi,		
mortality in twin pregnancy: Findings from 60	Howard Sobel et al. 2018.	We conducted a secondary analysis of individual level data from 60	Early neonatal mortality among twins was significantly higher when compared
		nationally-	to singleton neonates

low- and middle-	representative	(adjusted odds ratio
income countries	Demographic and Health Surveys including 521 867 singleton and 14 312 twin births. We investigated the occurrence of deaths within the first week of life in twins compared to singletons and the effect of place and attendance at birth; also, the role of caesarean sections against vaginal births was examined, globally and after countries stratification per caesarean sections rates. A multi-level logistic regression was used accounting for homogeneity within country, and homogeneity within twin pairs.	(aOR) 7.6; 95% confidence interval (CI) = 7.0-8.3) in these 60 countries. Early neonatal mortality was also higher among twins than singletons when adjusting for birth weight in a subgroup analysis of those countries with data on birth weight (n = 20; less than 20% of missing values) (aOR = 2.8; 95% CI = 2.2-3.5). For countries with high rates (>15%) of caesarean sections (CS), twins delivered vaginally in health facility had a statistically significant (aOR = 4.8; 95% CI = 2.4-9.4) increased risk of early neonatal mortality compared to twins delivered through caesarean sections. Home twin births without SBA was associated with increased mortality compared to twins delivering at home with SBA (aOR = 1.3; 95% CI = 1.0-1.8) and with vaginal birth in health facility (aOR = 1.7; 95% CI = 1.4-2.0).

### 2.4.3 In Cameroon

Title and place of study	Authors and place of study	Setting	Results
Outcomes of Twin	William Ako	This was a hospital-	Women with twin
Delivery at the	Takang1,2, Dobgima	based, cross-	gestations were
Bamenda Health	Walters Pisoh2,	sectional analytic	mostly aged between
District, North West	Tcheumbe Josiane	study done at the	25 and 34 years with a mean maternal age
, in the second second	Nyeumenou1, Enow	Bamenda Health	of $28.6 \pm 5.8$ years,
Region Cameroon			more than half
	Robinson Mbu1,	District in three	(60%) of them were
	Mary Bi Shu	selected hospitals	multiparous with
	Atanga, 2018.	(Bamenda Regional	family histories of
		Hospital, CMA	twin, and business
		Nkwen, and IHC	was their main occupation (58.2%).
		Azire) from the 1 st	The prevalence of
		of January to the	twin gestations at the
		10th of May 2018.	Bamenda Health
		_	District was 2.8%.
		55 women with twin	As compared to
		pregnancies and 55	singleton deliveries, twin deliveries were
		women with	associated with
		singleton	adverse fetal
		pregnancies at	outcomes such as
		gestational ages of	prematurity (born
		28 completed weeks	before 37 completed weeks) which was
		and above who came	about 6 times higher
			among twins than
		for delivery and who	singleton babies
		consented to the	(OR: 5.6, 95% CI:
		study were included.	2.2 - 14.3, p <
			0.001), birth
			asphyxia (Apgar score < 7 at 5th min)
			that was 15 times
			higher in twin than
			singleton births (OR:
			15.3, 95% CI: 2 -

	116.6, $p < 0.001$ )
	and low birth weight
	(birth weight < 2500
	grams) that was 15.6
	times increased in
	twin than singleton
	births (OR: 15.6,
	95% CI: 3.6 - 67.8, p
	< 0.001). There were
	5.5 times increased
	cesarean sections
	among women with
	twin pregnancies
	compared to women
	with singleton
	pregnancies (OR:
	5.5, 95% CI: 2.2
	·
	13.9, $p < 0.001$ ).
	There was no
	association between
	twin delivery and
	postpartum
	haemorrhage (p >
	0.05). Conclusion:
	Twin deliveries were
	associated with
	adverse fetal
	outcomes
	(prematurity, birth
	asphyxia, and low
	birth weight) in the
	three health facilities
	where we carried out
	the study. Cesarean
	section was higher
	among women with
	twin gestations
	compared to women
	with singleton
	gestations.
	0.00000000

Pregnancies	Tchene Nguefack	It was a case-control	Some independent
Outcome after	Charlotte, bourdanne	study carried out in	factors associated
Assisted	Tekouake Didier et	four health facilities	with ART were: age
Reproductive	al. 2021	in Douala-	over 45 years [aOR: 7.55; 95% CI (1.55 -
Technology: A		Cameroon, over a	36.76); p: 0.01],
Multicenter Case		period of five years.	twin pregnancies
		period of five years.	[aOR: 16.55; 95%
Control Study in a			CI (7.91 - 34.60); p
Low Income Setting			< 0.01], Cervical cerclage [aOR: 3.04;
Douala, Cameroon			95% CI (1.23 -
			7.50); p: 0.01],
			miscarriages [aOR:
			11.73; 95% CI (5.07
			- 27.10); p: 0.01],
			elective cesarean
			section [aOR: 4.63; 95% CI (2.27 -
			9.45); p: 0.01] and
			low birth weight
			[aOR: 3.32; 95% CI
			(1.90 - 5.82); p <
			0.01]. Women who
			conceived by ART
			were older with higher rates of
			multiple pregnancy
			and complications.
			We recommend
			transfer of a single
			embryo.
Triple Gestations in	E Nkwabong,	This retrospective	A total of 43 cases
Two University	F Lhagadang,	study, carried out in	were analyzed. The most common
Teaching Hospitals	R Mbu,	2 university	complications that
in Yaounde,	PN Nana,	hospitals in Yaounde	occurred during
Cameroon	L Kouam,	(Cameroon) over a	pregnancy were
	PC Ngassa.	6-year period, was	preterm delivery and pre-eclampsia.
	2011	done to evaluate the	Twenty seven
		complications that	women (62.8%)

1	
occurred during	delivered vaginally
triple pregnancies as	and 16 (37.2%) were
	delivered by
well as the mode of	caesarean section
delivery of triplets.	with the most
	common indications
	being mal
	presentation and
	cord prolapse of the
	1st triplet. In
	patients who have
	proper antepartum
	monitoring, it is
	possible to pre-select
	cases for trial of
	vaginal delivery
	because vaginal
	delivery is possible
	and carries no
	significant risk for
	the foetuses.

**CHAPTER 3: METHODOLOGY** 

### 3 METHODOLOGY

### 3.1 TYPE OF STUDY

We carried out a retrospective cohort study.

### 3.2 SITE OF STUDY

Our study was carried out in two reference hospitals in Yaoundé. These hospitals are the Yaoundé Gynaecology, Obstetrics and Paediatrics Hospital and the Yaoundé Central Hospital.

### The Yaoundé Gynaecology, Obstetrics and Paediatrics Hospital

It is a reference health facility created in 2002 and specializes in mother and child health care. Its gynaecology/obstetrics 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 in the heart of Yaoundé has one of the biggest and most specialized maternity unit with over 72 in-patient beds, 6 delivery tables, 2 service operating theatres and a large highly trained staff. It records about 219 deliveries per month.

All the afore mentioned hospitals have been chosen for this study because of their great patient turnover, adequate follow up and anticipated clear records.

### 3.3 DURATION OF STUDY

The study was carried out over a duration of seven months (November 2023 to May 2024).

### 3.4 STUDY POPULATION

Our study population consisted of files of pregnant women who delivered in the selected hospitals from January 2018 to December 2022.

### 3.4.1 Inclusion criteria

Exposed group:

- Files of pregnant women with multifetal gestations who were admitted in labor and delivered in these hospitals.
- Complete patient records.

### Unexposed group:

• Files of women with singleton pregnancies who were admitted in labor and delivered just after the cases of multifetal pregnancy matched for maternal age (+/-), gestational age(+/-) and parity (+/-).

### 3.4.2 Exclusion criteria

• Files of women with incomplete information.

### 3.4.3 Non-inclusion criteria

• Files of women with comorbidities such as gestational diabetes and hypertension who delivered during the same period.

### 3.5 SAMPLING

### 3.5.1 Sampling method

Recruitment was consecutive until our sample size was attained.

### 3.5.2 Sample size estimation

Based on our study design, the sample size was calculated as shown below:

$$n = \left[ \frac{2 * (Z_{\alpha} + Z_{\beta})^{2} * p * (1 - p)}{(p_{0} - p_{1})^{2}} \right]$$

 $P_0$ = The proportion of women in the unexposed group who will develop the complication considered.

 $P_1$ = The proportion of women in the exposed (risk) group who will develop the same complication.

$$P = (P_0 + P_1) / 2$$

 $\alpha = 0.05$ 

 $Z_{\alpha} = 1.96$ 

 $\beta = 0.1$ 

 $Z_{\beta} = 1.28$ 

### Therefore **n**= **a minimum of 79 participants**

With ratio 1 exposed: 1 unexposed.

### 3.6 PROCEDURE

### 3.6.1 Administrative formalities

Firstly, we wrote and presented a research protocol that was approved by the supervisors, after which we obtained research authorization from the management of the hospitals and ethical clearance from the Institutional Review Board of the Faculty of Medicine of the University of Yaoundé I.

### 3.6.2 Recruitment and data collection

Delivery records were used to identify women with multifetal and singleton gestations who delivered in the selected hospitals during the period ranging from 2018 to 2022 inclusive. We then proceeded to the archives to collect the files for studies. For every exposed case or multifetal delivery, the next singleton delivered matched for age and parity was considered as the unexposed case. Data were extracted from their files according to working variables unto the worksheet for appropriate data management and analysis.

### 3.6.2.1 Study Variables

For the exposed and unexposed cases, information of interest was collected with the help of a data collection worksheet. This worksheet was designed, internally validated by supervisors, tested and then adapted for the study. The following were searched for;

- 1. Sociodemographic and obstetrical data: This included age, region of origin, marital status, profession, level of education, religion, gravidity and parity.
- 2. Clinical variables: We obtained information on the sex of neonate(s), gestational age, ANC, ultrasound data, mode of delivery, history of multiple gestations, APGAR score, birth weight, foetal length, foetal head circumference, fetal mid-upper arm circumference.
- 3. Complications: This included fetal death, prematurity, neonatal asphyxia, neonatal sepsis, other immediate neonatal morbidities encountered.

### 3.7 STUDY RESOURCES

### 3.7.1 Materials for data collection

- Pre-established consent forms
- Pre-established questionnaires
- Rim of A4 papers
- Patients' medical records
- Pens, pencils, ...

### 3.7.2 Human resources

• Main investigator:

BATEBE-AGBOR REGINA NKIEH

7<sup>th</sup> Year - General Medicine, FMBS UYI

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reginabatebe@gmail.com

- Supervisors
- Statistician

### 3.8 DATA ANALYSIS

Data from completed and validated data collection sheet were entered into and analysed using the IBM SPSS (International Business Machine Statistical Package for Social Sciences). Pearson's chi square test will be used for comparison between categorical data and Student's T-test for numerical data. The exposed and the unexposed group characteristics were compared using relative risk. This study was done within a confidence interval of 95% and a value of P< 0.05 was considered significant.

### 3.8.1 Material for data management

- Computer
- Scientific calculator
- Microsoft software package
- USB flash drive
- Smart phone

### 3.9 ETHICAL CONSIDERATIONS

Before embarking on data collection, ethical clearance was requested and obtained from the ethical committee of the Faculty of Medicine and Biomedical Sciences. We equally obtained administrative authorizations from the management of the Yaoundé, Gynaecology Obstetrics and Paediatrics Hospital and Yaoundé Central Hospital to carry out the study.

Confidentiality was ensured by assigning randomly generated codes to every participant and these codes used at every stage of documentation.

All the data collected was used only for the research.

**CHAPTER 4: RESULTS** 

### 4.1 DIAGRAMMATIC REPRESENTATION OF RECRUITMENT PROCESS

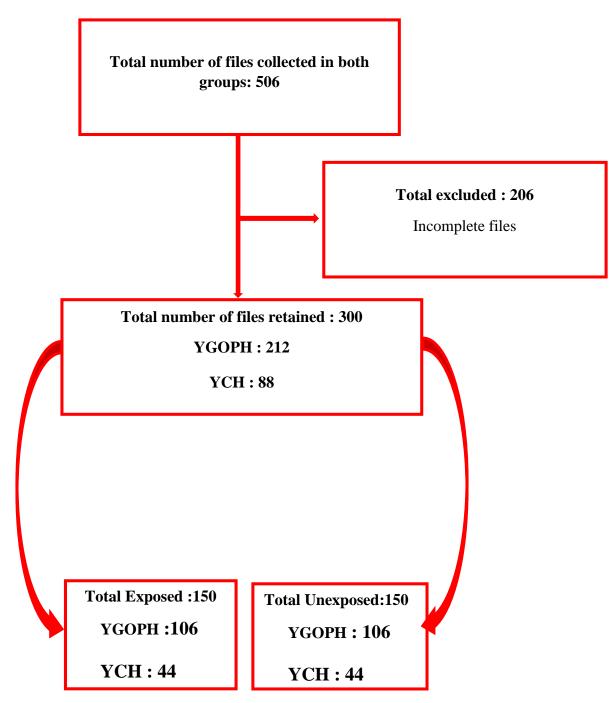


Figure 13: Recruitment flow chart.

For this study, we went through all patient records in the Obstetrics and Gynecology services of the YGOPH and the YCH from Jan 1<sup>st</sup> 2019 to Dec 31<sup>st</sup> 2022. Out of the 506 files evaluated, 206 were found to be incomplete. A total of 300 files were retained in our study. We had 150 files in the exposed group and 150 in the unexposed group giving a ratio of 1:1.

### 4.2 TYPES OF MULTIFETAL PREGNANCIES

Table III: Types of multifetal pregnancies

Types	Frequency N=150	Percentage (%)
Twins	134	89.3
Triplets	16	10.7
Quadruplets	0	0.0
Quintuplets	0	0.0

The number of twins and triplets were 134 and 16 respectively, giving a total of 316 neonates from the exposed group. There were no quadruplets nor quintuplets in the study.

### 4.3 SOCIODEMOGRAPHIC PROFILE OF THE STUDY POPULATION

The tables (III and IV) below describe the sociodemographic profiles of our study population.

Table IV: Population distribution by age and marital status

Variables	Exposed group	Unexposed group	RR	p-value
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
Age groups (in years)				
[15-19]	13 (8.7)	17 (11.3)	0.74 (0.34-1.58)	0.282
[20-24]	37 (24.7)	36 (24.0)	1.03 (0.61-1.75)	0.500
[25-29]	34 (22.7)	49 (32.7)	<b>0.64</b> (0.32-1.01)	0.035
[30-34]	40 (26.7)	30 (20.0)	1.45 (0.84-2.49)	0.110
[35-39]	21 (14.0)	16 (10.7)	1.36 (0.68-2.72)	0.241
≥ 40	5 (3.3)	2 (1.3)	2.55 (0.48-13.36)	0.224
Marital status				
Married	73 (48.7)	58 (38.7)	1.50 (0.95-2.37)	0.051
Single	77 (51.3)	92 (61.3)	0.66 (0.42-1.05)	0.051

Women within the age group 25-29 were the most protected in the two groups (**RR 0.64, 95% CI 0.32-1.01, p<0.035**). The highest number of multifetal pregnancies occurred among women aged between 30-34 (26.7%).

Table V: Population distribution by others sociodemographic characteristics

Variables	Exposed group	Unexposed group	RR	p-value
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
Level of education				
Primary	5 (3.3)	6 (4.0)	0.82 (0.24-2.77)	0.500
Secondary	39 (26.0)	32 (21.3)	1.29 (0.75-2.21)	0.208
High school	60 (40.0)	42 (28.0)	1.71 (1.05-2.78)	0.019
University	46 (30.7)	70 (46.7)	0.50 (0.31-0.81)	0.003
Occupation				
Informal sector	67 (44.7)	54 (36.0)	1.43 (0.90-2.28)	0.079
Student	30 (20.0)	36 (24.0)	0.79 (0.45-1.37)	0.243
Civil servant	18 (12.0)	21 (14.0)	0.83 (0.42-1.64)	0.366
Private sector	20 (13.3)	18 (12.0)	1.12 (0.57-2.23)	0.431
Unemployed	15 (10.0)	21 (14.0)	0.68 (0.33-1.38)	0.187
Region of origin				
Grand-North	10 (6.7)	15 (10.0)	0.64 (0.27-1.48)	0.202
Centre	61 (40.7)	50 (33.3)	1.37 (0.85-2.19)	0.116
Littoral	4 (2.7)	8 (5.3)	0.48 (0.14-1.65)	0.189
North-West	4 (2.7)	2 (1.3)	2.02 (0.36-11.24)	0.342
South-West	2 (1.3)	2 (1.3)	1.00 (0.13-7.19)	0.689
West	64 (42.7)	67 (44.7)	0.92 (0.58-1.45)	0.408
East	3 (2.0)	1 (0.7)	3.04 (0.31-29.56)	0.311
South	0 (0.0)	2 (1.3)	/	0.249
Foreigner	2 (1.3)	3 (2.0)	0.66 (0.10-4.02)	0.500
Religion				
Christian	135 (90.0)	132 (88.0)	1.22 (0.59-2.53)	0.356
Muslim	15 (10.0)	16 (10.7)	0.93 (0.44-1.95)	0.500
Others	0 (0.0)	2 (1.3)	/	0.249

The highest level of education among women in the exposed group was high school (40.0% vs. 28.0%) in contrast to women in the unexposed group who were mostly university graduates(46.7% vs. 30.7%) ( $\mathbf{p} < 0.05$ ). Women in the informal sector were the most represented in both groups, i.e. 44.7% vs. 36.0% but this was not statistically significant ( $\mathbf{p} = 0.079$ ). There were no differences with respect to region of origin and religion.

## 4.4 OBSTETRICAL PROFILE AND COMORBIDITIES OF OUR STUDY POPULATION

The tables (V and VI) below describe the obstetrical profile and comorbidities of our study population

Table VI: Population distribution according to personal and family obstetrical characteristics

Variables	Exposed group	Unexposed group	RR	P
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
Gravidity				
Pimigravidarum	34 (22.7)	50 (33.3)	0.58 (0.35-0.97)	0.027
Paucigravidarum	49 (32.7)	63 (42.0)	0.67 (0.41-1.07)	0.060
Multigravidarum	38 (25.3)	29 (19.3)	1.41 (0.81-2.44)	0.134
Grand multigravidarum	29 (19.3)	8 (5.3)	4.25 (1.87-9.65)	< 0.001
Parity				
Primiparous	41 (27.3)	66 (44.0)	0.47 (0.29-0.77)	0.002
Pauciparous	57 (38.0)	61 (40.7)	0.89 (0.56-1.42)	0.361
Multiparous	32 (21.3)	19 (12.7)	1.87 (1.01-3.47)	0.032
Grand multiparous	20 (13.3)	4 (2.7)	5.61 (1.87-16.85)	< 0.001
History of multifetal pro	egnancy			
Yes	5 (3.3)	1 (0.7)	5.13 (0.59-44.51)	0.107
No	145 (96.7)	149 (99.3)	1	
Family history of multif	etal pregnancy			
Yes	3 (2.0)	0 (0.0)	/	0.124
No	147 (98.0)	0 (0.0)	/	0.124

Grand multigravidity and grand multiparity were associated with multifetal pregnancies. Women who were grand multigravida had 4.25 times the risk of having multifetal pregnancies (**RR 4.25**, 95% **CI 1.87-9.65**, **p< 0.001**). In the same order, women who were grand multiparous had 5.16 times the risk of having multifetal pregnancies (**RR 5.61**, 95% **CI 1.87-16.85**, **p<0.001**)

Table VII: Population distribution according to comorbidities and lifestyle

Variables	Exposed group	Unexposed group	RR	P
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
Comorbidities				
None	140 (93.3)	135 (90.3)	1.55 (0.67(3.58)	0.202
HIV infection	3 (2.0)	11 (7.3)	0.25 (0.07-0.94)	0.026
Hepatitis B	3 (2.0)	2 (1.3)	1.51 (0.24-9.17)	0.500
Hypertension	2 (1.3)	0 (0.0)	/	0.249
Diabetes	1 (0.7)	0 (0.0)	/	0.500
Hepatitis C	0 (0.0)	1 (0.7)	/	0.500
Lifestyle				
Alcohol consumption	11 (7.3)	7 (4.7)	1.61 (0.60-4.29)	0.233
Tobacco consumption	1 (0.7)	1 (0.7)	1.00 (0.06-16.13)	0.751

Comorbidities were dominated by HIV infection in all study groups, i.e. 2.0% in the exposed group and 7.3% in the unexposed group (**p=0.026**). Alcohol consumption was frequent in 7.3% of women among the exposed group and in 4.7% of women among the unexposed group but the difference was not statistically significant (p=0.233).

### 4.5 ANC CHARACTERISTICS OF OUR STUDY POPULATION

Table VIII: Population distribution according to ANC characteristics

Variables	Exposed group	Unexposed group	RR	p-value
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
Number of ANC				
0	1 (0.7)	1 (0.7)	1.00 (0.06-16.13)	0.751
1-3	89 (59.3)	78 (52.0)	1.34 (0.85-2.12)	0.123
4	18 (12.0)	25 (16.7)	0.68 (0.35-1.31)	0.161
5-7	36 (24.0)	39 (26.0)	0.89 (0.53-1.51)	0.395
≥ 8	6 (4.0)	7 (4.7)	0.85 (0.27-2.59)	0.500
Qualification of ANC				
provider				
No follow-up pregnancy	1 (0.7)	1 (0.7)	1.00 (0.06-16.13)	0.751
Gynaecologist	8 (5.3)	13 (8.7)	0.59 (0.23-1.47)	0.183
General practitioner	105 (70.0)	106 (70.7)	0.96 (0.59-1.59)	0.500
Midwife	36 (24.0)	30 (20.0)	1.26 (0.73-2.18)	0.243

Most women in our study had undergone 1 to 3 ANCs, 59.3% and 52.0% respectively in the exposed and unexposed groups (p=0.123). The majority of these ANCs were carried out by a general practitioner (70.0% vs. 70.7%; p=0.500). Neither of these had any significant association with multifetal pregnancies.

Table IX: Population distribution according to prophylactic measures during pregnancy

*				-
Variables	Exposed group	Unexposed group	RR	p-value
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
Antitetanic vaccin				
< 2	29 (19.3)	35 (23.3)	0.78 (0.45-1.37)	0.241
≥ 2	121 (80.7)	115 (76.7)	1.27 (0.72-2.21)	0.241
Slept under treated				
mosquito net				
Yes	92 (61.3)	83 (55.3)	1.28 (0.80-2.02)	0.174
No	58 (38.7)	67 (44.7)	1	
Iron / folic acid consum	nption			
Yes	118 (78.7)	107 (71.3)	1.48 (0.87-2.51)	0.091
No	32 (21.3)	43 (28.7)	1	

The majority of women had received at least two doses of antitetanic vaccine (89.7% vs. 76.7%; p=0.241), slept under an impregnated mosquito net (61.3% vs. 55.3%; p=0.174) and had taken iron/folic acid (78.7% vs. 71.3%; p=0.091). Neither of these had any significant association with multifetal pregnancies.

### 4.6 PATHOLOGIES IN PREGNANCY

Table X: Distribution of the population according to pathologies in pregnancy

Pathologies during	Exposed group	Unexposed group	RR	p-value
pragnancy				
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
None	134 (88.7)	142 (94.0)	0.49 (0.21-1.15)	0.075
Malaria	11 (7.3)	7 (4.7)	1.61 (0.60-4.29)	0.233
Anaemia	1 (0.7)	0 (0.0)	/	0.500
Urinary tract infection	0 (0.0)	1 (0.7)	/	0.500
Genital tract infection	2 (66.7)	0 (0.0)	/	0.300
Cervical insufficiency	1 (0.7)	0 (0.0)	/	0.500
Preeclampsia	1 (0.7)	0 (0.0)	/	0.500

Pathologies developed during pregnancy were dominated by malaria, which accounted for 7.3% of cases among exposed women, versus 4.7% of cases among unexposed women but this was not statistically significant (p<0.075).

### 4.7 MATERNAL OUTCOME OF PREGNANCIES IN THE STUDY POPULATION

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

Variables	Exposed group	Unexposed group	RR	p-value
	N=150; n(%)	N=150; n(%)	(CI at 95%)	
Mode of delivery				
Cesarian section	58 (38.7)	34 (22.7)	1.70 (1.19-2.44)	0.002
Vaginal delivery	92 (61.3)	116 (77.3)	0.79 (0.68-0.92)	0.002
Post partum complication	ons			
No complication	144 (96.0)	147 (98.0)	0.98 (0.94-1.01)	0.251
Post partum haemorrage	4 (2.7)	3 (2.0)	1.33 (0.30-5.85)	0.500
Puerperal infection	1 (0.7)	0 (0.0)	/	0.500
Preeclampsia/Eclampsia	1 (0.7)	0 (0.0)	/	0.500

Women with multifetal pregnancies had 1.70 times the risk of delivering through caesarean section (**RR 1.70, 95% CI 1.19-2.44, p=0,002**). Post-partum haemorrhage occurred in both groups without any statistical significance.

### 4.8 FETAL AND NEONATAL OUTCOME OF THE STUDY POPULATION

Table XII: Fetal characteristics at delivery

Variables	Exposed group	Unexposed group	RR	p-value
	N=316; n(%)	N=150; n(%)	(CI at 95%)	
Gestational age at deli	ivery (in weeks)			
< 28	21 (6.6)	3 (2.0)	3.32 (1.01-10.96)	0.023
[28-31]	48 (15.2)	27 (18.0)	0.84 (0.54-1.29)	0.260
[32-34]	77 (24.4)	26 (17.3)	1.40 (0.94-2.09)	0.054
[35-36]	68 (21.5)	13 (8.7)	2.48 (1.41-4.34)	< 0.001
≥ 37	102 (32.3)	81 (54.0)	0.59 (0.48-0.74)	< 0.001
Notion of fetal detress	<u> </u>			
Yes	96 (30.4)	35 (23.3)	1.30 (0.93-1.82)	0.070
No	220 (69.6)	115 (76.7)	1	

Neonates born following multifetal pregnancies had more than 3 folds the risk of having extremely premature deliveries (**RR 3.22, 95% CI 1.01-10.96, p=0.023**). Delivery at gestational age ≥37 weeks was protective (**RR 0.59, 95% CI 0.48-0.74, p<0,001**).

Table XIII: Neonatal and evolutionary characteristics of new-borns

Variables	Exposed group	Unexposed group	RR	p-value
	N=316; n(%)	N=150; n(%)	(CI at 95%)	
Sex				
Male	160 (50,6)	91 (60.7)	0.83 (0.70-0.98)	0.027
Female	156 (49.4)	59 (39.3)	1	
Birth weight (in				
grams)				
< 1500	82 (25.9)	24 (16.0)	1.62 (1.11-3.04)	0.010
[1500-2000[	68 (21.5)	15 (10.0)	2.46 (1.35-4.48)	0.001
[2000-2500[	81 (25.6)	18 (12.0)	2.13 (1.33-3.42)	< 0.001
[2500-4000[	84 (26.6)	89 (59.3)	0.44 (0.35-0.56)	< 0.001
$\geq 4000$	1 (0.3)	4 (2.7)	0.11 (0.01-1.05)	0.039
Hypotophy				
Yes	14 (4.4)	1 (0.7)	6.64 (0.88-50.06)	0.022
No	302 (95.6)	149 (99.3)	1	
Apgar score				
0	17 (5.4)	2 (1.3)	4.03 (0.94-17.23)	0.028
1-6	33 (10.4)	13 (8.7)	1.20 (0.65-2.22)	0.337
≥ 7	266 (84.2)	135 (90.0)	0.93 (0.87-1.01)	0.058
Complications after bin	rth			
Neonatal asphyxia	2 (0.6)	1 (0.7)	0.94 (0.08-10.38)	0.689
Neonatal resuscitation	96 (30.4)	34 (22.7)	1.34 (0.95-1.88)	0.051
Neonatal infection	6 (1.9)	4 (2.7)	0.71 (0.20-2.48)	0.409
Mortality				
Intrapartal death	20 (6.3)	2 (1.3)	4.74 (1.12-20.04)	0.011
Early neonatal death	17 (5.4)	5 (3.3)	1.61 (0.60-4.29)	0.234

The male sex was protective in multifetal pregnancies (RR 0.83, 95% CI 0.70-0.98, p<0.027). Multifetal pregnancies were associated with low birth weight (RR 1.62, 95% CI 1.11-3.04, p=0.01), fetal hypotrophy (RR 6.64, 95% CI 0.888-50.06, p=0.022), APGAR score at 0 at birth (RR=4.03, 95% CI 0.94-17.23, P=0.028) and intrapartal death (RR 4.74, 95% CI 1.12-20.04, P=0.011).

# 4.9 INDEPENDENT FACTORS ASSOCIATED TO MULTIFETAL PREGNANCIES: MULTIVARIATE BINARY LOGISTIC REGRESSION ANALYSIS.

Table XIV: Independent factors associated with multifetal pregnancies

Variables	Exposed group	Unexposed group	aRR	Adjusted
				p-value
	N=316; n(%)	N=150; n(%)	(CI at 95%)	
Gestational age at delive	ery (in weeks)			
≥ 37	102 (32.3)	81 (54.0)	0,95 (0,56-1,62)	0,874
Notion of fetal detress				
Yes	96 (30.4)	35 (23.3)	0,54 (0,09-3,16)	0,501
Birth weight (in grams)				
[2500-4000[	84 (26.6)	89 (59.3)	0,27 (0,16-0,47)	< 0.001
Hypotrophy				
Yes	14 (4.4)	1 (0.7)	3,28 (0,4-26,07)	0,260
Apgar score				
0	17 (5.4)	2 (1.3)	1,50 (0,11-19,48)	0,753
Complications after birt	th			
Neonatal resuscitation	96 (30.4)	34 (22.7)	1,90 (0,32-11,11)	0,474
Mortality				
Intrapartal death	20 (6.3)	2 (1.3)	2,20 (0,17-27,15)	0,537

After multivariate analysis using the binary logistic regression method for variables with a p-value strictly less than 0.10, neonates in the exposed group were significantly less likely to fall within the birth weight range of 2500-4000 grams (aRR: 0.27, 95% CI 0.16-0.47; adjusted p < 0.001).

**CHAPTER 5: DISCUSSION** 

### **MULTIFETAL PREGNANCIES**

Multifetal pregnancies are considered high risk due to the increased incidence of perinatal mortality and morbidity worldwide[5]. The highest incidence of multiple pregnancies has been found in low and middle-income countries particularly in Sub-Saharan Africa[4]. This is quite common in our setting occurring in about 2.8% of pregnancies[1]. These pregnancies can imply an increased risk for women and children because of higher rates of obstetrical complications. It is therefore important to understand the relationship between these pregnancies and their outcomes. We therefore carried out a retrospective cohort study to evaluate the immediate neonatal outcome following multifetal pregnancies and compared the outcome with that of singleton pregnancies. Our results confirmed some of the findings from previous studies, that the outcome from these pregnancies are poorer than those of singleton pregnancies.

### Limitations of the study

A possible limitation of our study is the fact that it was carried out in Yaoundé and in two hospitals only therefore the results cannot reflect the burden of multifetal pregnancies in the general population.

### Sociodemographic characteristics of the study population

Women within the age group 25-29 years were the most protected in the two groups (RR 0.64, 95% CI 0.32-1.01, p<0.035). The highest number of multifetal pregnancies occurred among women aged between 30-34 (26.7%), the mean maternal age of the women was  $27.9\pm6.2$  years. This is similar to results published in Kenya in 2014 and in Ethiopia in 2022 which revealed mean maternal ages of  $26\pm5$  years and 26.6 years respectively[36,37].

The highest level of education among women in the exposed group was high school (40.0% vs. 28.0%) in contrast to women in the unexposed group who were mostly university graduates (46.7% vs. 30.7%) ( $\mathbf{p} < \mathbf{0.05}$ ). This is contrary to the results published in Cameroon in 2022 which showed the highest level of education among women with multifetal pregnancies to be secondary [1].

### Obstetrical profile and comorbidities of the study population

Grand multigravidity and grand multiparity were associated with multifetal pregnancies. Women who were grand multigravida had 4.25 times the risk of having multifetal pregnancies (**RR 4.25**, **95% CI 1.87-9.65**, **p< 0.001**). In the same order, women who were grand multiparous had 5.16 times the risk of having multifetal pregnancies (**RR 5.61**, **95% CI 1.87-16.85**, **p<0.001**). These findings are similar to a study done in Nigeria in 2011 which showed that multiple pregnancies occurred mostly among grand multiparous women [4].

There was no statistically significant association between personal/family history of multifetal pregnancy and the occurrence of multifetal pregnancy. This is contrary to the results published in Cameroon in 2022 which showed 65.5% of cases of multifetal pregnancies had a family history of multifetal pregnancy compared to 2% in our study. This discrepancy may be due to the difference in the sample size[1].

### **Pregnancy follow-up**

Most women in our study had only 1 to 3 antenatal contacts, 59.3% and 52.0% respectively in the exposed and unexposed groups (p=0.123). This is contrary to results published in Nigeria in 2013 which showed that 61.5% of their study population had 4 or more antenatal contacts[38]. This can be explained by the fact that most women in our setting were not well informed on the importance of antenatal contacts or due to limited resources since most of them worked in the informal sector.

There was no statistically significant difference between pathologies developed during singleton and multifetal pregnancies. This is contrary to results published in India in 2016 which revealed a significant association between multifetal pregnancies and pathologies such as anaemia[39]. This is could be due to the fact that our study was retrospective therefore data concerning these pathologies might have been poorly filled or absent.

### Maternal and foetal outcome of multifetal pregnancies

Women with multifetal pregnancies had 1.70 times the risk of delivering through caesarean section (**RR 1.70**, 95% **CI 1.19-2.44**, **p=0,002**). This correlates with a study carried out in Kenya in 2014 and in India in 2017 revealing that women with multifetal pregnancies had four times the risk of delivering through caesarean section [36,40]. This can be explained by the increased risk of malpresentation coupled with the higher rates of obstetrical

complications such as placenta praevia/abruption, preeclampsia in these pregnancies. Consequently, healthcare providers often opt for caesarean section to mitigate these risks and ensure the safety of both mother and babies.

Women with multifetal pregnancies had more than 3 folds the risk of having extremely premature deliveries (**RR 3.22, 95% CI 1.01-10.96, p=0.023**). These findings are supported by other studies. For instance, a study carried out at the Jimma University in Southwest Ethiopia in 2015 showed that the mean gestational age at delivery for twin deliveries was 35.1±2.5 weeks (p=0.002)[41]. A similar study carried out in the USA in 2021 showed that the mean GA for singleton was significantly higher at 38.30 weeks of gestation as against 36.39 weeks in twin pregnancies[20]. The results published in Nigeria in 2013 equally reported having a mean gestational age of 36.8 vs 38.7 weeks for twin and singleton deliveries respectively[38]. This prematurity can be explained by the fact that preterm premature rupture of membranes (PPROM) occurs more frequently in multifetal gestations coupled with uterine distension that occurs in these pregnancies as well as other factors such as increased incidence of placental abnormalities and other obstetrical complications.

The male sex was protective in multifetal pregnancies (**RR 0.83, 95% CI 0.70-0.98, p<0.027**). Multifetal pregnancies were associated with low birth weight (**RR 1.62, 95% CI 1.11-3.04, p=0.01**), fetal hypotrophy (**RR 6.64, 95% CI 0.888-50.06, p=0.022**), and APGAR score of 0 at birth (**RR=4.03, 95% CI 0.94-17.23, P=0.028**). These results are consistent with those published from a study done in Cameroon in 2022 which revealed low birth weight and neonatal aspyxia in twins compared to singletons [1]. These results are most likely due to the fact that most of these babies are born prematurely. This can also be due to factors such as placental insufficiency as well as increased hormonal and physical demands which can impact the nutritional status of the foetuses.

In terms of mortality, neonates born to women in the exposed group were 4 times more likely to die during delivery than those born to women in the unexposed group(**RR 4.74, 95% CI 1.12-20.04, P=0.011**). These findings are similar to those published in Nepal in 2015 which revealed that perinatal mortality is four times higher in twins and six times higher in triplets as compared to singletons[8]. A study carried out in Guinea equally had similar findings in 2017 with a twin-singleton rate ratio for neonatal mortality of 5.0 (95% CI 4.4-5.6)[42]. This can be explained by the poor monitoring of the pregnancy as most women (59.3%) had attended

just between 1-3 ANCs and probably due to inadequate neonatal resuscitation. Furthermore, because of the increased rates of low birth weight and prematurity in these pregnancies, the risk of perinatal mortality increases due to a variety of complications such as respiratory distress syndrome caused by immature lungs.

### **Independent variables associated to multifetal pregnancies**

However, after multivariate logistic regression analysis, the only independent variable found to be associated with multifetal pregnancies was low birth weight. Neonates born following multifetal pregnancies were significantly less likely to fall within the birth weight range of 2500-4000 (aRR: 0.27, 95% CI 0.16-0.47; adjusted p < 0.001).

Immediate neonatal outcome following multifetal pregnancies in two hospitals in Yaoundé
CONCLUSION AND RECOMMENDATIONS

### **CONCLUSION**

At the end of this study which had as main objective to evaluate the immediate neonatal outcome following multifetal pregnancies in two hospitals in Yaoundé, we can draw the following conclusions;

- Multifetal pregnancies mostly occurred among women in high school, aged between 30-34, who were grand multigravida and grand multiparous.
- Neonates born following multifetal pregnancies were most likely to be males, extremely premature, small-for-gestational age and have poor APGAR scores at birth.
- Multifetal pregnancies were associated with adverse neonatal outcomes such as low birth weight.
- Neonates born following multifetal pregnancies were more likely to have a low birth weight compared to singletons.

### RECOMMENDATIONS

Following our study, we kindly recommend the following;

### To pregnant women

- To respect the recommended WHO program for antenatal consultations.
- To be cautious and seek medical attention as soon as they notice any signs of preterm labor.

### To the health personnel

- To provide specialized prenatal care to women with multifetal pregnancies tailored towards their unique needs. This involves close monitoring of maternal and fetal health, regular ultrasound examinations to assess fetal growth and well-being.
- To educate pregnant women about the signs of preterm labor and encourage them to seek prompt medical attention if they experience any symptoms.

### To hospitals

- To establish a better archiving system for medical records.
- To prioritize the implementation of standardized protocols and guidelines for the management of multifetal pregnancies, ensuring consistency and quality of care across all clinical settings.

### To the scientific community

- To conduct studies investigating the long-term health outcomes of children born following multifetal pregnancies, including neurodevelopmental outcomes, cardiovascular health, and metabolic health, can provide valuable insights into the impact of these pregnancies beyond the neonatal period.
- To prioritize research focused on identifying novel methods for preventing and managing complications associated with multifetal pregnancies such as preterm birth can inform the development of evidence-based clinical guidelines and interventions to improve neonatal outcomes.

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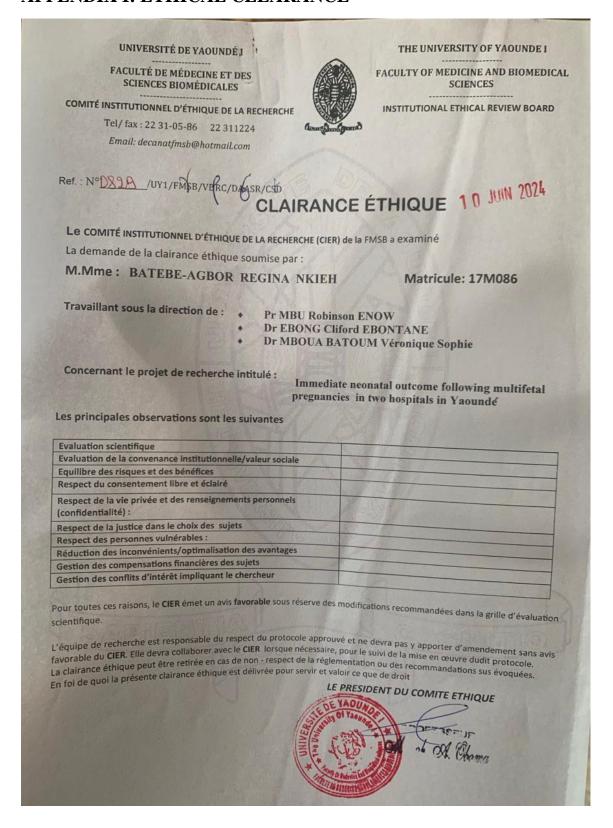
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**APPENDIX** 

### **APPENDIX**

### APPENDIX I: ETHICAL CLEARANCE



### **APPENDIX II: RESEARCH AUTHORISATION 1**

REPUBLIQUE DU CAMEROUN Paix-Travail-Patrie

MINISTERE DE LA SANTE PUBLIQUE

HOPITAL GYNECO-OBSTETRIQUE ET PEDIATRIQUE DE YAOUNDE

HUMILITE - INTEGRITE - VERITE - SERVICE



REPUBLIC OF CAMEROQN Peace-Work-Fatherland

MINISTRY OF PUBLIC HEALTH

YAOUNDE GYNAECO-OBSTETRIC AND PEDIATRIC HOSPITAL

HUMILITY - INTEGRITY - TRUTH - SERVIC

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

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

## AUTORISATION N° (AD /CIERSH/DM/2024 CLAIRANCE ETHIQUE

Le Comité Institutionnel d'Ethique de la Recherche pour la Santé Humaine (CIERSH) a examiné le 21 février 2024, la demande d'autorisation et le Protocole de recherche intitulé « multifetal pregnancies and immediate neonatal outcome in two hospitals in Yaounde » soumis par l'étudiant BATEBE AGBOR REGINA NKIEH.

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.

BATEBA AGBOR REGINA NKIEH, 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 2 8 FEV 2024

LE PRESIDENT

f MBU Robinson Directeur Général

HGOPY

### **APPENDIX III: RESEARCH AUTHORISATION 2**

REPUBLIQUE DU CAMEROUN Paix-Travail-Patrie

MINISTERE DE LA SANTE PUBLIQUE

SECRETARIAT GENERAL

DIRECTION DE L' HOPITAL CENTRAL DE YAOUNDE

SECRETARIAT MEDICAL

N° 020 24 AP/MINSANTE/SG/DHCY/CM/SM

REPUBLIC OF CAMEROUN Peace-Work-Fatherland

MINISTRY OF PUBLIC HEALTH

GENERAL SECRETARY

DIRECTORATE OF CENTRAL HOSPITAL OF YAOUNDE

MEDICAL SECRETARY

Yaoundé, le 0-7 FEV 2024

### **ACCORD DE PRINCIPE**

Je soussigné Professeur FOUDA Pierre Joseph, Directeur de l'Hôpital Central de Yaoundé, marque mon Accord de Principe à Madame BATEBE-AGBOR REGINA NKIEH, étudiante en 7ème année de Médecine générale à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I, sous le thème « MULTIFETAL PREGNANCIES AND IMMEDIATE NEONATAL OUTCOME IN TWO HOSPITALS IN YAOUNDE» dans le service de Gynécologie et Obstétrique à l'Hôpital Central de Yaoundé, sous la codirection du docteur EBONG Cliford.

#### Ampliations:

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



### APPENDIX IV: DATA COLLECTION SHEET

**Topic:** IMMEDIATE NEONATAL OUTCOME FOLLOWING MULTIFETAL PREGNANCIES IN TWO HOSPITALS IN YAOUNDE

Date://	Questionnaire number:
Patient Code://	

Number	Variable	Answer			
	1. SOCIODEMOGRAPHIC VARIABLES				
1.1	Exposed group=1, Unexposed group=2				
1.2	Recruitment site:Yaounde Central Hospital=1, Yaounde				
	Gynaecology,Obstetrics and Pediatrics Hospital=2				
1.3	Age: 15-19=1, 20-24=2, 25-29=3, 30-34=4, 35-39=5, >/40=6				
1.4	Marital status: Married=1, Single=2, Divorced=3, Widow=4				
1.5	Level of education: None=1, Primary=2, secondary(6eme-3eme)=3,				
	High School(2 <sup>nd</sup> -Tle)=4, University=5				
1.6	Occupation: Civil=1, Private=2, Informal=3, Student=4,				
	Housewife=5, Unemployed=6				
1.7	Region of origin: Extreme north = 1; North = 2; Adamawa = 3;				
	Centre = 4; Littoral = 5; North West = 6; South West = 7; West = 8;				
	East = 9; South = $10$				
1.8	Religion: Christian=1, Muslim=2, Atheist=3				
1.9	Gravdity: 1-2=1, 3-4=2, 5-6=3, 7-8=4, 9-10=5,>10=6				
1.10	Parity: 1-2=1, 3-4=2, 5-6=3, 7-8=4, 8-9=5, >10=6				
	2. OBSTETRIC HISTORY				
2.1	History of multifetal pregnancy? Yes=1, No=2				
2.2	If yes, what was the fetal number? One =1, Two=2, Three=3,				
	>three=4				
2.3	What was the mode of delivery of the multifetal pregnancy?				
	Vaginal=1, C-section=2				

	3. PAST MEDICAL HISTORY	
3.1	Medical conditions: Hypertension=1, Diabetes=2, HIV=3,	
	Hepatitis=4, Others=5, None=6	
3.2	Do you smoke? Yes=1, No=2	
3.3	Do you consume alcohol? Yes=1, No=2	
3.4	Have you ever had an ART? Yes=1, No=2	
3.5	If yes, which one? IVF=1, Ovulation induction=2, Others=3	
3.6	Family history of multifetal pregnancy? Yes=1, No=2	
	4. FOLLOW-UP OF PREGNANCY	
4.1	Gestational age at time of diagnosis: 1st Trimester=1, 2nd	
	Trimester=2, 3 <sup>rd</sup> Trimester=3	
4.2	Number of antenatal consultations done: <8=1, >8=2	
4.3	Gestational age at first antenatal consultation: 1 <sup>st</sup> Trimester=1, 2 <sup>nd</sup>	
	Trimester=2, 3 <sup>rd</sup> Trimester=3	
4.4	Antenatal consultations done by: Gynaecologist = 1; Medical doctor	
	= 2; Midwife = 2; Nurse = 3	
4.5	Number of obstetrical ultrasounds done: <3=1, >3=2	
4.6	Number of foetuses : One =1, Two=2, Three=3, >three=4	
4.7	Fetal or placental abnormalities on echography?Yes=1, No=2	
4.8	HIV done? Yes = $1$ ; No = $2$	
4.9	Hepatitis B done? Yes = 1; No = 2	
4.10	Hepatitis C done? Yes = 1; No = 2	
4.11	Syphilis done? Yes = 1; No =2	
4.12	Toxoplasmosis done? Yes = 1; No = 2	
4.13	Anaemia in pregnancy? Yes = 1; No = 2	
4.14	Did you take daily iron and folic acid? Yes = 1; No = 2	
4.15	Number of antitetanic vaccine taken: <2=1, >2=2	
4.16	Insecticide treated long lasting mosquito nets? Yes = 1; No = 2	
4.17	Any pathologies during pregnancy? Yes = 1; No = 2	
4.18	If yes ,which?Malaria=1, UTI=2, Other=3	
4.19	Mode of delivery: Vaginal delivery=1, C-Section=2, Instrumental	
	delivery=3	
4.20	If C-section, circumstances of C-section: Elective=1, Emergency=2	
4.21	Qualification of surgeon: Consultant=1, Resident in Obstetrics and	
	Gynaecology (Specify level) ,Other=3	
4.22	If> 1 foetus, interval between 1 foetus and the next (in minutes): <15	
	=1, 15-30 =2, >30=3	

5.FOETAL OUTCOME		
5.1	Gestational age at delivery (in weeks): <37=1, 37-42=2, >42=3	
5.2	Sex of neonate(s): Male=1, Female=2	
5.3	Birth weight(s):<1000g=1, 1000-1499g=2,1500-2000-2499g=3	
	2500g-3500g=4, >3500g=5	

5.4	Fetal length(s) in cm: <50=1, >50cm=2	
5.5	Fetal head circumference(s) in cm : <30=1, 30-35=2,>35=3	
5.6	Fetal mid upper arm circumference(s) in cm: <11.5=1,11.5-12.5>2,	
	>12.5=3	
5.7	APGAR Score at 5 minutes: <7=1, >7=2	
5.8	Any notion of fetal distress? Yes=1, No=2	
5.9	Was there neonatal resuscitation? Yes=1, No=2	
5.10	Fetal demise? Yes=1, No=2	

### APPENDIX V: ANTI-PLAGIARISM REPORT

