

REPUBLIC OF CAMEROON

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**MINISTRY OF HIGHER
EDUCATION**

THE UNIVERSITY OF YAOUNDE 1

**FACULTY OF MEDICINE AND
BIOMEDICAL SCIENCES**



REPUBLIQUE DU CAMEROUN

Paix-travail-patrie

**MINISTERE DE
L'ENSEIGNEMENT SUPERIEUR**

UNIVERSITE DE YAOUNDE 1

**FACULTE DE MEDECINE ET DES
SCIENCES BIOMEDICALES**

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY

**PREGNANCY FOLLOWING TREATMENT OF ECTOPIC
PREGNANCY IN THREE HIGHLY TURNOVER HOSPITALS IN
YAOUNDE.**

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

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DEDICATION



To my lovely parents,

**NSANGOU Adamou and MFOUT Adama Epse
NSANGOU**

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KEY:

HOD: Head of Department

P= Professor

AP= Associate Professor

SL= Senior Lecturer

L= Lecturer

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

I make these promises solemnly, freely and upon my honour.

SUMMARY

Introduction: Ectopic pregnancy (EP) is a major public health problem worldwide due to its frequency and severity. It is the first cause of maternal mortality in the first trimester of pregnancy, especially in developing countries.

Objectives: The main objective was to evaluate spontaneous pregnancy following different methods of treatment of ectopic pregnancy in three hospitals in Yaoundé.

Methods: We conducted a retrospective descriptive study covering a period of 5 years from 1st January 2018 to 31st December 2022 in the Yaoundé Gynaecology Obstetrics and Pediatrics hospital, Yaoundé Central hospital and Efoulan district hospital. In these hospitals, we identified files of cases treated for EP. Clinical data were exploited and we actively called the women to find out if they ever became pregnant after treatment and what happened to the pregnancies. Clinical and fertility outcome were then obtained through phone calls. We obtained information concerning intrauterine pregnancies, miscarriages, live births (LB), repeat EPs, the time between treatment and first intrauterine pregnancies and compared with method of treatment.

Results: We examined 293 files and 150 files conformed to the inclusion criteria. Ectopic pregnancies were found among women aged between 25 and 29 years, with a mean age of 28.3 ± 5.5 years. The study population was made mostly of students 31.3% and 48.0% of them had attained a higher level of education. Majority were single (67.3%) and most were primiparous (75.3%). Sexually transmitted infections (STIs) were found among 55.3% of the cases, and the most common organism was *Chlamydia trachomatis*. The overall spontaneous pregnancy rate was 76.0%. With respect to method of treatment, 24.2% of pregnancies occurred following medical treatment, 57.0% following laparotomy and 18.6% following minimally invasive surgery. About 49.1% of pregnancies were carried to term irrespective of method of treatment. There were 30.7% of repeat EPs and 26.6% miscarriages.

Conclusion: The prevalence of subsequent pregnancy following treatment of ectopic pregnancy was high irrespective of the method of treatment. Laparotomy was associated with the highest rate of subsequent pregnancies.

Keywords: Ectopic; pregnancy; spontaneous; outcome; recurrent.

RESUME

Introduction: La grossesse extra-utérine (GEU) est un problème majeur de santé publique dans le monde en raison de sa fréquence et de sa gravité. Elle est la première cause de mortalité maternelle au premier trimestre de la grossesse, surtout dans les pays en développement.

Objectifs: L'objectif principal était d'évaluer la grossesse spontanée après différents modes de traitement de la grossesse extra-utérine dans trois hôpitaux de Yaoundé.

Méthodes: Nous avons mené une étude descriptive rétrospective couvrant une période de 5 ans, du 1er janvier 2018 au 31 décembre 2022, à l'Hôpital de Gynéco-Obstétrique et Pédiatrique de Yaoundé, à l'Hôpital central de Yaoundé et à l'Hôpital de district d'Efoulan. Dans ces hôpitaux, nous avons identifié les dossiers des cas traités pour GEU. Les données cliniques ont été exploitées et nous avons activement contacté les femmes pour savoir si elles étaient tombées enceintes après le traitement et ce qui était advenu des grossesses. Les résultats cliniques et de fertilité ont ensuite été obtenus par des appels téléphoniques. Nous avons obtenu des informations concernant les grossesses intra-utérines, les fausses couches, les naissances vivantes, les GEU récurrentes et le délai entre le traitement et les premières grossesses intra-utérines, et les avons comparés selon la méthode de traitement.

Résultats: Nous avons examiné 293 dossiers et 150 dossiers ont répondu aux critères d'inclusion. Les grossesses extra-utérines ont été retrouvées chez des femmes âgées de 25 à 29 ans, avec un âge moyen de $28,3 \pm 5,5$ ans. La population étudiée était principalement composée d'étudiantes (31,3 %) et 48,0 % d'entre elles avaient atteint un niveau d'éducation supérieur. La majorité était célibataire (67,3 %) et la plupart étaient primipares (75,3 %). Les infections sexuellement transmissibles (IST) ont été retrouvées chez 55,3 % des cas, et l'organisme le plus courant était *Chlamydia trachomatis*. Le taux global de grossesse spontanée était de 76,0 %. En ce qui concerne la méthode de traitement, 24,2 % des grossesses sont survenues après un traitement médical, 57,0 % après une laparotomie et 18,6 % après une chirurgie mini-invasive. Environ 49,1% des grossesses ont été menées à terme, quelle que soit la méthode de traitement. Il y avait 30,7 % de GEU récurrentes et 26,6 % de fausses couches.

Conclusion: La prévalence de la grossesse ultérieure après le traitement de la GEU était élevée, quelle que soit la méthode de traitement. La laparotomie était associée au taux le plus élevé de grossesses ultérieures.

Mots-clés: Extra-utérine; grossesse; spontanée; résultats; récidivante.

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LIST OF ABBREVIATIONS

ACOG	: American College of Obstetricians and Gynecologist
CDG	: Center for Disease Control
CL	: Corpus Luteum
CS	: Cesarean Section
EDH	: Efoulan District Hospital
EP	: Ectopic Pregnancy
FMBS	: Faculty of Medicine and Biomedical sciences
GA	: Gestational Age
GnRH	: Gonadotrohin Releasing Hormone
IUP	: Intra Uterine Pregnancy
LMP	: Last Menstrual Period
MIS	: Minimally Invasive Surgery
REP	: Repeat Ectopic Pregnancy
RCOG	: Royal College of Obstetricians and Gynaecologist
STIs	: Sexually transmitted Infections
US	: Ultrasound
UYI	: University of Yaoundé 1
WHO	: World Health Organisation
YUTH	: Yaoundé University Teaching Hospital
YCH	: Yaoundé Central Hospital
YGOPH	: Yaoundé Gynaecology Obstetric Pediatrics

CHAPTER 1: INTRODUCTION

1.1 BACKGROUND

Ectopic pregnancy (EP) is defined as the implantation of product of conception out of the normal site in the uterine cavity. It is a gynecological condition considered to be the leading cause of maternal death during the first trimester of pregnancy according to the World Health Organization (WHO) [1]. It can have different locations, the most common being the fallopian tube. It is common due to increase in sexually transmitted infections, including *Chlamydia trachomatis*, adnexal adhesions and induced abortions [2]. In African developing countries, where most of the women tend to present at the rupture stage (with an unstable hemodynamic state), it is an important cause of maternal deaths, with a case fatality rates around 1–3%; 10 times higher than reported in industrialized countries [3–5]. A delay in diagnosis most often leads to severe complications (rupture and hemoperitoneum) and consequently to surgical treatment by laparotomy with salpingectomy [6,7]. Over the last few decades, the incidence of EP has steadily increased around the world. In the Western countries, it varies between 1–2% [8,9]. Yet this incidence is higher in developing countries, especially in Cameroon where it reaches 4.23% [10-13]. Some Swedish studies have demonstrated that the increased in EP's incidence was strongly associated to a rise in the incidence of Pelvic Inflammatory Disease (PID) and some sexually transmitted infections (STIs) [14,15].

There are other risk factors that have been associated with EP including prior EP, previous tubal surgery, documented tubal pathology, history of infertility, cigarette smoking, assisted reproduction technologies (ARTs), multiple lifetime sexual partners, older maternal age, and in utero diethylstilbestrol (DES) exposure [16–20]. In 2013 in the United States, the prevalence of ectopic pregnancy was 2.38% in New York, 2.07% in California and 2.2% in Illinois [21]. Research carried out on this subject at the Conakry University Hospital in 2012, found a prevalence of ectopic pregnancy of 1.30% and a mortality rate of 1.8% [22,23]. The incidence of EP ranges from 1-2% globally [24].

In Cameroon, an incidence of 0.79% was found in the year 2000 at the Yaounde University Teaching Hospital[25], 2.3% incidence from 1998 to 2008 in the Bafoussam Regional Hospital and 3.45% in the Sangmelima District Hospital in 2008[27]. Case fatality rate of ectopic pregnancy is 10 times higher in our environment compared to high income countries [28-30]. These different studies did not evaluate the subsequent fertility of patients independently of treatment methods. This study will go a long way to improve on quality care of patients with EP and provide baseline data for future studies.

1.2 RATIONALE

Ectopic pregnancies are responsible for approximately 10% of all maternal mortality and are the leading cause of pregnancy-related deaths during the first trimester and mainly related to internal hemorrhage [31-32]. In addition to maternal mortality and other related complications, ectopic pregnancy is an economic burden. There is paucity of information related to the occurrence of pregnancy following various methods of treatment of ectopic pregnancy in our milieu. This study is designed to respond to information gaps that exists.

1.3 RESEARCH QUESTIONS

1. What proportion of women become pregnant after treatment of EP?
2. What method of treatment of ectopic pregnancy favours subsequent pregnancies?

1.4 RESEARCH HYPOTHESIS

Spontaneous pregnancy following treatment of ectopic pregnancy may depend on the method of treatment.

1.5 OBJECTIVES OF THE STUDY

1.5.1 Main objective

The main objective was to study the occurrence of pregnancy following treatment of ectopic pregnancy in three highly turnover hospitals in Yaoundé.

1.5.2 Specific objectives

1. Describe the socio-demographic and clinical profiles of patients treated for ectopic pregnancy.
2. Determine the prevalence of pregnancies following the various methods of treatment of ectopic pregnancies.
3. Determine the prevalence of repeat ectopic pregnancies following treatment of ectopic pregnancies.
4. Compare the prevalence of ectopic pregnancy following the various methods of treatment of ectopic pregnancies.

1.6 DEFINITION OF OPERATIONAL TERMS

For all purposes and intents, the following definitions shall be adopted [3,9,10]

Ovulation: is the release of an egg from an ovary during the menstrual cycle.

Pregnancy: is a term used to describe the period in which a fetus develops inside a woman's uterus.

Ectopic Pregnancy: a pregnancy in which the fertilized ovum implants in a location other than the normal uterine endometrium.

Spotting: staining, streaking or spots of blood noted on the sanitary pad.

Tubal pregnancy: a pregnancy that occurs within the fallopian tube.

Interstitial pregnancy: a pregnancy that occurs within the interstitial portion of the fallopian tube (i.e., the segment that connects the tube to the endometrial cavity).

Complicated Ectopic Pregnancy: ectopic pregnancy associated with severe bleeding (e.g., hemoperitoneum, vaginal bleeding), abdominal pain with or without shock.

Uncomplicated Ectopic Pregnancy: ectopic pregnancy without any features of complicated pregnancy. May resolve spontaneously in some cases.

Heterotopic pregnancy: a rare condition involving multiple gestations, in which one is intrauterine and another ectopic. Occurs more frequently in patients undergoing infertility treatments e.g., in vitro fertilization.

Intrauterine pregnancy: pregnancy that occurs when a fertilized ovum implants and starts to develop within the uterus, where it is supposed to be.

First trimester: From 0-14 weeks days of gestation.

Ultrasound: is a radiological technique that involves sending soundwaves with very high frequencies through the body and receiving their echoes to visualize internal structures and organs.

Pregnancy test: is a test that measures a hormone in the body called human chorionic hormone (HCG) which is produced during pregnancy.

Corpus luteum: it is a temporary yellow hormone-secreting body in the female reproductive system that is formed in the ovary each menstrual period.

Ovum transmigration: is an event in which the pregnancy occurs contralateral to where ovulation was produced.

Selection bias: a general term for different types of systematic errors that may occur if study subjects are inappropriately selected or a large number of subjects are lost to follow-up.

CHAPTER 2: LITERATURE REVIEW

2.1 INTRODUCTION

Ectopic pregnancy (EP) is a clinical condition that results from the implantation of a fertilized ovum outside the normal uterine cavity. It is a common cause of morbidity and mortality in women of reproductive age globally and the most common cause of maternal mortality in the first trimester, it accounts for up to 12.5% of maternal mortality in Cameroon. Apart from maternal morbidity and mortality, EP is also associated with foetal loss, repeat ectopic gestation and impairment of subsequent fertility. The incidence of EP ranges from 1-2% globally. In Cameroon, an incidence of 0.79% was found in the year 2000 at the Yaounde University Teaching Hospital, 2.3% incidence from 1998 to 2008 in the Bafoussam Regional Hospital and 3.45% in the Sangmelima District Hospital in 2008. Case fatality rate of Ectopic pregnancy is 10 times higher in our environment compared to high income countries. The goal of this research was to provide data that will serve as basis for interventional programs designed to prevent and decrease the morbidity and mortality due to ectopic pregnancy.

2.1.1 Definition

Ectopic pregnancy is defined as a pregnancy in which the implantation of the embryo occurs outside the uterine cavity, most frequently in one of the two fallopian tubes or, more rarely, in the abdominal cavity or the cervix.

2.1.2 Epidemiology

It is the leading cause of maternal death in the first trimester of pregnancy due to hemorrhage. The current incidence of ectopic pregnancy is difficult to estimate accurately from available data (hospitalizations) because inpatient hospital treatment of ectopic pregnancy has decreased and multiple health care visits for a single ectopic pregnancy have increased [1,2]. The Center for Disease Control (CDC) published the data of incidence of ectopic pregnancy in US [3]. The prevalence of ectopic pregnancy among women who go to an emergency department with first trimester bleeding, pain, or both ranges from 6 to 16%[4].

2.2 RECALL

2.2.1 REVIEW OF ANATOMY

2.2.1.1 The uterus

The uterus is a thick-walled, pear shaped hollow muscular organ, which lies within the lesser pelvis with its body lying on the urinary bladder and its's/ cervix lying between the urinary bladder and the rectum.

The adult uterus is usually anteverted and anteflexed so that the mass lies over the bladder, with its position changing relative to the degree of fullness of the bladder and rectum or stage of pregnancy.

The non-gravid uterus varies in size, ranging from approximately 7.5cm long, 5cm in diameter, 2cm thick and weighs approximately 90g.

The uterus is divided into 2 main parts; the body, which forms the superior 2/3 of the organ, includes the fundus of the uterus, the rounded part that lies superior to the uterine ostia. The body lies between the layers of the broad ligament and is freely movable. It has 2 surfaces, visceral and interstitial.

The body is demarcated from the cervix by the isthmus.

The wall of the uterus consists of 3 layers;

- The outermost serosal perimetrium. The serosa, or outermost layer, consists of a thin layer of connective tissue. It is distinct from the parametrium, a subserosa extension of the uterus between the layers of the broad ligament
- The middle layer called the myometrium, which is made up of thick smooth muscles, majority of the uterine blood vessels and nervous fibers. It is responsible for the contracting force of the uterus during labor.
- The innermost layer or the endometrium, which firmly adheres to the myometrium and is subjected to monthly cyclical changes to its structure and function under the influence of various hormone. Shedding of this layer is responsible for menstruation.

The vascularization of the uterus is achieved mainly from the uterine arteries, with potential collateral supply from the ovarian arteries.

The uterine veins enter the broad ligaments with the arteries and form the uterine venous plexus on each side of the cervix.

The vein drains into the iliac vein.

The lymphatic drainage of the endometrium is achieved through lymphatics that are confined to the basalis layer

The uterus gets its innervation by the uterovaginal plexus which is a branch of the hypogastric plexus.

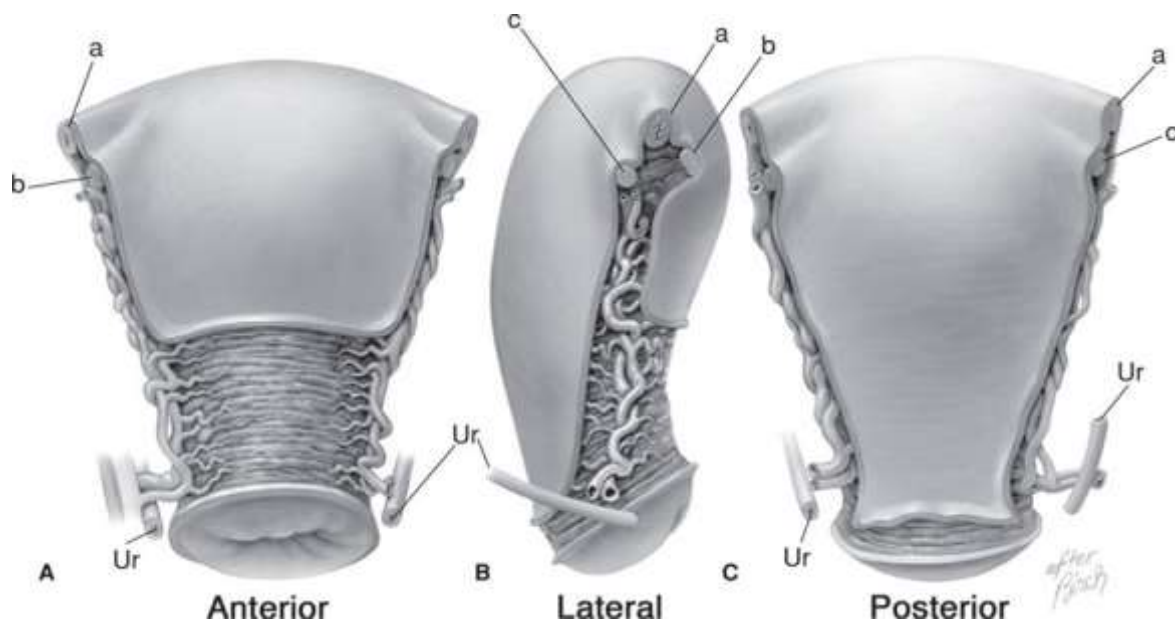


Figure 1: Anterior(A), right lateral(B), and posterior(C) views of the uterus of an adult woman. a= fallopian tube; b=round ligament; c= utero-ovarian ligament; Ur= ureter[18]

2.2.1.2 The cervix

The cervical portion of the uterus is fusiform and open at each end by small apertures—the internal and external cervical os. Proximally, the upper boundary of the cervix is the internal os, which corresponds to the level at which the peritoneum is reflected up onto the bladder. The upper cervical segment the portio supravaginalis, lies above the vagina's attachment to the cervix. It is covered by peritoneum on its posterior surface, the cardinal ligaments attach laterally, and it is separated from the overlying bladder by loose connective tissue. The lower cervical portion protrudes into the vagina as the portio vaginalis. Before childbirth, the external cervical os is a small, regular, oval opening. After labor, especially vaginal child- birth, the orifice is converted into a transverse slit that is divided such that there are the so-called anterior and posterior cervical lips. If torn deeply during labor or delivery, the cervix may heal in such a manner that it appears irregular, nodular, or stellate. The portion of the cervix exterior to the external os is called the ectocervix and is lined predominantly by nonkeratinized stratified

squamous epithelium. In contrast, the endocervical canal is covered by a single layer of mucin-secreting columnar epithelium, which creates deep cleft like infoldings or “glands.” Commonly during pregnancy, the endocervical epithelium moves out and onto the ectocervix in a physiological process termed eversion.

The cervical stroma is composed mainly of collagen, elastin, and proteoglycans, but very little smooth muscle. Changes in the amount, composition, and orientation of these components lead to cervical ripening prior to labor onset. In early pregnancy, increased vascularity within the cervix stroma beneath the epithelium creates an ectocervical blue tint that is characteristic of Chadwick sign. Cervical edema leads to softening Goodell sign, whereas isthmic softening is Hegar sign.

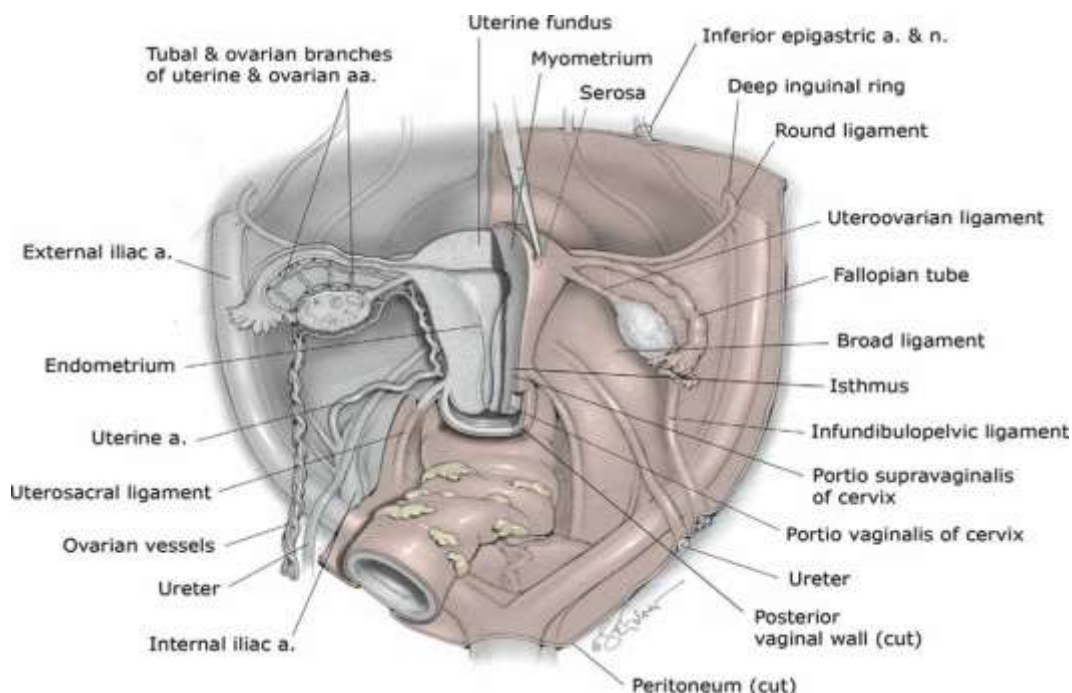


Figure 2 : Uterus, adnexa, and associated anatomy[6]

2.2.1.3 The fallopian tube

The Fallopian tube can be anatomically divided into 03 different parts. The isthmus, ampulla, and the infundibulum.

Proximally, there is the isthmus with a narrow 2-3mm lumen which adjoins the uterus, and gradually widens to about 5-8mm more laterally for form the ampulla.

Lastly, the infundibulum is a funneled- shaped fimbriated distal extremity of the tube which opens to the abdominal cavity and surrounds the ovary, collecting the oocyte at the time of ovulation.

The distal tubal musculature of the Fallopian tube undergoes constant rhythmic contractions varies with cyclical ovarian hormonal changes.

The tubal mucosa consists of ciliated secretory cells and is most abundant at the fimbriated extremity and sparse elsewhere. These cilia produce a current which is directed towards the uterine cavity creating a peristaltic wave which is important for ovum transport.

The Fallopian tubes are richly supplied by the ovarian and uterine arteries.

Nervous supply is achieved by extensive sympathetic innervation. This nerve supply derives partly from the ovarian plexus and partly from the uterovaginal plexus, with sensory afferent fibers being derived from T10.

Functions of the fallopian tubes:

- Movement of cilia and contraction of the muscular layer facilitate the transport of the ovum to the uterus for implantation
- Secretion of nutrients for gametes
- Sperm transport

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.

These changes occur at the level of the ovaries and the endometrium and it enables normal pregnancy or shedding during menstruation. The average age of menarche and menopause is 12yrs old and 51 years respectively.

Day 1 of the menstrual cycle is the first day of fresh bleeding

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:**

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.

❖ **The menstrual phase:**

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.

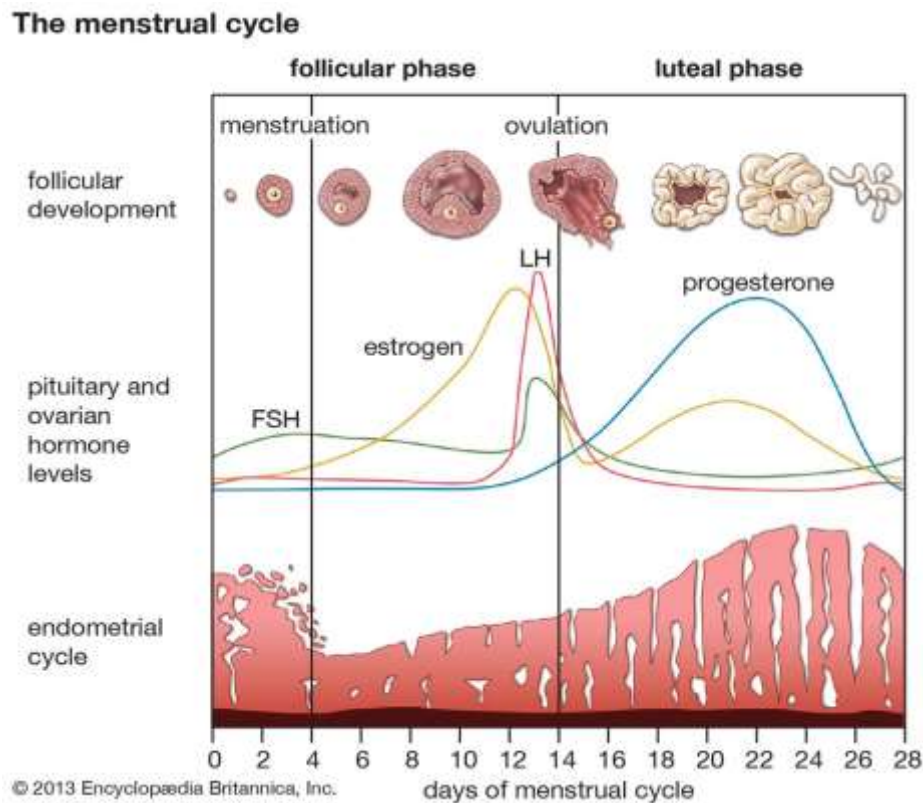


Figure 3 : The menstrual cycle [26]

2.2.2.2 Fertilization.

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

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 of 2 nuclei and intermingling of maternal and paternal chromosomes leads to the formation of the zygote.

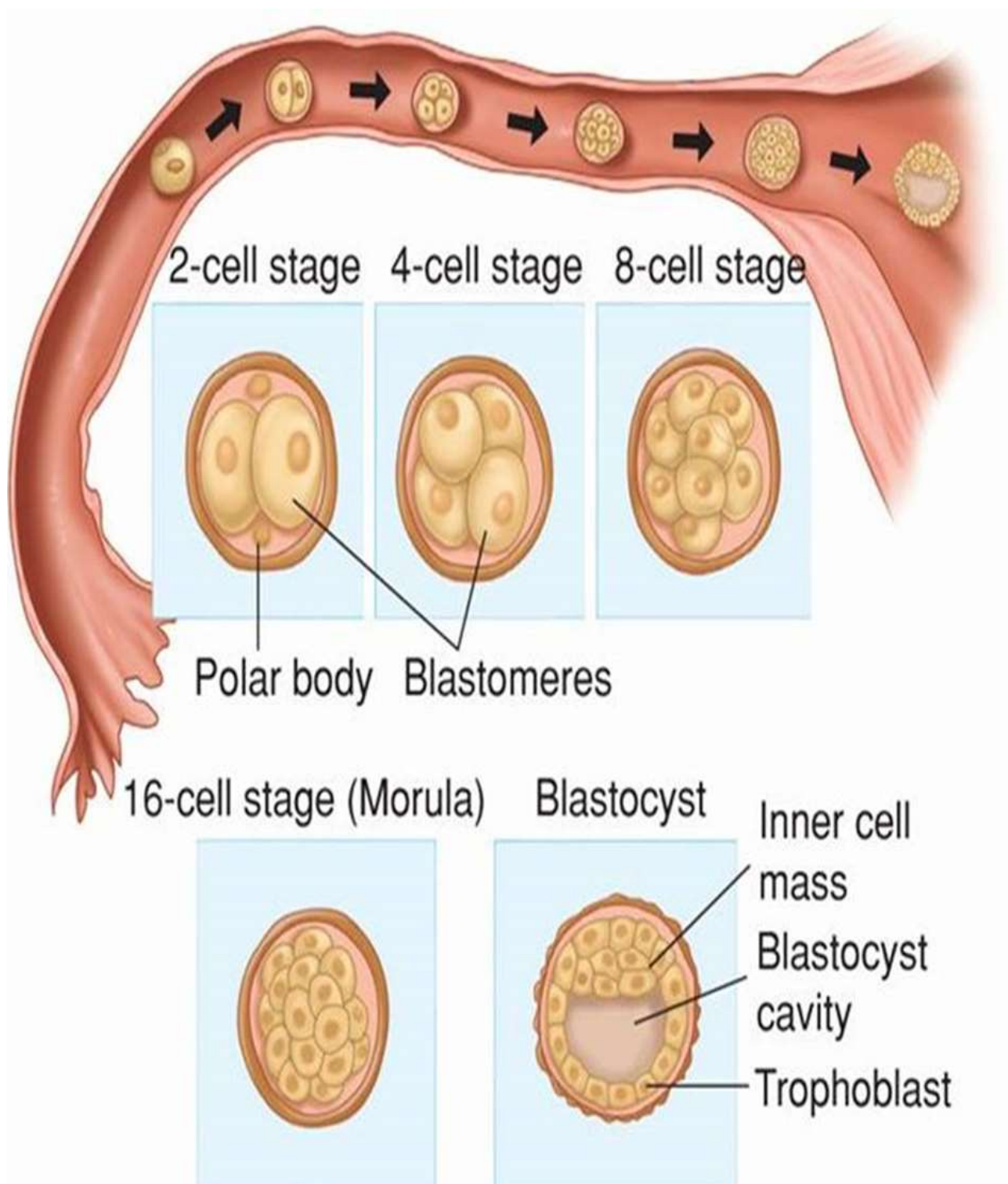


Figure 4 : Zygote cleavage and blastocyst formation[18]

The zygote:

The result of fertilization is a 46-chromosome diploid cell which undergoes cleavage and division to form the blastomere. The zygote undergoes slow cleavage for 03 days while still within the Fallopian tube. Further division leads to the production of a ball of cells called the morula. This ball of cells enters the uterine cavity 3 days after fertilization.

Gradually, fluid is accumulated between the morula and cells which leads to the formation of the early blastocyst.

Blastocyst implantation

Implantation of blastocyst occurs about 6-7 days after fertilization has occurred. This occurs in 3 different steps.

- Apposition: during apposition, the blastocyst makes initial contact with the uterine wall.
- Adhesion: here, there is increased physical contact between the blastocyst and the uterine wall.
- Invasion: penetration and invasion of the syncytiotrophoblast and cytotrophoblast into the endometrium, inner 3rd of the myometrium and uterine vasculature.

for implantation to occur, the endometrium readies itself appropriately with the help of estrogen and progesterone which are being produced by the corpus luteum. This process of uterine receptivity is limited to days 20-24 of the cycle.

The adherence of the blastocyst to the endometrial wall is mediated by cell surface receptors at the site of implantation that interact with the blastocyst receptor.

The blastocyst initially loosely adheres to the endometrium by apposition with the most common site of this process being the upper posterior wall.

2.2.2.3 Normal pregnancy.

Physiological changes in pregnancy. Summary

Table I: Physiological changes in pregnancy[15]

	T1 (1–14 wks)	T2 (14–28 wks)	T3 (28 wks– term) Term = 37–42 wks	During Labor	9-Month Period
Serum alkaline phosphatase					↑
Plasma prolactin	↑				↑ 10–20 times nonpregnant level
Cortisol and other corticosteroids	↑ from 12 wks	↑	↑		↑ to 3–5 times nonpregnant levels
Glucagon					↑
Insulin sensitivity	↑	↓ at 20 wks	↓		
Fasting insulin levels		↑ at 20 wks	Peak at 32 wks		
Plasma volume	↑	↑	↑		↑ by 50%
Red blood cell (RBC) mass	↑	↑	↑		↑ by 18–30%
Mean corpuscular volume (MCV)	↔ or ↑ from 82–84 fL		↑ from 86–100 fL or more		
Neutrophils	↑	↑	↑ to 30 wks		
Erythrocyte sedimentation rate (ESR)	↑				↑
Albumin blood levels	↓	↓ from 3.5–2.5 g/100 mL	↓ by 22%		
Total globulin		↑ by 0.2 g/100 mL			
Total proteins		↓ by 20 wks from 7–6 g/100 mL			
Thyroxine-binding globulin					↑ (Thyroxine-binding globulin levels double)
Total plasma cholesterol	↓ by 5%	↑	↑		↑ by 24–206%
Low-density lipoprotein (LDL)					↑ by 50–90%
Very low-density lipoprotein (VLDL)			Peaks at 36 wks		↑ by 36%
High-density lipoprotein (HDL)		↑ by 30%	Decreases from T2		↑ by 10–23%
Triglycerides			Reach 2–4 times nonpregnant level at 36 wks		↑ by 90–570%
Lipoprotein (a)	↑	↑ until 22 wks	↓ to nonpregnant levels		↔
Uterine contractions		Begin at 20 wks	↑		

2.3 COMPLICATIONS OF PREGNANCY

Many problems can be faced during early and late pregnancy. These complications may affect the mother, fetus or both. Some complications are:

- Hyperemesis gravidarum
- Bleeding in early and late pregnancy
- Hypertension in pregnancy
- Gestational diabetes
- Infections (Malaria, urinary tract infections (UTI), HIV, Hepatitis etc)
- Premature rupture of membranes (PRM)
- Preterm labor etc....

2.3.1 Risk factors of EP:

Table II: Risk factors of ectopic pregnancy[6,7]

Degree of risk	Risk factors
High	Previous ectopic pregnancy
	Previous tubal surgery
	Tubal ligation
	Tubal pathology
	In utero DES exposure
	Current IUD use
Moderate	Infertility
	Previous cervicitis (gonorrhea, chlamydia)
	History of pelvic inflammatory disease
	Multiple sexual partners
	Smoking
Low	Previous pelvic/abdominal surgery
	Vaginal douching
	<i>Early age of intercourse (<18 years)</i>

2.4 Etiopathogenesis:

In tubal ectopic pregnancy, implantation typically occurs in the wall of the tube, in the connective tissue beneath the serosa. There may be little or no decidual reaction and minimal defense against the permeating trophoblast. The trophoblast invades blood vessels, causing local hemorrhage. A hematoma in the subserosal space enlarges as pregnancy progresses. Progressive distention of the tube eventually leads to rupture. Vaginal bleeding is of uterine origin and is caused by endometrial involution and decidual sloughing. Atypical changes in the endometrium may be suggestive of ectopic pregnancy. The Arias-Stella reaction consists of hyperchromatic, hypertrophic, irregularly shaped nuclei, and foamy, vacuolated cytoplasm. These changes can be seen in normal pregnancy and in miscarriage and therefore are not diagnostic of ectopic pregnancy. Occasionally, endometrial tissue may be passed as a so-called decidual cast. Superficial secretory endometrium usually is present, but no trophoblastic cells are seen.

2.4.1 Location

The most common site for an ectopic pregnancy to implant is the Fallopian tube (the tubes stretching from the uterus to the ovaries, which the fertilised egg passes through on its way to the womb in a normal pregnancy). Over **90%** of ectopic pregnancies are located within the tubes.

Approximately 70% of ectopic pregnancies are located within the ampulla, which is the widest portion of the tube, at the ovarian end. 12% are located in the isthmic portion of the tube, which is the narrower part of the tube that links to the uterus, and 11% are found in the fimbriae, the finger- like projections which surround the ovary.

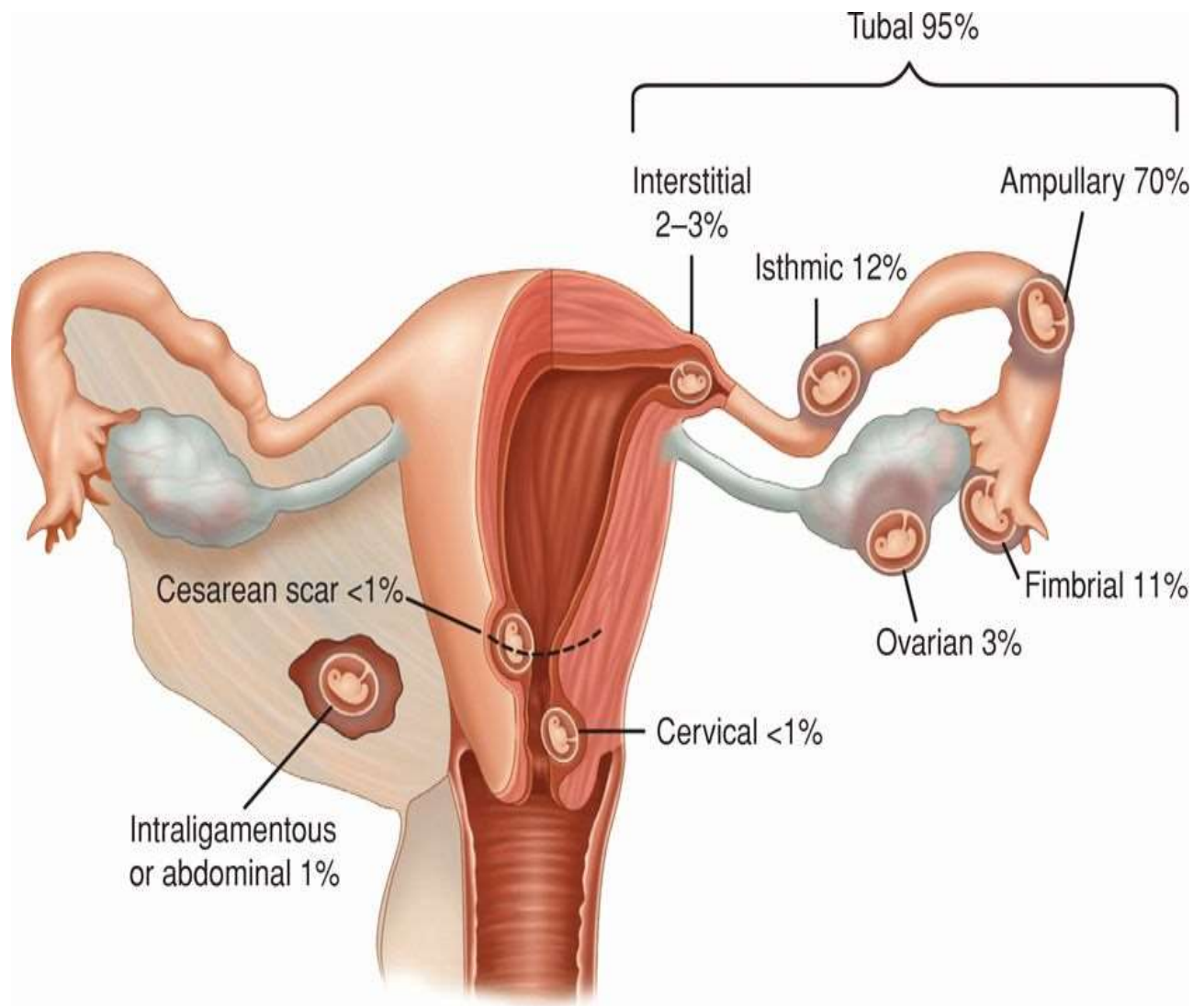


Figure 5 : Various sites of ectopic implantations with their percentages[9,10]

2.5 Clinical presentation

2.5.1 Type of description: Unruptured Ectopic Pregnancy

2.5.2 Circumstances of discovery:

Women who consults in early pregnancy for amenorrhea

Women of childbearing age consulting for pelvic pain or metrorrhagia

2.5.3 Clinical signs

The following symptoms may assist in the diagnosis of ectopic pregnancy:

1. Pain—Pelvic or abdominal pain is present in close to 100% of cases. Pain can be unilateral or bilateral, localized or generalized. The presence of subdiaphragmatic or shoulder pain is more variable, depending on the amount of intra-abdominal bleeding.

2. Bleeding—Abnormal uterine bleeding, usually spotting, occurs in roughly 75% of cases and represents decidual sloughing. A decidua cast is passed in 5–10% of ectopic pregnancies and may be mistaken for products of conception.

3. Amenorrhea—Secondary amenorrhea is variable. Approximately half of women with ectopic pregnancies have some spotting at the time of their expected menses and thus do not realize they are pregnant.

4. Other symptoms include; syncope—Dizziness, lightheadedness, and/or syncope is present in one-third to one-half of cases and represent advanced stages of intra-abdominal bleeding.

2.5.4 Physical Examination

The physical examination of patients with ectopic pregnancy is highly variable and often unhelpful. Patients frequently present with benign examination findings, and adnexal masses are rarely found. Patients in hemorrhagic shock from ruptured ectopic may not be tachycardic.

Some physical findings that have been found to be predictive (although not diagnostic) for ectopic pregnancy include the following:

- Presence of peritoneal signs
- Cervical motion tenderness
- Unilateral or bilateral abdominal or pelvic tenderness - Usually much worse on the affected side

Abdominal rigidity, involuntary guarding, and severe tenderness, as well as evidence of hypovolemic shock, such as orthostatic blood pressure changes and tachycardia, should alert the clinician to a surgical emergency; this may occur in up to 20% of cases. However, midline abdominal tenderness or a uterine size of greater than 8 weeks on pelvic examination decreases the risk of ectopic pregnancy.

On pelvic examination, the uterus may be slightly enlarged and soft, and uterine or cervical motion tenderness may suggest peritoneal inflammation. An adnexal mass may be palpated but is usually difficult to differentiate from the ipsilateral ovary.

The presence of uterine contents in the vagina, which can be caused by shedding of endometrial lining stimulated by an ectopic pregnancy, may lead to a misdiagnosis of an incomplete or complete abortion and therefore a delayed or missed diagnosis of ectopic pregnancy.

2.5.5 Laboratory studies

2.5.5.1 Serum β -hCG level

Finding: \uparrow β -hCG

➤ Additional considerations

Increased β -hCG is verifiable from the eighth day after ovulation. β -hCG discriminatory level: the β -hCG level at which an IUP is typically visible on ultrasound.

- Cutoff is typically β -hCG > 1,500–2,000 mIU/mL.
- Inability to visualize pregnancy on ultrasound above the β -hCG discriminatory level may suggest ectopic pregnancy.
- Multiple pregnancies may have higher β -hCG levels.

Serial β -hCG measurements (every 48 hours). Better diagnostic accuracy than a single β -hCG level in differentiating intrauterine from ectopic pregnancies

Findings after 48 hours;

The expected percentage increase in β -hCG for normal IUPs is determined based on the initial level.

- Initial level < 1500 mIU/mL: > 49% expected increase
- Initial level 1500–3000 mIU/mL: > 40% expected increase
- Initial level > 3000 mIU/mL: > 33% expected increase

Falling β -hCG levels may indicate a failed IUP (e.g., spontaneous abortion) or an ectopic pregnancy.

- A drop of > 21% suggests failed IUP.
- A drop of < 21% is more likely to indicate an ectopic pregnancy.
- An insufficient decline in serial β -hCG measurements following induced abortion should raise suspicion for ectopic pregnancy.

Other laboratory studies:

- Control blood count (CBC): Anemia may be seen in patients with vaginal bleeding.
- Blood type and screen: ABO and Rh testing to identify patients who might need Rho immunization
- Liver function test and BUN: to determine baseline liver and renal function
- Pregnancy test

2.5.5.2 Imaging

a) Transvaginal ultrasound (TVUS)

Indication: best initial imaging for determining the location of the pregnancy.

❖ Supportive findings

Empty uterine cavity in combination with a thickened endometrial lining

Possible free fluid within the pouch of Douglas (unspecific)

❖ Additional findings in tubal pregnancy

Possible extraovarian adnexal mass

❖ **Tubal ring sign (blob sign):** an echogenic ring that surrounds an unruptured ectopic pregnancy [20]

❖ Additional findings in interstitial pregnancy

Interstitial line sign: an echogenic line that extends from the gestational sac into the upper uterus (thought to be the echogenic appearance of the interstitial portion of the tube)

A thin myometrial layer (< 5 mm) surrounding the gestational sac

b) Transabdominal ultrasound (TAUS)

- Can be used to exclude differential diagnoses (e.g., acute appendicitis)
- Provides a general picture of the pelvic anatomy and upper abdomen but is less sensitive than transvaginal ultrasound (TVUS) in detecting extrauterine pregnancy

c) Exploratory laparoscopy

Indications :

Unstable patients suspected of having an ectopic pregnancy

In pregnancy of unknown location if the location is still uncertain after 7–10 days

d) Endometrial biopsy

Indication:

Consider only in cases of pregnancy of unknown location where **nonviability** is certain.

❖ Findings

Ectopic pregnancy: decidualization of the endometrium without chorionic villi or fetal parts

Intrauterine pregnancy loss

2.5.5.3 Diagnosis

Diagnosis of ectopic pregnancy has improved significantly due to advances in ultrasound technology, rapid and sensitive serum hormone assays, increased awareness and understanding of the associated risk factors. Despite this, around half of the women with an eventual diagnosis of ectopic pregnancy are not diagnosed at their first presentation. Early diagnosis reduces the risk of tubal rupture and allows more conservative medical treatments to be employed.

Currently, diagnosis in unruptured ectopic pregnancy is achieved using a combination of transvaginal ultrasonography and measurement of serum β -hCG concentrations. One of the key elements in the diagnosis is the exclusion of a viable or non-viable IUP. Diagnosis can be straightforward when a transvaginal ultrasound scan (TVS) positively identifies an IUP or ectopic pregnancy. However, TVS fails to identify the location of a pregnancy in a significant number of women and such women are currently diagnosed as having a ‘pregnancy of unknown location’



Figure 6 : Transvaginal ultrasound images of an intrauterine pregnancy (IUP) and ectopic pregnancy[20]

(A) An IUP at 6 weeks. The central dark area is the intrauterine gestational sac and within the sac is a circular ringed structure that is the yolk sac. The small oval structure below the yolk sac is the fetus. (B) An ectopic pregnancy. To the right of the image is the normal uterus and to the left of the uterus is the doughnut-shaped ectopic pregnancy.

Useful ultrasonographic findings in the diagnosis of ectopic pregnancy:

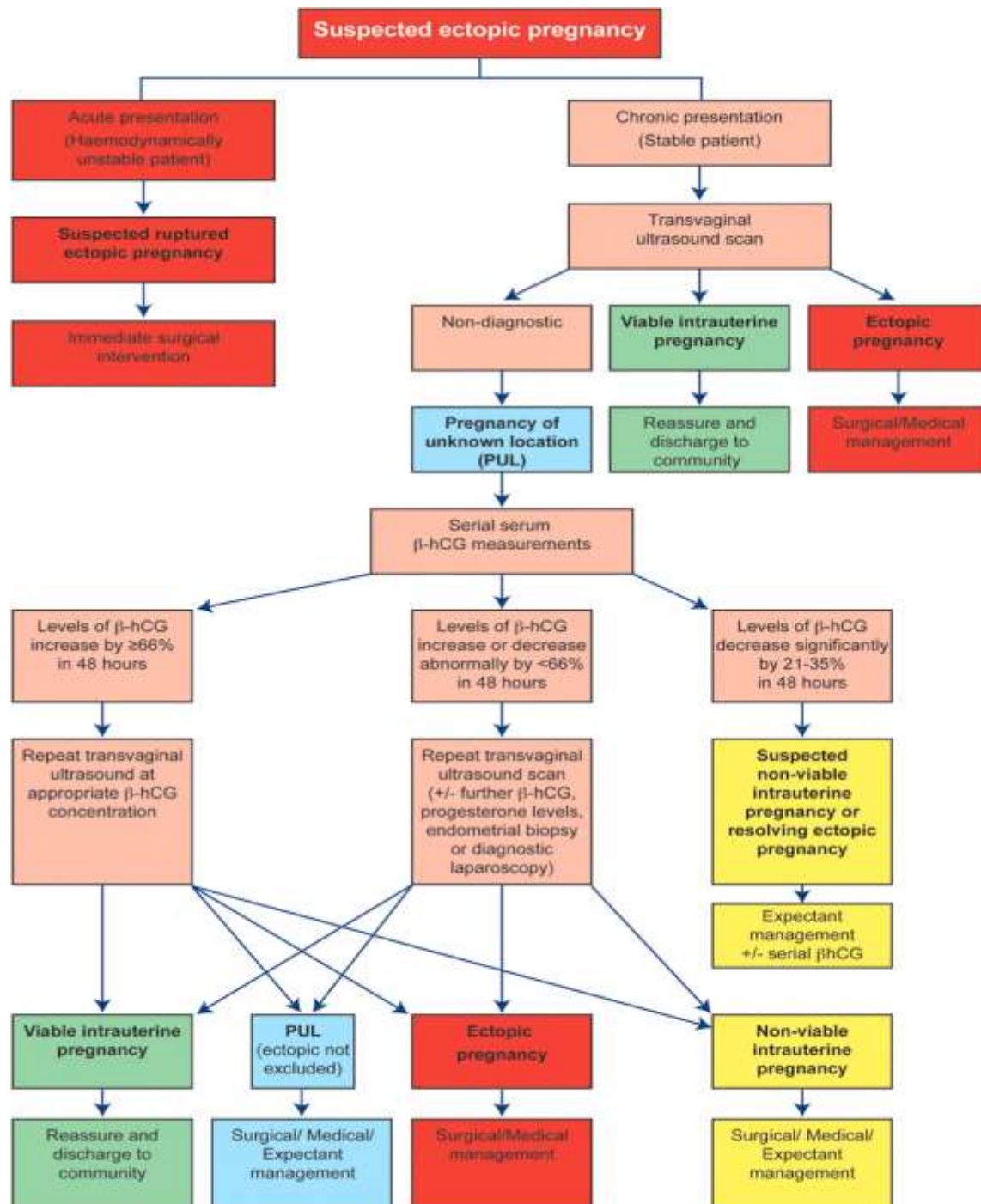
- Absence of intrauterine pregnancy (IUP)
- Positive identification of an ectopic pregnancy mass: inhomogenous mass, empty adnexal gestation sac or adnexal sac containing yolk sac or fetal pole
- Free fluid (i.e. blood): suggestive of ectopic pregnancy in the absence of IUP, but not diagnostic (small amount may be physiological)

2.6 Management

Ectopic pregnancy may be managed surgically, medically or expectantly. In these days of increasing outpatient diagnosis and management it is important to remember the risks of ruptured ectopic pregnancy. Clear documentation of diagnostic and management strategies – with clinical, sonographic and biochemical assessment of the patient – is therefore important. Which management is most appropriate depends on ongoing assessment and on numerous

clinical factors. Management is tailored to individual patients, based on their presentation and on the severity of their condition, suitability of treatment options and patient preference.

Table III: Diagnosis and management pathway[7,8]



2.6.1 Surgery

Surgical management is imperative in the clinical scenario of a ruptured ectopic pregnancy. A laparoscopic approach is preferable to an open approach in a patient who is haemodynamically

stable. Laparoscopic procedures are associated with shorter operative times, less intraoperative blood loss, shorter hospital stays and lower analgesia requirements. Laparotomy should be reserved for patients who present with rupture and are in a state of hypovolaemic shock and compromise. If the contralateral tube is healthy, the preferred option is salpingectomy, where the entire Fallopian tube, or the affected segment containing the ectopic gestation, is removed. A salpingostomy is the removal of the ectopic pregnancy, by dissecting it out of the tube, leaving the Fallopian tube in situ in an attempt to preserve fertility on that side.

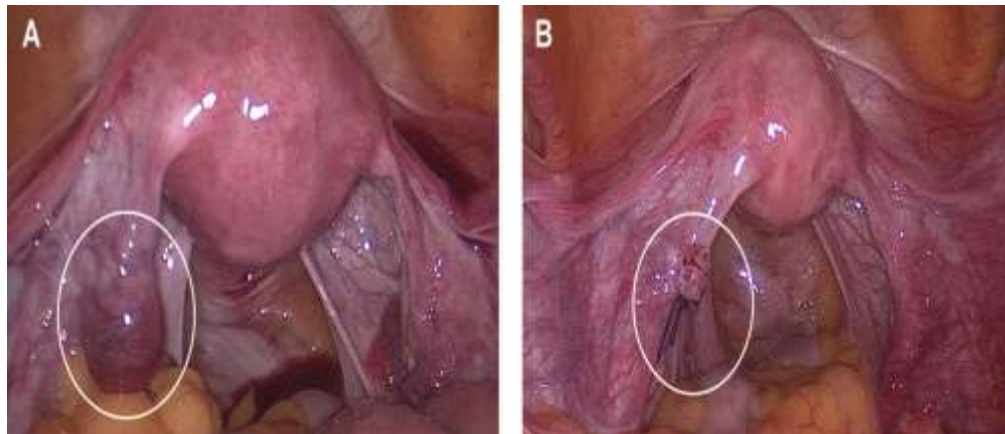


Figure 7 : (A) Left tubal ectopic pregnancy at laparoscopy. (B) Tubal ectopic pregnancy has been removed by salpingectomy.[3]

In the presence of contralateral tubal disease, a laparoscopic salpingostomy should be considered if future fertility is desired. Persistent trophoblast is the main concern after a salpingostomy. This is usually detected by a failure of serum β -hCG levels to fall and is more common following active tubal bleeding, where the ectopic pregnancy size was >2 cm or if serum β -hCG concentrations are >3000 IU/l or rising prior to surgery. Women should be followed up with serial β -hCG measurements and systemic methotrexate treatment may be required if the levels fail to fall as expected. While the short-term costs of postoperative follow-up and treatment of persistent trophoblast are greater following a salpingostomy, the potential avoidance of the subsequent need for assisted conception will make it more cost effective compared with salpingectomy.

2.6.2 Medical treatment with methotrexate

Medical treatment is useful for patients with an unruptured tubal ectopic pregnancy who are haemodynamically stable and have minimal symptoms and a low volume of free intraperitoneal fluid on ultrasound scan. Intramuscular methotrexate is the most widely used and successful medical therapy for ectopic pregnancy and is generally administered in a single-dose protocol.

Methotrexate is a folic acid antagonist that targets rapidly dividing cells and arrests mitosis. In ectopic pregnancy, the drug prevents the proliferation of cytotrophoblast cells, reducing cell viability and β -hCG secretion and thus progesterone support for the pregnancy. This facilitates the resolution of the ectopic pregnancy and tissue remodelling.

After assessing patient suitability for medical management, body surface area is calculated using height and weight measurements. In addition, a baseline full blood count and renal and liver function tests are obtained. In general, apart from some abdominal discomfort 1–3 days after treatment and abdominal bloating, side effects are not common and return to normal activities is quicker than after surgery. Potential serious side effects such as significant hepatotoxicity, bone marrow toxicity or alopecia are extremely rare with ectopic pregnancy treatment regimens. Patients require careful monitoring to ensure complete resolution of the ectopic gestation using serial assessment of β -hCG levels every 4–7 days (protocols vary between units) until the β -hCG level is <5 IU/l.

Inclusion criteria for medical management of ectopic pregnancy with methotrexate:

➤ Patient characteristics

Would prefer medical option

Willing to attend follow-up for up to 6 weeks

Willing to abstain from alcohol for 7 days following the treatment

Not breastfeeding or willing to stop

➤ Clinical features

Haemodynamically stable

Minimal abdominal pain

➤ Ultrasound scan findings

No fetal heart activity or clear yolk sac in adnexal mass

Small amount of free fluid

Unlikely to be early intrauterine pregnancy failure

➤ Serum beta-human chorionic gonadotrophin (β -hCG) concentrations

Usually < 3000 IU/l (Although limits of <5000 IU/l are used in some units and earlier studies, treatment success rates are higher when this more commonly used lower limit applies.)

➤ Medical history

No active peptic ulcer disease

No severe medical conditions including renal disease, hepatic disease, severe anaemia, leucopenia or thrombocytopenia

➤ Should not be on concurrent medication

Non-steroidal anti-inflammatory agents (NSAIDs), aspirin, penicillins, sulphonamides, trimethoprim, tetracyclines, diuretics, phenytoin, antimalarials, ciclosporin, retinoids, probenecid, folic acid, hypoglycaemics, live vaccines, nephrotoxic or hepatotoxic drugs

The commonly used single-dose methotrexate treatment regimen involves a deep intramuscular injection at a dose of 50 mg/m² of the calculated body surface area. Approximately 14–20% of patients receiving single-dose treatment will require a repeat dose, usually decided on following a fall of the β -hCG concentration of less than 15% from Day 4 to 7 after treatment. This timescale is used as methotrexate can cause a transient rise in serum β -hCG after initial treatment. Approximately 10% of women will require surgical intervention, although most of these are for slowly falling β -hCG levels rather than for acute tubal rupture. However, rupture still remains a possibility during treatment. Close treatment surveillance, and staff and patient awareness of potential treatment failure, are vital.

Two much less common uses of methotrexate for the treatment of ectopic gestation are the multi-dose protocol and direct injection of methotrexate into the ectopic pregnancy. The multi-dose regimen consists of methotrexate treatment on Days 1, 3, 5 and 7 to a maximum of four doses. Methotrexate treatment is very successful for small stable ectopic pregnancies.

2.6.3 Expectant management

Some ectopic pregnancies resolve spontaneously through either regression or tubal abortion, without causing harm to the patient. Expectant management is a conservative strategy consisting of observation and assessment of whether the ectopic pregnancy is continuing to resolve spontaneously and successfully without intervention. A suitable candidate for expectant management must have an ectopic pregnancy with no evidence of rupture, be clinically stable and asymptomatic, and have consistently declining β -hCG concentrations. A low serum

progesterone is also a possible marker of suitability for the expectant approach. Follow-up should be between one and three times weekly with β -hCG measurement and ultrasonography as required. Expectant management is reported to be most useful when the initial β -hCG is <1000 IU/l. A rapidly declining β -hCG level also appears to predict a favourable outcome. Success rates between 47% and 82% are reported, depending on the patient's initial status. The importance of compliance with follow-up and ease of access to the hospital should be emphasised. If β -hCG levels remain static or decline suboptimally, consideration should be given to reverting to surgical or medical management.

2.6.3.1 Predictive Score for ectopic pregnancy

Table IV: Fernandez predictive score of EP[21]

Elements	1	2	3
Gestational age (in days)	49wks	42<GA<49	>42
Beta HCG level (muI/ml)	<1000	1000-5000	>5000
Progesterone level (ng/ml)	<5	5-10	>10
Abdominal pain	Absent		Spontaneous
Hemoperitoneum (ml)	0	0-100	>100
Hematocele (cm)	<1	1-3	>3

Interpretation :

If

Score<11, => therapeutic abstention

11-13 => medical treatment

>13 => surgical treatment

2.6.3.2 Differential diagnosis

- Obstetrical bleeding
 - Threatened abortion
 - Incomplete abortion
 - Hydatiform mole

- Incidental bleeding
 - Torsion of an ovarian cyst
 - Tubal ovarian abscess
 - PID
 - Hemorrhagic corpus luteum

2.7 Prognosis

The condition is fatal for the fetus.

In the short run: the vital prognosis is compromised by the hemorrhage

In the long run: the functional prognosis of women operated for EP is poor; 30% remain sterile, 70% will be able to conceive and carry the pregnancy to term.

Future fertility: depends primarily on the fertility status prior to the ectopic pregnancy

Recurrence: Approx. 15 to 30%

Recent publications

Table V: Recent publications in the World

TITLE AND PLACE OF STUDY	AUTHOR AND YEAR OF STUDY	SAMPLING AND SETTING	RESULTS
Fertility outcome after ectopic pregnancy and use of an intrauterine device at the time of the index ectopic pregnancy	A. Bernoux, N. Job-Spira, E. Germain, J. Coste, J. Bouyer April 2014	A prospective population-based cohort study was undertaken using the Australasian Maternity Outcomes Surveillance System between May 1, 2013, and April 30, 2014, in hospitals in Australia with greater than 50 births per year.	The 70 women lost to follow-up included fewer IUD users than did the group followed (12 versus 29%), but there was no difference between the two groups for the main fertility factors except tubal damage, which was more frequent in women lost to follow-up (50 versus 30%, not significant).
The effect of appendectomy in future tubal infertility and ectopic pregnancy	Elraiyah T, Hashim Y, Elamin M, Erwin PJ, Zarroug AE. 12 May 2014	We systematically searched multiple electronic databases from inception through May 2013 for randomized trials and observational studies.	Our meta-analysis based on seven observational studies provided evidence that previous appendectomy is not associated with increased incidence of infertility in women (OR = 1.03, 0.86-1.24, P = 0.71). This finding was further augmented by several noncomparative cohorts that discussed the same issue and reported nearly the same conclusion; however, these

			studies pointed toward putative negative impact of surgery for complicated appendicitis on fertility. Our second meta-analysis revealed the effect of appendectomy on ectopic pregnancy was found to be significant based on a pooled estimate from four studies (OR = 1.78, 95% confidence interval = 1.46-2.16, P < 0.0001).
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IN AFRICA

Table VI: Recent publications in Africa

Management of ectopic pregnancies in a district hospital, Gauteng, South Africa	Doudou K. Nzaumvila, Indiran Govender and Gboyega A. Ogunbanjo 3 May 2018	The study was conducted at Odi District Hospital, located in Mabopane, a township in Gauteng province, 45 km north of Tshwane, South Africa (SA). This was a cross-sectional study.	We analysed 263 completed patient records. The incidence rate was 22 per 1000 live births. The mean age was 28.9 years (SD \pm 6.09), 57% were within the age group of 25–34 years, 90.9% were single and 85.2% were unemployed.
Risk factors of ectopic pregnancy	Luis R. Hoyos a c, Sejal Tamakuwala b c, Anupama Rambhatla c, Harpreet Brar c, Gustavo Vilchez d, Jenifer Allsworth e, Javier Rodriguez-	Retrospective, quasi-experimental case-control study of cervical ectopic pregnancy (CEP) cases from 2000-2013. Two groups were selected as controls, patients with tubal ectopic (TEP) and intrauterine pregnancies (IUP)	21 cases were identified and 126 controls included, 63 TEP and IUP each. A binary <u>logistic regression</u> model was used to analyze whether statistically significant preceding factors from a <u>bivariate analysis</u> could predict CEP. Compared to

	Kovacs c f, Awoniyi Awonuga c, July 2015	without a history of TEP, matched by year of pregnancy and randomly sampled in a 1:3 case-control ratio per each study group.	patients with IUP, CEP patients had a higher history of <u>elective abortions</u> , D&C and cervical excisional procedures, with a high effect size (>0.7). Compared to patients with TEP, CEP patients had a higher history of D&C and cervical excisional procedures, with a high effect size ($>.7$). The risk of CEP was significantly higher with a prior history of D&C compared to an IUP (aOR 1.4; 95% CI, 1.1–9.1; $p = 0.04$) and a TEP (aOR 6.1; 95% CI, 1.8–21.2; $p = 0.04$).
Incidence of ectopic pregnancy (EP) in St. Luke's Hospital, Anua in Uyo metropolis, Nigeria, 2012	Etuknwa Bassey Tom, FRCS1, Azu Onyemaechi Okpara, PhD2, Peter Aniekan Imo, MD1, Ekandem Gabriel John, PhD1, Olaifa Kayode, BSc1, Aquaisua Aquaisua Nyong, MSc1, Ikpeme Enobong, MSc1	A five-year retrospective study (2000-2004) was carried out, examining all cases of EP registered in the medical files of records in the casualty, maternity and surgical departments of St. Luke's Hospital, Anua in Uyo metropolis, which before the advent of the University of Uyo Teaching Hospital, in 2002, was the hub of medical activities in Akwa Ibom State.	Within the period under study, 2,3951 pregnancies was registered in that hospital out of which 72 cases of ectopic pregnancies was reported (3/1,000 pregnancies). Most of the affected females were young single women and students with 81.9% of them between 21 and 30 years of age. Mortality was 1.4% in the study. Related risk factors included pelvic inflammatory disease, previous history of abortions, infertility and a previous history of EP. These problems are compounded by social issues leading to

			multiple sexual partners and financial stress resulting from the palpable poverty in Nigeria today
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IN CAMEROON

Table VII: Recent publications in Cameroon

Incidence, risk factors, clinical presentation and treatment of ectopic pregnancy in the Limbe and Buea Regional Hospitals in Cameroon	Atabong Emmanuel Njingu ^{1,2} , Samuel Nambile Cumber ^{3,4,5} , Meh Martin Geh ^{1,6} , Mandeng Ma Linwa Edgar ¹ , Claude Ngwayu Nkfusai ^{7,&} , John Palle Ngunde ¹ , Gregory Edie Halle-Ekane ¹ December 2016	This was a retrospective nested case control study carried out in the maternity of the Limbe and Buea Regional Hospitals (LRH and BRH respectively) from December 2006 to December 2016. These two hospitals are the main referral centers in the South West Region of Cameroon. cases of EP with intraoperative findings not consistent with EP were excluded from the study. A ratio for control vs cases of 3:1 was obtained. The control group was obtained by systematic random sampling. Incomplete files were used in the calculation of the incidence but were excluded from the final analysis.	A total of 247 cases of EP were registered out of 17221 deliveries giving an incidence of 1.43% in ten years. History of pelvic inflammatory disease (OR = 3.10, CI (1.76-5.44), p < 0.001), previous EP (OR = 10.22, CI (2.61-14.82), p < 0.001), History of induced abortion (OR = 2.68, CI (3.32-9.73), p < 0.001), history of adnexa surgery (OR = 4.37, CI (2.17-10.32), p < 0.001) and history of appendectomy (OR = 2.16, CI (0.99-6.64) p < 0.001), were also found to be associated with increased risk of EP. More than five percent (5.52%) of the patients were in shock at presentation. Diagnosis was confirmed mainly by use of ultrasound (78.53%) and treatment was
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			principally by laparotomy (97.55%) with salpingectomy (95.60%). Most (90.18%) of ectopic pregnancies were ruptured at presentation. Only 2.45% of cases were managed medically with the use of methotrexate.
Maternal mortality in Cameroon, 7 May 2015	<u>Pierre-Marie Tebeu</u> , ^{1,2,&} <u>Gregor y Halle-Ekane</u> , ³ <u>Maxwell Da Itambi</u> , ¹ <u>Robinson Enow Mbu</u> , ⁴ <u>Yvette Mawamba</u> , ¹ and <u>J oseph Nelson Fomulu</u> ¹	This was a hospital-based case-control study approved by the National Ethical Committee. Data was collected from January 1st, 2006 to December 31st, 2010, in the Obstetrics and Gynecology Unit of the Yaoundé University Teaching Hospital.	During the study period, there were 9045 live births and 26 maternal deaths. The MMR for the study period was 287.5 per 100 000 live births. Among the cases of maternal deaths with known causes, direct causes accounted for 75% of maternal deaths and indirect causes for the remaining 25%. With regard to the direct causes, hemorrhage was the leading cause of maternal deaths (29.2%). There were 6 cases of postpartum hemorrhage (PPH) and a case of Placenta Praevia. The causes of PPH were bleeding disorders (3/6), uterine atony (2/6) and complete retention of the placenta (1/6). The second

			common cause of Maternal Mortality was complications of abortion (25%) and these were sepsis (4/6) and severe anemia (2/6). Other causes of MM were ectopic pregnancy (3/24, 12.5%), and hypertensive diseases of pregnancy (2/24, 8.3%).
The role of minimally-invasive and noninvasive methods in the management of EP in the Yaounde Gynaeco-Obstetric and Pediatric Hospital, Cameroon	Foumane P, Mboudou ET, Mbakop S, Dohbit JS, Belinga E, Doh AS. 2010	This was a retrospective and descriptive study, carried out in the Gynaecology service during the period from January 1st 2004 to December 31st 2008.	In total, 372 cases of EP were recorded during the 5 years during which 8779 deliveries took place, giving a frequency of EP of 4.23%. Of the 372 EP cases, only 281 files were usable. Minimally or successfully non-invasive treatment of EP has been carried out in 59 patients (21.00% of all cases). Medical treatment was successful in 37 patients (13.17% of all cases and 62.71% of minimally or non-invasive treatment cases).
Perceptions of antenatal care services by pregnant women	<u>Gregory Edie Halle Ekane</u> <u>Edie¹, Thomas Egbe</u>	An observational analytic cross-sectional study was carried out amongst pregnant women attending selected	Geographical accessibility and perceived quality of care were the predominant reasons for choosing or

attending government health centres in the Buea Health District, Cameroon: a cross sectional study, May 2015	<u>Obinchemti¹, Emmanuel Njuma</u> <u>Tamufor², Martin Mafany</u> <u>Njie², Theophile Nana</u> <u>Njamen¹, Eric Akum Achidi</u>	government health centres in the Buea Health District. We recruited 385 consenting pregnant women for the study. Demographic and clinical data were collected using structured questionnaires. The data was entered into Microsoft Excel and exported to Epi-Info (Version 3.5.1) for analysis.	changing a site for ANC. One third of respondents (30.1%) attended a health centre out of their catchment health area with Buea Town health centre receiving the highest proportion of women out of the health area (56.8% of attendees). Knowledge about antenatal care varied and majority of respondents (96.4%) were satisfied with the antenatal services received. However, there were elements of dissatisfaction with health centre services, poor sitting facilities, amenities, few health education talks and poor nursing skills. High educational level (high school and university) ($X(2) = 8.714$; $p = 0.01$) and first time pregnancy ($X(2) = 4.217$; $p = 0.04$) were significantly associated with poor satisfaction.
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CHAPTER 3: RESEARCH METHODOLOGY

3.1 TYPE OF STUDY

We carried out a retrospective descriptive study

3.2 STUDY SITES

Files were studied from 3 different hospitals

1. The Efoulan District hospital (EDH)

It is located at the heart of town in Yaoundé, Cameroon and has of gynecologists. The hospital has a dedicated mother and child unit which provides diversified medical care to children and pregnant women. The patient turnout is big with about 420 antenatal consultations per month, 3250 deliveries per year a cesarian section rate at 33.6% and that ectopic pregnancy of 12%.

2. The Yaoundé Gynaecology Obstetrics and Pediatrics hospital (YGOPH)

It is a reference health facility created in 2002 and specializes in mother and child health care. Its gynecology/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 Gynecology. The rate of cesarian section is 37% and that of ectopic pregnancy 10%.

3. The Yaoundé Central hospital (YCH)

This reference hospital located in the heart of Yaoundé has one of the biggest and most specialized maternity units with over 72 in patient beds, 6 delivery tables, 2 service operating theatres, 11 gynecologists and a large highly trained staff. It records about 2628 deliveries per year.

All the afore mentioned hospitals were chosen for this study because of their great patient turn over, good follow up and clear records.

3.3 DURATION OF STUDY AND PERIOD

The study was carried out on a duration of 7 months and covered a period of 5 years (from 1st of January 2018 to 31st of December 2022).

3.4 STUDY POPULATION

Files of women of childbearing age who were treated for ectopic pregnancy in the three hospitals were included in the study.

3.4.1 Inclusion criteria:

- All files of women of childbearing age diagnosed and treated for ectopic pregnancy by different treatment methods within the period 2018 to 2022.
- Women who accepted to take part in the study through phone calls.

3.4.2 Exclusion criteria

Files of women operated upon for indications other than ectopic pregnancy. Women who could not be reached on phone, and who did not want to participate were excluded.

3.4.3 Non-inclusion criteria

All participants who underwent bilateral salpingectomy and participants with non exploitable files were not included.

3.5 Sample Size estimation

3.5.1 Sampling method

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

3.5.2 Sample size estimation

Based on the study design, the sample size was estimated using the formula;

$$n = p*(1-p)*(Z\alpha/d)^2$$

Where;

n= population sample size

p= prevalence of cases of pregnancy after treatment of ectopic pregnancy, estimated to be 3% in our population.

$Z\alpha$ = the confidence interval 1.96 for 95%

d= level of precision estimated to 5%

$$n = 0.03*(1-0.03)*(1.96/0.05)^2$$

So, our minimum estimated sample size was 45.

3.6 PROCEDURE

3.6.1 Administrative procedure

A research proposal was written and approved by the supervisors, after which we obtained a research authorization from the different directors of the concerned hospitals, and ethical clearance from the Institutional Review Board of the Faculty of Medicine and Biomedical sciences of the University of Yaoundé I.

3.6.2 Data collection:

Once the administrative phase was completed, we went to the theater records, maternity records and identified all the cases of ectopic pregnancy treated by the various methods in the hospitals. After which, we went to the various archives to look for the records. We studied all the files and made phone calls to have active information on fertility status after treatment of ectopic pregnancy.

3.6.3 Variables studied:

We reviewed the medical records and obtained the sociodemographic profiles of patients treated for EP. These included:

- Ages
- Marital status
- Level of education
- Profession
- Religion of origin

For the Clinical variables, we collected information on the following :

- Symptoms, gravidity, parity, history of abortion, history of sexually transmitted infections, use of method of contraceptives, number of sexual partners, history of infertility
- History of pelvic surgery
- Gestational age
- Type of treatment carried out(laparotomy or ceolioscopy)
- Site of location of EP

We made phone calls and obtained the following information:

- Spontaneous IU pregnancies
- Repeat Ectopic pregnancies
- Pregnancies by method of treatment
- Outcome of pregnancies
- Time lapse between treatment and subsequent pregnancy

3.7 Data collection and analysis

Data were collected using a standard questionnaire that was conceived internally, validated, and adapted for the study. Data was entered into the Census and Survey Processing System (CSPro) version 7.5 software then transferred to and analyzed using Stata/SE version 17 software. Descriptive statistics were expressed as means with standard deviation for quantitative variables, after confirming normal distribution of the dataset while categorical variables were expressed as frequency and percentage. The Pearson's Chi square test was used to compare prevalences (proportions). Statistically significance was set at a two-sided p value < 0.05

3.8 Materials used

Material for data management included;

- Computer
- USB flash drive
- Scientific calculator
- Typing software
- Smart phone

3.9 HUMAN RESOURCES

- Principal Investigator : (myself)
- Study director and codirectors
- Statistician

3.10 ETHICAL CONSIDERATIONS

Ethical clearance was requested and obtained from the ethical committee of the Faculty of Medicine and Biomedical Sciences to carry out the study. The proposal and questionnaire form were submitted to the management of health facilities involved for the study site to obtain authorisation.

Confidentiality was assured by assigning codes for every participant and the codes were used to label all documentations and not the names of the patients.

The data collected were used for the research purpose only.

CHAPTER 4: RESULTS

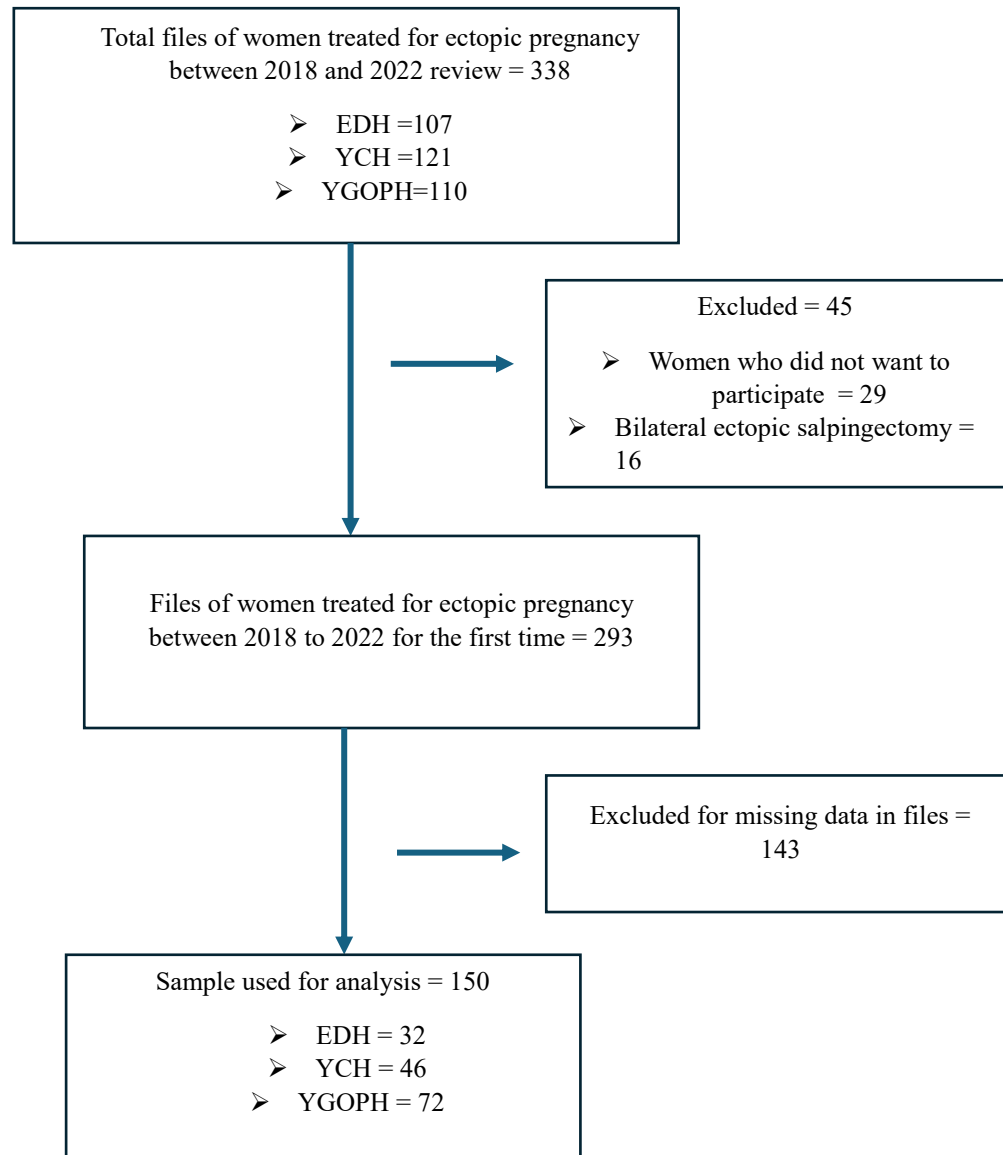


Figure 8: DIAGRAMATIC REPRESENTATION OF THE RECRUITEMENT PROCESS

In total, we successfully recruited **150 women** .

Table VIII: Distribution according to sociodemographic characteristics of study participants

Characteristic	Frequency (n=150)	Percentage
Age	28.3±5.5	
[15-19[3	2.0
[20-24[33	22.0
[25-29[61	40.7
30+	53	35.3
Profession		
Student	47	31.3
Housewife	41	27.3
Civil servant	36	24.0
Others	26	17.4
Level of education		
None	10	6.7
Primary	31	20.7
Secondary	72	48.0
University	37	24.6
Religion		
Christian	139	92.7
Muslim	7	4.7
Others	4	2.6
Marital status		
Single	101	67.3
Married	46	30.7
Widow	1	0.7
Divorced	2	1.3
Nationality		
Cameroonian	150	100
Foreigner	0	0
Region of origin		
West	46	30.7
North-West	7	4.7
South-West	2	1.3
East	7	4.7
North	2	1.3
Far-North	3	2.0
Adamaoua	2	1.3
Centre	65	43.3
Littoral	6	4.0
South	10	6.7

The study population was made mostly of students 31.3% and 48.0% of them had attained a secondary level of education. Majority were single (67.3%) and 92.7% were Christians.

Table IX: Clinical characteristics of study participants

Characteristic	Frequency (n=150)	Percentage
Gravidity		
G1-G2	66	44.0
G3-G4	49	32.7
G5-G6	27	18.0
> G6	8	5.3
Parity		
P0 – P2	113	75.3
P3 – P4	28	18.7
> P4	9	6.0
History of STIs		
Yes	108	72.0
No	42	28.0
History of abdomino-pelvic surgery		
Yes	38	25.3
No	112	74.7
Cumulative sexual partners		
< 3	37	24.7
≥ 3	113	75.3
Infertility before EP		
Yes	9	6.0
No	141	94.0
Smoking		
Yes	2	1.3
No	148	98.7

The women were of low gravidity 44.0% and low parity 75.3% with histories of STIs 72.0%

Table X: Distribution according to type of STIs and history of abdomino-pelvic surgery

Characteristic	Frequency (n=150)	Percentage
Type of STIs		
Chlamydia <i>trachomatis</i>	83	55.3
Gonorrhea	1	0.7
Mycoplasma <i>hominis</i>	20	13.3
Ureaplasma <i>urealyticum</i>	3	2.0
Others	1	0.7
None	42	28.0
History of abdomino-pelvic surgery		
Cesarean section	25	16.7
Coeloscopy	1	0.7
Myomectomy	1	0.7
Laparotomy	10	6.7
Others	2	1.3
None	112	74.7

Chlamydia *trachomatis* was isolated from 55.3% of cases and 16.7% have had cesarean deliveries.

Table XI: Distribution according to type of treatment recieved

Type of treatment	Frequency (n=150)	Percentage
Medical	29	19.3
Laparotomy	95	63.3
• Conservative	13	13.7
• Radical	82	86.3
Minimally invasive surgery	26	17.3
• Conservative	15	57.7
• Radical	11	42.3

Participants treated by medical treatment recorded a rate of 19.3%, 63.3% by laparotomy and 17.3% by minimally invasive surgery. Radical surgery was done in 86.3% of laparotomies and 42.3% of minimally invasive surgeries.

Table XII: Prevalence of subsequent pregnancy by treatment method

	Total (n=150)	Medical	laparotomy	Minimal invasive	P value
Pregnancy after ectopic pregnancy					
Yes	114(76.0)	26(22.8)	67(58.7)	21(18.42)	0.089
No	36(24.0)	3(8.3)	28(77.7)	5(13.8)	

After treatment of ectopic pregnancy, the prevalence of subsequent pregnancy was 76.0% in the whole sample. This prevalence was highest amongst those who received laparotomy treatment (58.7%), 22.8% after medical and lowest amongst those who received minimally invasive treatment (18.42%). Nevertheless, the difference in prevalence between the three groups of treatment was not statistically significant.

Table XIII: Outcome of pregnancy by method of treatment

Characteristics	Total (n=114)	Medical (n=26)	Laparotomy (n=67)	Minimally invasive (n=21)	P value
Time lapse between EP and current pregnancy/months					
< 6	2(1.75)	0(0)	2(2.99)	0(0.0)	0.195
[6 – 12[34(29.8)	12(46.2)	19(28.4)	3(14.3)	
[12 – 24[58(50.9)	12(46.2)	32(47.8)	14(66.7)	
≥ 24	20(17.5)	2(7.7)	14(20.9)	4(19.0)	
Nature of pregnancy					
Spontaneous	107(93.9)	26(24.3)	61(57.0)	20(18.6)	0.260
Medically assisted	7(6.1)	7(0.0)	6(9.0)	1(4.8)	
Location of pregnancy					
Intra-uterine	79(69.3)	22(84.6)	48(71.6)	9(42.9)	0.007
Ectopic	35(30.7)	4(15.4)	19(28.4)	12(57.1)	

The time lapse between 12-24 months was favorable for spontaneous pregnancies following treatment of ectopic pregnancy irrespective of the method of treatment. Pregnancies were 69.3% intra-uterine and 30.7% repeat ectopic pregnancies.

Table XIV: Outcome of subsequent pregnancy after initial ectopic pregnancy

Characteristic	Total (n=114)	Medical (n=26)	Laparotomy (n=67)	Minimally invasive (n=21)	P value
Outcome of intra-uterine					
Miscarriage	56(37.7)	10(38.5)	31(46.8)	15(71.4)	0.196
Preterm delivery	15(13.1)	5(19.2)	9(13.4)	1(4.8)	
Term delivery	43(49.1)	11(42.3)	27(40.3)	5(23.8)	

The highest rate of term deliveries was observed in patients who underwent medical with over 49.1% reaching full term. Minimally invasive surgery and laparotomy treatment had lower rates of term deliveries 23.8% and 40.3% respectively. Despite these differences, the P value of 0.196 indicates that the variations are not statistically significant.

CHAPTER 5: DISCUSSION

1. Sociodemographic Characteristics

The average age of the study population was 28.3 ± 5.5 years. This result is close to that reported in Cameroon in 2012, where the reported average age was 26.46 ± 5.42 years, with the most affected age group being 25-30 years [9]. In our case series, the dominant age was 25-29 years old (40.7%). This age was similar to that found in similar studies. This corresponds to the age of reproduction and peak sexual activity[6]. The highest incidence of ectopic pregnancy was noted amongst nulliparous and pauciparous women (75.3%). This observation has also been made by almost all the authors who estimated that ectopic pregnancy is associated to low parity [10,14] .

There were 101 single women, accounting for 67.3% of the study population, and 48.0% had secondary level of education. Most participants were Christians (92.7%) and all participants were Cameroonians, with the Centre region being the most represented (43.3%).

This result is similar to that reported in earlier studies in Cameroon in 2010 and 2012, where single women were predominant [37].The result could be explained by the fact that these patients were exposed to multiple sexual partners, which is a source of infection.

2. Gynecological History and Risk Factors for Ectopic Pregnancy (EP)

With respect to parity, 113 patients, or 75.3%, were primiparous. Clinically, 44.0% were in their first or second pregnancy (G1-G2), and 75.3% had between zero to two previous births (P0-P2). This result differs from a study in 2010 in Cameroon which found a predominance of EP among multiparous women [37].

Chlamydia trachomatis was the pathogenic sexually transmissible infection found among most of the cases. This tallies with results of previous studies carried out in Yaoundé and in Douala [1,9]. A study carried out in Gabon in 2002 identified Chlamydia *trachomatis* as 31.5% among cases of sexually transmitted infections and noted that the increase in the incidence of ectopic pregnancies coincided with the increase in the incidence of salpingitis[39]. This could be explained by the damage caused by the infection to the fallopian tubes, preventing normal migration of the embryo. The lesions caused by infections of the adnexa are responsible for scars that significantly reduce tubal patency and motility.

A history of pelvic surgery was found among 14.3% of the patients. This result is close to that reported in earlier studies in Cameroon in 2009 where a history of pelvic surgery was found in 12.9% of cases of ectopic pregnancy with 8,65 being tubal surgery[1]. This result differs from

that found in Cameroon in 2009[1,9]. This difference can be explained by the sizes of the different samples, but both past histories remains a risk factor for EP.

3. Prevalence of repeat ectopic pregnancy following treatment method

The overall prevalence of repeat ectopic pregnancy among those who had a subsequent pregnancy was 30.7%. This varied significantly among the treatment methods:

- Minimally Invasive Surgery: 57.1%
- Laparotomy: 28.4%
- Medical Treatment: 15.4%

The difference in repeat ectopic pregnancy rates was statistically significant ($P=0.007$), indicating that the treatment method impacts the risk of recurrent ectopic pregnancies.

4. Comparison of reproductive outcomes after treatment methods of ectopic pregnancy

Comparing the prevalence of repeat ectopic pregnancies post-treatment, minimally invasive surgery had the highest rate (57.1%), followed by laparotomy (28.4%) and medical treatment (15.4%). This suggests that while minimally invasive surgery might be less invasive, it carries a higher risk for repeat ectopic pregnancies compared to other treatment methods.

Among those who achieved subsequent pregnancies, the breakdown by treatment type was as follows:

- Laparotomy: 58.7%
- Medical: 22.8%
- Minimally Invasive Surgery: 18.4%

Though laparotomy had the highest prevalence of subsequent pregnancies, the difference in pregnancy rates among the treatment types was not statistically significant ($P=0.089$).

This study showed that spontaneous pregnancy was significantly higher after laparotomy treatment than medical treatment.

5. Spontaneous conception rate after treatment of ectopic pregnancy by method

The prevalence of subsequent pregnancy after treatment of ectopic pregnancy was 76.0%. This indicates a relatively high likelihood of achieving pregnancy post-treatment, reflecting either effective fertility-preserving interventions or the natural fertility potential of the participants.

After medical treatment of EP, there was a spontaneous conception rate of 22.8%. This result is similar to that found in 2021 in Cameroon, which reported a conception rate of 32.3% after medical treatment of EP, but lower than that reported in a similar study in 2022 in Turkey, which reported a rate of 83.2% after EP treatment by medical treatment [10,14]. This difference could be explained by the fact that our study evaluated women treated by both surgical and medical methods.

6. Time lapse between treatment and Conception

The distribution of time lapse suggests that a majority of subsequent pregnancies occurred within 12-24 months post-treatment, irrespective of the treatment type. This indicates a general pattern of recovery and readiness for a new pregnancy within that period. However, the non statistical significance ($P=0.195$) implies that the type of treatment does not significantly impact the timing of the next pregnancy. This result is similar to studies carried out in 2015 and 2022 in Cameroon which reported conception time lapse of 12 months and 11.82 ± 7.46 months, respectively[10,11]. This result could be explained firstly by the fact that the desire for pregnancy after EP treatment is not always immediate, secondly by the time required for the resorption of the gestational sac, which averages 2 to 8 weeks according to a study carried out in 2022 in Saudi Arabia [41]. Forty pregnancies, or 54.4%, reached full term, this indicates that the outcome of subsequent intra-uterine pregnancies following initial ectopic pregnancy treatment do not significantly differ across the three types of treatment (medical, laparotomy, and minimally invasive surgery). The rates of miscarriage, preterm delivery, and term delivery were fairly consistent suggesting that the type of treatment does not have a significant impact on the outcome of subsequent intra-uterine pregnancies.

This information is crucial for counseling patients post-ectopic pregnancy treatment, as it provides reassurance that the likelihood of a successful term delivery is not significantly influenced by the type of treatment they receive for their initial ectopic pregnancy. This can help in making informed decisions about treatment options based on other factors such as recovery time, invasiveness, and personal preferences.

Limitations

A potential limitation to this study was the fact that the study was conducted in three hospitals in Yaoundé, which may limit the generalizability of the findings to other regions of Cameroon or to different populations with varying sociodemographic characteristics.

CONCLUSION

At the end of the study, we could conclude as follows:

- The average age of the study population was 28.3 ± 5.5 years, the most affected age group was 25-29 years and they were mostly nulliparous and pauciparous.
- The overall prevalence of subsequent pregnancies following treatment for ectopic pregnancy, was 76.0%.
- The rate of repeat ectopic pregnancy varied significantly by treatment method, with minimally invasive surgery having the highest rate followed by medical treatment.
- Laparotomy resulted in the highest rate of subsequent pregnancies, followed by medical treatment and minimally invasive surgery.
- Laparotomy was associated with a significantly higher rate of spontaneous conception compared to medical treatment and minimally invasive surgery.

RECOMMENDATIONS

To pregnant women

- Should consult a gynecologist concerning any event of pelvic pain and/or vaginal bleeding occurring during the first-trimester. This is important for early diagnosis and timely management based on the etiology of ectopic pregnancy.
- Should prevent STI's by limiting numerous sexual partners
- Should have a regular check -up following treatment of ectopic pregnancy
- Should be positive about treatment of ectopic pregnancy

To health care personnels

- To raise awareness among patients about the impact of ectopic pregnancy on reproductive outcome by providing comprehensive counseling.
- To promote awareness campaigns on the prevention of sexually transmitted infections, thereby reducing the risks of ectopic pregnancy and other complications.
- To implement and widely disseminate protocols for the different treatment method of ectopic pregnancy for effective and early management.

To the YGOPH, EDH and YCH

- To ensure better management of the archives units to facilitate data collection.

To the FMBS of Yaoundé

- To encourage longitudinal prospective studies aimed at better evaluating spontaneous pregnancies after ectopic pregnancy and improve data accuracy.
- To carry out studies with a larger sample size and expanding the study to include more diverse populations and longer follow-up periods which would enhance the generalizability and comprehensiveness of the findings.
- To evaluate the risk of having repeat ectopic pregnancy.

To the Ministry of Public Health

- To ensure that all hospitals should be equipped with necessary diagnostic tools like transvaginal ultrasounds and have access to free methotrexate.

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APPENDIX

APPENDIX I:

UNIVERSITÉ DE YAOUNDÉ I
FACULTÉ DE MÉDECINE ET DES
SCIENCES BIOMÉDICALES
COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE
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THE UNIVERSITY OF YAOUNDE I
FACULTY OF MEDICINE AND BIOMEDICAL
SCIENCES
INSTITUTIONAL ETHICAL REVIEW BOARD

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CLAIRANCE ÉTHIQUE 10 JUN 2024

Le COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE (CIER) de la FMSB a examiné
La demande de la clairance éthique soumise par :

M.Mme : MAKWET NSANGOU CHIRIFATOU

Matricule: 17M002

Travaillant sous la direction de :

- ♦ Pr MBU Enow Robinson
- ♦ Dr EBONG Clifford EBONTANE

Concernant le projet de recherche
intitulé :

**Pregnancy following treatment of ectopic pregnancy
in three highly turnover hospitals in Yaoundé**

Les principales observations sont les suivantes

Evaluation scientifique	
Evaluation de la convenance institutionnelle/valeur sociale	
Equilibre des risques et des bénéfices	
Respect du consentement libre et éclairé	
Respect de la vie privée et des renseignements personnels (confidentialité) :	
Respect de la justice dans le choix des sujets	
Respect des personnes vulnérables :	
Réduction des inconvénients/optimalisation des avantages	
Gestion des compensations financières des sujets	
Gestion des conflits d'intérêt impliquant le chercheur	

Pour toutes ces raisons, le CIER émet un avis favorable sous réserve des modifications recommandées dans la grille d'évaluation scientifique.


L'équipe de recherche est responsable du respect du protocole approuvé et ne devra pas y apporter d'amendement sans avis favorable du CIER. Elle devra collaborer avec le CIER lorsque nécessaire, pour le suivi de la mise en œuvre dudit protocole. La clairance éthique peut être retirée en cas de non - respect de la réglementation ou des recommandations sus évoquées. En foi de quoi la présente clairance éthique est délivrée pour servir et valoir ce que de droit

LE PRESIDENT DU COMITE ETHIQUE



[Signature]

APPENDIX II:

<p>REPUBLIQUE DU CAMEROUN Paix-Travail-Patrie</p> <p>MINISTERE DE LA SANTE PUBLIQUE</p> <p>HOPITAL GYNECO-OBSTETRIQUE ET PEDIATRIQUE DE YAOUNDE</p> <p>HUMILITE – INTEGRITE – VERITE – SERVICE</p>		<p>REPUBLIC OF CAMEROON Peace-Work-Fatherland</p> <p>MINISTRY OF PUBLIC HEALTH</p> <p>YAOUNDE GYNAECO-OBSTETRIC AND PEDIATRIC HOSPITAL</p> <p>HUMILITY – INTEGRITY – TRUTH – SERVICE</p>
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**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° 593 /CIERSH/DM/2024


CLAIRANCE ETHIQUE

Le Comité Institutionnel d'Ethique de la Recherche pour la Santé Humaine (CIERSH) a examiné le 24 janvier 2024, la demande d'autorisation et le Protocole de recherche intitulé « **pregnancy following treatment of ectopic pregnancy in three highly turnover hospitals in Yaounde** » soumis par l'étudiant MAKWEK NSANGOU CHIRIFATOU.

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.

MAKWEK NSANGOU CHIRIFATOU devra se conformer au règlement en vigueur à HGOPY et déposer obligatoirement une copie de leurs travaux à la Direction Médicale de ladite formation sanitaire.

Yaoundé, le **08 FEV 2024**



LE PRESIDENT

[Signature]

Prof MBU Robinson
Directeur Général
HGOPY

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

APPENDIX III:

<p>REPUBLIQUE DU CAMEROUN Paix-Travail-Patrie ***** MINISTRE DE LA SANTE PUBLIQUE ***** SECRETARIAT GENERAL ***** DIRECTION DE L'HOPITAL CENTRAL DE YAOUNDE ***** SECRETARIAT MEDICAL N° <u>005</u> / AP/MINSANTE/SG/DHCY/CM/SM</p>		<p>REPUBLIC OF CAMEROON Peace-Work-Fatherland ***** MINISTRY OF PUBLIC HEALTH ***** GENERAL SECRETARY ***** DIRECTORATE OF CENTRAL HOSPITAL OF YAOUNDE ***** MEDICAL SECRETARY Yaoundé, le <u>12-9-JAN 2024</u></p>
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ACCORD DE PRINCIPE

Je soussigné Professeur FOU DA Pierre Joseph, Directeur de l'Hôpital Central de Yaoundé, marque mon Accord de Principe à Madame MAKWET NSANGOU Chirifatou , étudiante en 7^{ème} année de Médecine Générale à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I , sous le thème « PREGNANCY FOLLOWING TREATMENT OF ECTOPIC PREGNANCY IN THREE HIGHLY TURNOVER 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.

Pour Le Directeur et par ordre
Le Conseiller Médical.



Dr. Ngoko Pierre Ngoko Logo

APPENDIX IV:

<p>REPUBLIQUE DU CAMEROUN ----- Paix - Travail - Patrie ----- MINISTERE DE LA SANTE PUBLIQUE ----- DELEGATION REGIONALE DU CENTRE ----- DISTRICT DE SANTE D'EFOULAN ----- HOPITAL DE DISTRICT D'EFOULAN -----</p>		<p>REPUBLIC OF CAMEROON ----- Peace-Work-Fatherland ----- MINISTRY OF PUBLIC HEALTH ----- CENTER REGIONAL DELEGATION ----- EFOULAN HEALTH DISTRICT ----- EFOULAN DISTRICT HOSPITAL -----</p>
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N° 1645 /AR/MSP/DRSPC/DSE/HDYDEIII.

AUTORISATION DE RECHERCHE

Je soussigné **Dr LOMBO LOMBO Landry**, Directeur de l'Hôpital de District d'Efoulan certifie qu'une autorisation administrative d'effectuer une enquête portant sur le thème « *Pregnancy following treatment of ectopic pregnancy in three highly turnover hospitals in Yaoundé* », est accordée **MAKWET NSANGOU CHIRIFATOU**, étudiante en 7^{ème} année Médecine générale, à la Faculté de Médecine et des Sciences Biomédicales, de l'Université de YAOUNDE I.

L'éthique et la confidentialité sont à respecter ;

Au terme de cette Recherche, une copie sera déposée à la bibliothèque de l'Hôpital de District d'Efoulan.

COPIE
- INTERESSE (E)
- ARCHIVES/CHRONO

Yaoundé, le 18 JAN 2024



LE DIRECTEUR
Dr Lombo Landry
Médecin
Directeur HD Efoulan

APPENDIX V: PATIENT QUESTIONNAIRE FORM

Topic: Pregnancy following treatment of ectopic pregnancy in three highly turnover hospitals in Yaoundé

Date: ____\ ____\ ____\

Questionnaire No: ____

Patient code: ____/____/____/____/

Number	Variable	Values	
1- Sociodemographic and clinical profiles of patient			
1.1.	File number	_____	
1.2.	Recruitment site	/__/_/	1. HGOPY ; 2. HCY; 3.EDH
1.3.	Age group	/__/_/	1. <20 ; 2. [20-24] ; 3. [25-29] ;4[30+]
1.4.	Profession	/__/_/	1. Student ; 2. housewife ; 3. civil servant; others_
1.5.	Marital status	/__/_/	1. Single; 2. Married ; 3. widow ; 4. Divorced
1.6.	Level of education	/__/_/	1. None ; 2. Primary; 3. Secondary ; 4. University
1.7.	Religion	/__/_/	1. Christian ; 2. Muslim ; 3.others_
1.8.	Nationality	/__/_/	1. Cameroon ; 2. Foreigner
1.9.	Region of origin	/__/_/	1. West; 2. North-west ; 3. South-west ; 4. East ; 5. North ; 6. Far north; 7. Adamaoua ; 8. Centre ; 9.Littoral ; 10. South
1.10	Gravidity	/__/_/	G1-G2=1; G3-G4=2; G5-6=3; >G6=4
1.11	Parity	/__/_/ /__/_/	P0-P2=1; P3-P4=2; P5-P6=4; >P6=4
1.12	History of sexually transmitted diseases	/__/_/	Yes=1 No=2
1.13	If yes, which?	/__/_/	Chlamydiae=1; Gonorrhea=2; Mycoplasma=3; ureaplasma=4; others=5

1.14	History of previous abdomino-pelvic surgery	/_/_/	C/S=1; Ceolioscopy=2; Myomectomy=3; Laparotomy=4; others=5
1.15	Cumulated sexual partners	/_/_/	<3=1 >3=2
1.16	History of smoking	/_/_/	Yes=1 No=2
1.17	If yes, for how long?	/_/_/	<3=1 >3=2
1.18	History of infertility before EP	/_/_/	Yes =1 No=2

2- Pregnancy following treatment of EP			
2.1	Treatment received for EP	/_/_/	Yes=1 No=2
2.2	If yes, which method	/_/_/	Medical=1 Surgical=2

3-Prevalence of pregnancy following treatment of EP			
3.1.	Medical treatment	/_/_/	Pregnancy=1 No pregnancy=2
3.2.	If yes, was it?	/_/_/	IUP=1 Repeated EP=2
3.3.	If IUP, what was the outcome?	/_/_/	Miscarriage=1 Preterm=2 Term delivery=3
3.4.	Duration between treatment and pregnancy	/_/_/	0-6months=1 6-12months=2 12-18months=3 18-24months=4 >24months=5
3.5.	Spontaneous pregnancy	/_/_/	Yes=1 No=2
3.6.	Surgical treatment (laparotomy)	/_/_/	Pregnancy=1 No pregnancy=2
3.7.	If yes, was it?	/_/_/	IUP=1 Repeated EP=2
3.8.	If IUP, what was the outcome?	/_/_/	Miscarriage=1 Preterm=2 Term delivery=3



3.9.	Duration between treatment and pregnancy	/ _ /	0-6months=1 6-12months=2 12-18months=3 18-24months=4 >24months=5
3.10.	Spontaneous pregnancy	/ _ /	Yes=1 No=2
3.11.	Surgical treatment (minimally invasive)	/ _ /	Pregnancy=1 No pregnancy=2
3.12.	If yes, was it?	/ _ /	IUP=1 Repeated EP=2
3.13.	If IUP, what was the outcome?	/ _ /	Miscarriage=1 Preterm=2 Term delivery=3
3.14.	Duration between treatment and pregnancy	/ _ /	0-6months=1 6-12months=2 12-18months=3 18-24months=4 >24months=5
3.15.	Spontaneous pregnancy	/ _ /	Yes=1 No=2

4-Prevalence of EP following various methods of treatment			
4.1.	Method of treatment	/ _ /	Medical =1 Surgical =2
4.2.	If surgical,	/ _ /	Laparotomy =1 Minimally invasive =2
4.3.	If laparotomy,	/ _ /	Radical =1 Conservative =2
4.4.	If minimally,	/ _ /	Radical =1 Conservative =2

APPENDIX VI

Dupli Checker Plagiarism Report

Originality Report

 12.5% Plagiarized Content	 87.5% Unique Content	3178 Words	21993 Characters
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Topic: Pregnancy following treatment of ectopic pregnancy in three highly turnover hospitals in Yaoundé. SUMMARY Introduction: Ectopic pregnancy (EP) is a major public health problem worldwide due to its frequency and severity. It is the first cause of maternal mortality in the first trimester of pregnancy, especially in developing countries. Objectives: The main objective was to evaluate spontaneous pregnancy following different methods of treatment of ectopic pregnancy in three hospitals in Yaoundé. Methods: We conducted a retrospective descriptive study covering a period of 5 years from 1st January 2018 to 31st December 2022 in the Yaoundé Gynaecology Obstetrics and Pediatrics hospital, Yaoundé Central hospital and Efoulan district hospital. In these hospitals, we identified files of cases treated for EP. Clinical data were exploited and we actively called the women to find out if they ever became pregnant after treatment and what happened to the pregnancies. Clinical and fertility outcome were then obtained through phone calls. We obtained information concerning intrauterine pregnancies, miscarriages, live births (LB), repeat EPs, the time between treatment and first intrauterine pregnancies and compared with method of treatment. Results: We examined 293 files and 150 files conformed to the inclusion criteria. Ectopic pregnancies were found among women aged between 25 and 29 years, with a mean age of 28.3 ± 5.5 years. The study population was made mostly of students 31.3% and 48.0% of them had attained a higher level of education. Majority were single (67.3%) and most were primiparous (75.3%). Sexually transmitted infections (STIs) were found among 55.3% of the cases, and the most common organism was Chlamydia trachomatis. The overall spontaneous pregnancy rate was 76.0%. With respect to method of treatment, 24.2% of pregnancies occurred following medical treatment, 57.0% following laparotomy and 18.6% following minimally invasive surgery. About 49.1% of pregnancies were carried to term irrespective of method of treatment. There were 30.7% of repeat EPs and 26.6% miscarriages. Conclusion: The prevalence of subsequent pregnancy following treatment of ectopic pregnancy was high irrespective of the method of treatment. Laparotomy was associated with the highest rate of subsequent pregnancies. Keywords: Ectopic; pregnancy; spontaneous; outcome; recurrent. Methodology 1.1 TYPE OF STUDY We carried out a retrospective descriptive study 1.2 STUDY SITES Files were studied from 3 different hospitals 1. The Efoulan District hospital (EDH) It is located at the heart of town in Yaoundé, Cameroon and has of gynecologists. The hospital has a dedicated mother and child unit which provides diversified medical care to children and pregnant women. The patient turnout is big with about 420 antenatal consultations per month, 3250 deliveries per year a cesarian section rate at 33.6% and that ectopic pregnancy of 12%. 2. The Yaoundé Gynaecology Obstetrics and Pediatrics hospital (YGOPH) It is a reference health facility created in 2002 and specializes in mother and child health care. Its gynecology/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 Gynecology. The rate of cesarian section is 37% and that of ectopic pregnancy 10%. 3. The Yaoundé Central hospital (YCH) This reference hospital located in the heart of Yaoundé has one of the biggest and most specialized maternity units with over 72 in patient beds, 6 delivery tables, 2 service operating theatres, 11 gynecologists and a large highly trained staff. It records about 2628 deliveries per year. All the afore mentioned hospitals were chosen for this study because of their great patient turn over, good follow up and clear records. 1.3 DURATION OF STUDY AND PERIOD The study was carried out on a duration of 6 months and covered a period of 5 years (from 1st of January 2018 to 31st of December 2022). 1.4 STUDY POPULATION Files of women of childbearing age who were treated for ectopic pregnancy in the three hospitals were included in the study. 1.4.1 Inclusion criteria: • All files of women of childbearing age diagnosed and treated for ectopic pregnancy by different treatment methods within the period 2018 to 2022. • Women who accepted to

take part in the study through phone calls. 1.4.2 Exclusion criteria Files of women operated upon for indications other than ectopic pregnancy. Women who could not be reached on phone, and who did not want to participate were excluded. 1.4.3 Non-inclusion criteria All participants who underwent bilateral salpingectomy and participants with non exploitable files were not included. 1.5 Sample Size estimation 1.5.1 Sampling method Participants were consecutively recruited until the desired sample size was obtained. 1.5.2

Sample size estimation Based on the study design, the sample size was estimated using the formula; $n = p * (1-p) * (Z\alpha/d)^2$ 2 Where; n= population sample size p= prevalence of cases of pregnancy after treatment of ectopic pregnancy, estimated to be 3% in our population. $Z\alpha$ = the confidence interval 1.96 for 95% d= level of precision estimated to 5% $n = 0.03 * (1-0.03) * (1.96/0.05)^2$ 2 So, our minimum estimated sample size was 45. 1.6 PROCEDURE 1.6.1 Administrative procedure A research proposal was written and approved by the supervisors, after which we obtained a research authorization from the different directors of the concerned hospitals, and ethical clearance from the Institutional Review Board of the Faculty of Medicine and Biomedical sciences of the University of Yaoundé I. 1.6.2 Data collection: Once the administrative phase was completed, we went to the theater records, maternity records and identified all the cases of ectopic pregnancy treated by the various methods in the hospitals. After which, we went to the various archives to look for the records. We studied all the files and made phone calls to have active information on fertility status after treatment of ectopic pregnancy. 1.6.3 Variables studied: We reviewed the medical records and obtained the sociodemographic profiles of patients treated for EP. These included: Ages Marital status Level of education Profession Religion of origin For the Clinical variables, we collected information on the following : Symptoms, gravidity, parity, history of abortion, history of sexually transmitted infections, use of method of contraceptives, number of sexual partners, history of infertility History of pelvic surgery Gestational age Type of treatment carried out(laparotomy or celioscopy) Site of location of EP We made phone calls and obtained the following information: Spontaneous IU pregnancies Repeat Ectopic pregnancies Pregnancies by method of treatment Outcome of pregnancies Time lapse between treatment and subsequent pregnancy 1.7 Data collection and analysis Data were collected using a standard questionnaire

that was conceived internally, validated, and adapted for the study. Data was entered into the Census and Survey Processing System (CSPPro) version 7.5 software then transferred to and analyzed using Stata/SE

version 17 software. Descriptive statistics were expressed as means with standard deviation for quantitative variables, after confirming normal distribution of the dataset while categorical variables were expressed as frequency and percentage. The Pearson's Chi square test was used to compare prevalences (proportions). Statistically significance was set at a two-sided p value < 0.05 1.8 Materials used Material for data

management included; - Computer - USB flash drive - Scientific calculator - Typing software - Smart phone 1.9 HUMAN RESOURCES - Principal Investigator : (myself) - Study director and codirectors - Statistician 1.10

ETHICAL CONSIDERATIONS Ethical clearance was requested and obtained from the ethical committee of the Faculty of Medicine and Biomedical Sciences to carry out the study. The proposal and questionnaire form were submitted to the management of health facilities involved for the study site to obtain authorisation. Confidentiality was assured by assigning codes for every participant and the codes were used to label all documentations and not the names of the patients. The data collected were used for the research purpose only. Results Figure 1: DIAGRAMATIC REPRESENTATION OF THE RECRUITEMENT PROCESS In total, we successfully recruited 150 women . Total files of women treated for ectopic pregnancy between 2018 and 2023 review = 338 EDH =107 YCH =121 YGOPH=110 Excluded = 45 Women who did not want to participate = 29 Bilateral ectopic salpingectomy = 16 Files of women treated for ectopic pregnancy between 2018 to 2023 for the first time = 293 Excluded for missing data in files = 143 Sample used for analysis = 150 EDH = 32 YCH = 46 YGOPH = 72 Table I: Distribution according to sociodemographic characteristics of study participants

Characteristic Frequency Percentage (n=150) Age 28.3±5.5 [15-19[3 2.0 [20-24[33 22.0 [25-29[61 40.7 30+ 53 35.3 Profession Student 47 31.3 Housewife 41 27.3 Civil servant 36 24.0 Others 26 17.4 Level of education None 10 6.7 Primary 31 20.7 Secondary 72 48.0 University 37 24.6 Religion Christian 139 92.7 Muslim 7 4.7 Others 4 2.6 Marital status Single 101 67.3 Married 46 30.7 Widow 1 0.7 Divorced 2 1.3 Nationality Cameroonian 150 100 Foreigner 0 0 Region of origin West 46 30.7 North-West 7 4.7 South-West 2 1.3 East 7 4.7 North 2 1.3 Far-North 3 2.0 Adamaoua 2 1.3 Centre 65 43.3 Littoral 6 4.0 South 10 6.7 The study population was made mostly of students 31.3% and 48.0% of them had attained a secondary level of education. Majority were single (67.3%) and 92.7% were Christians. Table II: Clinical characteristics of study participants Characteristic Frequency (n=150) Percentage Gravidity G1-G2 66 44.0 G3-G4 49 32.7 G5-G6 27 18.0 > G6 8 5.3 Parity P0 – P2 113 75.3 P3 – P4 28 18.7 > P4 9 6.0 History of STIs Yes 108 72.0 No 42 28.0 History of abdomino-pelvic surgery Yes 38 25.3 No 112 74.7 Cumulative sexual partners < 3 37 24.7 ≥ 3 113 75.3 Infertility before EP Yes 9 6.0 No 141 94.0 Smoking Yes 2 1.3 No 148 98.7 The women were of low gravidity 44.0% and low parity 75.3% with histories of STIs 72.0% Table III: Distribution according to type of STIs and history of abdomino-pelvic surgery Characteristic Frequency (n=150) Percentage Type of STIs Chlamydia trachomatis 83 55.3 Gonorrhea 1 0.7 Mycoplasma hominis 20 13.3 Ureaplasma urealyticum 3 2.0 Others 1 0.7 None 42 28.0 History of abdomino-pelvic surgery Cesarean section

25 16.7 Coelioscopy 1 0.7 Myomectomy 1 0.7 Laparotomy 10 6.7 Others 2 1.3 None 112 74.7 Chlamydia trachomatis was isolated from 55.3% of cases and 16.7% have had cesarean deliveries. Table IV: Distribution according to type of treatment received Type of treatment Frequency (n=150) Percentage Medical 29 19.3 Laparotomy 95 63.3 • Conservative 13 13.7 • Radical 82 86.3 Minimally invasive surgery 26 17.3 • Conservative 15 57.7 • Radical 11 42.3 Participants treated by medical treatment recorded a rate of 19.3%, 63.3% by laparotomy and 17.3% by minimally invasive surgery. Radical surgery was done in 86.3% of laparotomies and 42.3% of minimally invasive surgeries. Table V: Prevalence of subsequent pregnancy by treatment method Total

(n=150) Medical laparotomy Minimal invasive P value Pregnancy after ectopic pregnancy Yes 114(76.0) 26(22.8) 67(58.7) 21(18.42) No 36(24.0) 3(8.3) 28(77.7) 5(13.8) 0.089 After treatment of ectopic pregnancy, the prevalence of subsequent pregnancy was 76.0% in the whole sample. This prevalence was highest amongst those who received laparotomy treatment (58.7%), 22.8% after medical and lowest amongst those who received minimally invasive treatment (18.42%). Nevertheless, the difference in prevalence between the three groups of treatment was not statistically significant. Table VI: Outcome of pregnancy by method of treatment Characteristics Total (n=114) Medical (n=26) Laparotomy (n=67) Minimally invasive (n=21) P value Time lapse between EP and current pregnancy/months < 6 2(1.75) 0(0) 2(2.99) 0(0.0) [6 – 12[34(29.8) 12(46.2) 19(28.4) 3(14.3) [12 – 24[58(50.9) 12(46.2) 32(47.8) 14(66.7) ≥ 24 20(17.5) 2(7.7) 14(20.9) 4(19.0) 0.195 Nature of pregnancy Spontaneous 107(93.9) 26(24.3) 61(57.0) 20(18.6) Medically assisted 7(6.1) 7(0.0) 6(9.0) 1(4.8) 0.260 Location of pregnancy Intra-uterine 79(69.3) 22(84.6) 48(71.6) 9(42.9) Ectopic 35(30.7) 4(15.4) 19(28.4) 12(57.1) 0.007 The time lapse between 12-24 months was favorable for spontaneous pregnancies following treatment of ectopic pregnancy irrespective of the method of treatment. Pregnancies were 69.3% intra-uterine and 30.7% repeat ectopic pregnancies. Table VII: Outcome of subsequent pregnancy after initial ectopic pregnancy Characteristic Total (n=114) Medical (n=26) Laparotomy (n=67) Minimally invasive (n=21) P value Outcome of intra-uterine Miscarriage 43(37.7) 10(23.2) 27(62.7) 5(46.5) Preterm delivery 15(13.1) 5(33.3) 9(60) 1(6.6) Term delivery 56(49.1) 11(19.6) 31(55.3) 15(26.7) 0.196 The highest rate of term deliveries was observed in patients who underwent laparotomy with with over 49.1% reaching full term. Minimally invasive surgery and medical treatment had lower rates of term deliveries 26.7% and 19.6% respectively. Despite these differences, the P value of 0.196 indicates that the variations are not statistically significant. CHAPTER 2: DISCUSSION 2.1 DISCUSSION 1. Sociodemographic Characteristics The average age of the study population was 28.3 ± 5.5

years. This result is close to that reported in Cameroon in 2012, where the reported average age was 26.46 ± 5.42 years, with the most affected age group being 25-30 years [9]. In our case series, the dominant age was 25-29 years old (40.7%). This age was similar to that found in similar studies. This corresponds to the age of reproduction and peak sexual activity[6]. The highest incidence of ectopic pregnancy was noted amongst nulliparous and pauciparous women (75.3%). This observation has also been made by almost all the authors who estimated that ectopic pregnancy is associated to low parity [10,14]. There were 101 single women, accounting for 67.3% of the study population, and 48.0% had secondary level of education. Most participants were Christians (92.7%) and all participants were Cameroonians, with the Centre region being the most represented (43.3%). This result is similar to that reported in earlier studies in Cameroon in 2010 and 2012, where single women were predominant [37]. The result could be explained by the fact that these patients were exposed to multiple sexual partners, which is a source of infection. 2. Gynecological History and Risk Factors for Ectopic Pregnancy (EP) With respect to parity, 113 patients, or 75.3%, were primiparous. Clinically, 44.0% were in their first or second pregnancy (G1-G2), and 75.3% had between zero to two previous births (POP2). This result differs from a study in 2010 in Cameroon which found a predominance of EP among multiparous women [37]. Chlamydia trachomatis was the pathogenic sexually transmissible infection found among most of the cases. This tallies with results of previous studies carried out in Yaoundé and in Douala [1,9]. A study carried out in Gabon in 2002 identified Chlamydia trachomatis as 31.5% among cases of sexually transmitted infections and noted that the increase in the incidence of ectopic pregnancies coincided with the increase in the incidence of salpingitis[39]. This could be explained by the damage caused by the infection to the fallopian tubes, preventing normal migration of the embryo. The lesions caused by infections of the adnexa are responsible for scars that significantly reduce tubal patency and motility. A history of pelvic surgery was found among 14.3% of the patients. This result is close to that reported in earlier studies in Cameroon in 2009 where a history of pelvic surgery was found in 12.9% of cases of ectopic pregnancy with 8,65 being tubal surgery[1]. This result differs from that found in Cameroon in 2009[1,9]. This difference can be explained by the sizes of the different samples, but both past histories remains a risk factor for EP. 3. Prevalence of repeat ectopic pregnancy following treatment method The overall prevalence of repeat ectopic pregnancy among those who had a subsequent pregnancy was 30.7%. This varied significantly among the treatment methods: - Minimally Invasive Surgery: 57.1% - Laparotomy: 28.4% - Medical Treatment: 15.4% The difference in repeat ectopic pregnancy rates was statistically significant (P=0.007), indicating that the treatment method impacts the risk of recurrent ectopic pregnancies. 4. Comparison of reproductive outcomes after treatment methods of ectopic pregnancy Comparing the prevalence of repeat ectopic pregnancies post-treatment, minimally invasive surgery had the highest rate (57.1%), followed by laparotomy (28.4%) and medical treatment (15.4%). This suggests that while minimally invasive surgery might be less invasive, it carries a higher risk for repeat ectopic pregnancies compared to other treatment methods. Among those who achieved subsequent pregnancies, the breakdown by treatment type was as follows: Laparotomy: 58.7% - Medical: 22.8% - Minimally Invasive Surgery: 18.4% Though laparotomy had the highest prevalence of

subsequent pregnancies, the difference in pregnancy rates among the treatment types was not statistically significant ($P=0.089$). This study showed that spontaneous pregnancy was significantly higher after laparotomy treatment than medical treatment. 5. Spontaneous conception rate after treatment of ectopic pregnancy by method The prevalence of subsequent pregnancy after treatment of ectopic pregnancy was 76.0%. This indicates a relatively high likelihood of achieving pregnancy post-treatment, reflecting either effective fertility-preserving interventions or the natural fertility potential of the participants. After medical treatment of EP, there was a spontaneous conception rate of 22.8%. This result is similar to that found in 2021 in Cameroon, which reported a conception rate of 32.3% after medical treatment of EP, but lower than that reported in a similar study in 2022 in Turkey, which reported a rate of 83.2% after EP treatment by medical treatment [10,14]. This difference could be explained by the fact that our study evaluated women treated by both surgical and medical methods. 6. Time lapse between treatment and Conception The distribution of time lapse suggests that a majority of subsequent pregnancies occurred within 12-24 months post-treatment, irrespective of the treatment type. This indicates a general pattern of recovery and readiness for a new pregnancy within that period. However, the non statistical significance ($P=0.195$) implies that the type of treatment does not significantly impact the timing of the next pregnancy. This result is similar to studies carried out in 2015 and 2022 in Cameroon which reported conception time lapse of 12 months and 11.82 ± 7.46 months, respectively[10,11]. This result could be explained firstly by the fact that the desire for pregnancy after EP treatment is not always immediate, secondly by the time required for the resorption of the gestational sac, which averages 2 to 8 weeks according to a study carried out in 2022 in Saudi Arabia [41]. Forty pregnancies, or 54.4%, reached full term, this indicates that the outcome of subsequent intra-uterine pregnancies following initial ectopic pregnancy treatment do not significantly differ across the three types of treatment (medical, laparotomy, and minimally invasive surgery). The rates of miscarriage, preterm delivery, and term delivery were fairly consistent suggesting that the type of treatment does not have a significant impact on the outcome of subsequent intra-uterine pregnancies. This information is crucial for counseling patients post-ectopic pregnancy treatment, as it provides reassurance that the likelihood of a successful term delivery is not significantly influenced by the type of treatment they receive for their initial ectopic pregnancy. This can help in making informed decisions about treatment options based on other factors such as recovery time, invasiveness, and personal preferences. Limitations A potential limitation to this study was the fact that the study was conducted in three hospitals in Yaoundé, which may limit the generalizability of the findings to other regions of Cameroon or to different populations with varying sociodemographic characteristics.