SUDAN UNIVERSITY OF SCIENCE & TECHNOLOGY
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Characterization of Female Infertility using Ultrasonography

توصيف عقم الإناث باستخدام التصوير بالموجات فوق الصوتية

A thesis submitted for the requirement of PhD degree in Medical Diagnostic Ultrasound

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الآيـــــــة

قال الله تعالي:

{ لله ملك السماوات والأرض يخلق ما يشاء يهب لمن يشاء إناثا ويهب لمن يشاء الذكور (49) أو يزوجهم ذكرانا وإناثا ويجعل من يشاء عقيما إنه عليم قدير (50) }

سورة الشورى اية (49-50)

Dedication

To my parents for their endless love, sacrifices, prayers, supports and advices

To my amazing husband who encouraged and supported me unconditionally

To my children (Lama, Khaled, Ahmed, Leen) each of whom have a special place in my heart

I dedicated this humble work

Acknowledgment

I would like to express my sincere gratitude and deep appreciation to my faithful supervisor Prof. Dr. Mohammed Alfadel who dedicated a lot of there precious time to give me invaluable assistance and guidance throughout the study and for sharing his knowledge with me thus promoting my skills and knowledge.

Many thanks and great appreciations extended to Dr. Mohammed Ahmed who assist to accomplish this work.

Abstract

Diagnosis of infertility includes several steps but mostly depend on qualitative conclusion therefore the main objective of this study was to characterize female infertility using ultrasonography. The data of this study collected from 180 patients 120 were infertile and 60 fertile. The study was conducted in in Mohammed bin Naif Medical center in Saudi Arabia in the period from December 2017 to December 2018. The result of this study showed that there were two variables that showed significance differences between the fertile and infertile female concerning laboratory test; they include FSH and PRL. In respect to ultrasonography all measurement concerning Rt and Lt ovary showed significance difference but uterus measurements were inconclusive. To classify the female as fertile and infertile using linear discriminant analysis stepwise method, four variables were chosen as the most discriminant one they include FSH, LH, Rt ovary width and Lt ovary length. The overall classification accuracy was 78.9%, for infertile was 70.8% and 95.0% for the fertile one. In conclusion differentiation between fertile and infertile female still an issue but using ovarian measurement with some laboratory test differentiations between fertile and infertile was possible.

المستخلص

تشخيص العقم يشمل عدة خطوات ولكن في الغالب تعتمد على الاستنتاج النوعي لذلك كان الهدف الرئيسي لهذه الدراسة هو توصيف العقم الأنثوي باستخدام الموجات فوق الصوتية. تم جمع بيانات هذه الدراسة من 180 مريضة ، منهم 120مريضة مصابات بالعقم و60 مريضة ذات خصوبة. تم إجراء هذه الدراسة في مركز محمد بن نايف الطبي في المملكة العربية السعودية في الفترة من ديسمبر 2017 إلى ديسمبر 2018. وأظهرت نتيجة هذه الدراسة وجود متغيرين أظهرا اختلافات معنوية بين المرأة الخصبة وغير الخصبة فيما يتعلق بالاختبار المختبري، وهما يتضمان FSH وPRL. في ما يتعلق بالموجات فوق الصوتية جميع القياس فيما يتعلق المبيض (اليمين و الشمال) أظهرت الدراسة وجود فرق معنوي فيما يتعلق بالخصوبة ولكن قياسات الرحم لم تكن حاسمة. تصنيف المرأة على أنها خصبة وغير خصبة. لتصنيف المرأة على أنها خصبة اوعقيمة تم استخدام التحليل التدريجي للتمييز الخطي ، وتم اختيار أربعة متغيرات على أنها الأكثر تمييزًا والتي تشمل FSH، LH، Rtعرض المبيض الايمن وطول المبيض الايسر كانت دقة التصنيف الإجمالية هي 78.9%، وكانت بالنسبة للمصابات بالعقم هي 70.8% ولذوات الخصوبة هي 95%. في الختام ، لا يزال التمايز بين الإناث في مشكلة الخصبة يمثل تحدي، لكن باستخدام قياسات المبيض مع بعض الاختبارات المعملية يصبح التمييز في موضوع الخصوبة ممكنًا

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LIST OF ABBREVIATION

LPD : LUTEAL PHASE DEFECT

LUF : LUTEAL UNRUPTURED FOLLICLE

GnRH : GONADOTROPIN-RELEASING HORMONE

FSH : FOLLICLE-STIMULATING HORMONE

TSH : THIROID STIMULATING HORMONE

LH : LUEINIZING HORMONE

PRL : PROLACTINE HORMONE

PCOS : POLYCYSTIC OVARIES SYNDROME

OHSS : OVARIAN HYPERSTIMULATION SYNDROME

HCG : HUMAN CHORIONIC GONADOTROPIN

AVM : ARTERIOVEINUS MALFORMATION

TVS : TRANSVAGINAL SCAN

DUB : DYSFUNCTIONAL UTERINE BLEEDING

HMB : HEAVY MENSTRUAL BLEEDING

AUB : ABNORMAL UTERINE BLEEDING

Chapter one

Introduction

Infertility means not being able to become pregnant after a year of trying. If a woman can get pregnant but keeps having miscarriages or stillbirths, that's also called infertility.

Infertility is fairly common. After one year of having unprotected sex, about 15 percent of couples are unable to get pregnant. About a third of the time, infertility can be traced to the woman. In another third of cases, it is because of the man. The rest of the time, it is because of both partners or no cause can be found.

There are treatments that are specifically for men or for women. Some involve both partners. Drugs, assisted reproductive technology, and surgery are common treatments. Happily, many couples treated for infertility go on to have babies.

1.1 Causes of infertility in women

There are many possible causes of infertility. Unfortunately, in about one-third of cases no cause is ever identified.

1.2 Ovulation disorders

Problems with ovulation are the most common cause of infertility in women, experts say. Ovulation is the monthly release of an egg. In some cases the woman never releases eggs, while in others the woman does not release eggs during come cycles.

1.3 Ovulation disorders can be due to:

- Premature ovarian failure - the woman's ovaries stop working before she is 40.
- PCOS (polycystic ovary syndrome) - the woman's ovaries function abnormally. She also has abnormally high levels of androgen. About 5% to 10% of women of reproductive age are affected to some degree. Also called Stein-Leventhal syndrome.
- Hyperprolactinemia - if prolactin levels are high and the woman is not pregnant or breastfeeding, it may affect ovulation and fertility.

- Poor egg quality - eggs that are damaged or develop genetic abnormalities cannot sustain a pregnancy. The older a woman is the higher the risk.
- Overactive thyroid gland
- Underactive thyroid gland
- Some chronic conditions, such as AIDS or cancer.

1.4 Problems in the uterus or fallopian tubes

The egg travels from the ovary to the uterus where the fertilized egg grows. If there is something wrong in the uterus or the fallopian tubes the woman may not be able to conceive naturally. This may be due to:

- Surgery - pelvic surgery can sometimes cause scarring or damage to the fallopian tubes. Cervical surgery can sometimes cause scarring or shortening of the cervix. The cervix is the neck of the uterus.
- Submucosal fibroids - benign or non-cancerous tumors found in the muscular wall of the uterus, occurring in 30% to 40% of women of childbearing age. They may interfere with implantation. They can also block the fallopian tube, preventing sperm from fertilizing the egg. Large submucosal uterine fibroid may make the uterus' cavity bigger, increasing the distance the sperm has to travel. Endometriosis - cells that are normally found within the lining of the uterus start growing elsewhere in the body.

1.5 Problem of the study:

The main cause of infertility usually is unknown and the usage of TAS for investigation mostly does not provides enough information about gynecological status, there for usage of TVS may reveal more information regarding the status of infertility causes integrated with laboratory test.

1.6 Objectives:

The general objective of this study was to characterize infertility in female using vaginal ultrasonography

Specific objectives:

- To measure the size of ovary and uterus.
- To find the ultrasound findings of the ovary and uterus.
- To find the difference between the collected data of fertile and infertile ladies.
- To correlate the finding with laboratory investigation.

1.7 Overviews of the Study:

This study will fall into five chapters with chapter one is an introduction, problem of the study, objectives and overview. Chapter two include literature review while chapter three include material used and the method of data collection and analysis. Chapter four presents the result of the study in a line graphs and table and finally chapter five which include the discussion, conclusion, recommendation and references.

Chapter two
Literature review

2.1 Female Reproductive Anatomy and Physiology

The female reproductive system is composed of both external and internal reproductive organs.

2.1.1 External Female Reproductive Organs

The external female reproductive organs collectively are called the vulva. The vulva serves to protect the urethral and vaginal openings.

The structures that make up the vulva include the monspubis, the labia majora and minora, the clitoris, the structures within the vestibule, and the perineum

2.1.2 Internal Female Reproductive Organs

The internal female reproductive organs consist of the vagina, uterus, fallopian tubes, and ovaries. These structures develop and function according to the specific hormone influences that affect fertility and childbearing (Fig.2.1).

Vagina

The vagina is a highly distensible musculomembranous canal situated in front of the rectum and behind the bladder. It is a tubular, fibromuscular organ lined with mucousmembrane that lies in a series of transverse folds called rugae. The rugae allow for extreme dilatation of the canal during labor and birth. The vagina is a canal that connects the external genitals to the uterus. It receives the penis and the sperm ejaculated during sexual intercourse, and it serves as an exit passage way for menstrual blood and for the fetus during childbirth. The front and back walls normally touch each other so that there is no space in the vagina except when it is opened (e.g., during a pelvic examination or intercourse). In the adult, the vaginal cavity is 3 to 4 inches long. Muscles that control its diameter surround the lower third of the vagina. The upper two thirds of the vagina lies above these muscles and can be stretched easily. During a woman's reproductive years, the mucosal lining of the vagina has a corrugated appearance and is resistant to bacterial colonization. Before puberty and after menopause (if the woman is not taking

estrogen), the mucosa is smooth due to lower levels of estrogen .The vagina has an acidic environment, which protects it against ascending infections. Antibiotic therapy, douching, perineal hygiene sprays, and deodorants upset the acid balance within the vaginal environment and can predispose women to infections.

Uterus

The uterus is a pear-shaped muscular organ at the top of the vagina. It lies behind the bladder and in front of the rectum and is anchored in position by eight ligaments, although it is not firmly attached or adherent to any part of the skeleton. A full bladder tilts the uterus backward; a distended rectum tilts it forward. The uterus alters its position by gravity or with change of posture, and is the size and shape of an inverted pear. It is the site of menstruation, implantation of a fertilized ovum, development of the fetus during pregnancy, and labor. Before the first pregnancy, it measures approximately 3 inches long, 2 inches wide and 1 inch thick. After a pregnancy, the uterus remains larger than before the pregnancy. After menopause, it becomes smaller and atrophies. The uterine wall is relatively thick and composed of three layers: the endometrium (inner most layer), the myometrium (muscular middle layer), and the perimetrium (outer serosal layer that covers the body of the uterus). The endometrium is the mucosal layer that lines the uterine cavity in non-pregnant women. It varies in thickness from0.5 mm to 5 mm and has an abundant supply of glands and blood vessels. The myometrium makes up the major portion of the uterus and is composed of smooth muscle linked by connective tissue with numerous elastic fibers. During pregnancy, the upper myometrium under goes marked hypertrophy, but there is limited change in the cervical muscle content. Anatomic subdivisions of the uterus include the convex portion above the uterine tubes (the fundus); the central portion (the corpus or body) between the fundus and the cervix; and the cervix, or neck, which opens into the vagina.

Cervix

The cervix, the lower part of the uterus, opens into the vagina and has a channel that allows sperm to enter the uterus and menstrual discharge to exit. It is composed of fibrous connective tissue. During a pelvic examination,the part of the cervix that protrudes into the upper end of the vagina can be visualized. Like the vagina, this part of the cervix is covered by mucosa, which is smooth, firm, and doughnut-shaped, with a visible central opening called the external OS (Fig.2.1). Before childbirth, the external cervical OS is a small, regular, oval opening. After childbirth, the opening is converted into a transverse slit that resembles lips. Except during menstruation or ovulation, the cervix is usually a good barrier against bacteria. The cervix has an alkaline environment, which protects the sperm from the acidic environment in the vagina. The canal or channel of the cervix is lined with mucus secreting glands. This mucus is thick and impenetrable to sperm until just before the ovaries release an egg (ovulation). At ovulation, the consistency of the mucus changes so that sperm can swim through it, allowing fertilization. At the same time, the mucus-secreting glands of the cervix actually become able to store live sperm for 2 or 3 days. These sperm can later move up through the corpus and into the fallopian tubes to fertilize the egg; thus, intercourse 1 or 2 days before ovulation can lead to pregnancy. Because some women do not ovulate consistently, pregnancy can occur at varying times after the last menstrual period. The channel in the cervix is too narrow for the fetus to pass through during pregnancy, but during labor it stretches to let the newborn through.

Corpus

The corpus, or the main body of the uterus, is a highly muscular organ that enlarges to hold the fetus during pregnancy. The inner lining of the corpus (endometrium) undergoes cyclic changes as a result of the changing levels of hormones secreted by the ovaries: it is thickest during the part of the menstrual

cycle in which a fertilized egg would be expected to enter the uterus and is thinnest just after menstruation. If fertilization does not take place during this cycle, most of the endometrium is shed and bleeding occurs, resulting in the monthly period. If fertilization does take place, the embryo attaches to the wall of the uterus, where it becomes embedded in the endometrium (about 1 week after fertilization); this process is called implantation .Menstruation then ceases during the 40 weeks (280 days) of pregnancy. During labor, the muscular walls of the corpus contract to push the baby through the cervix and into the vagina.

Fallopian Tubes

The fallopian tubes are hollow, cylindrical structures that extend 2 to 3 inches from the upper edges of the uterus toward the ovaries. Each tube is about 7 to 10 cm long (4 inches) and approximately 0.7 cm in diameter. The end of each tube flares into a funnel shape, providing a large opening for the egg to fall into when it is released from the ovary. Cilia (beating, hair-like extensions on cells) line the fallopian tube and the muscles in the tube's wall. The fallopian tubes convey the ovum from the ovary to the uterus and sperm from the uterus toward the ovary. This movement is accomplished via ciliary action and peristalsis.

If sperm is present in the fallopian tube as a result of sexual intercourse or artificial insemination, fertilization of the ovum can occur in the distal portion of the tube. If the egg is fertilized, it will divide over a period of 4 days while it moves slowly down the fallopian tube and into the uterus.

Ovaries

The ovaries are a set of paired glands resembling unshelled almonds set in the pelvic cavity below and to either side of the umbilicus. They are usually pearl-colored and oblong. They are homologous to the testes. Each ovary weighs from 2 to 5 grams and is about 4 cm long, 2 cm wide and 1 cm thick. The ovaries are not attached to the fallopian tubes but are suspended nearby from several ligaments,

which help hold them in position. The development and the release of the ovum and the secretion of the hormones estrogen and progesterone are the two primary functions of the ovary. The ovaries link the reproductive system to the body's system of endocrine glands, as they produce the ova (eggs) and secrete, in cyclic fashion, the female sex hormones estrogen and progesterone. After an ovum matures, it passes into the fallopian tubes.(Konar, 2013)

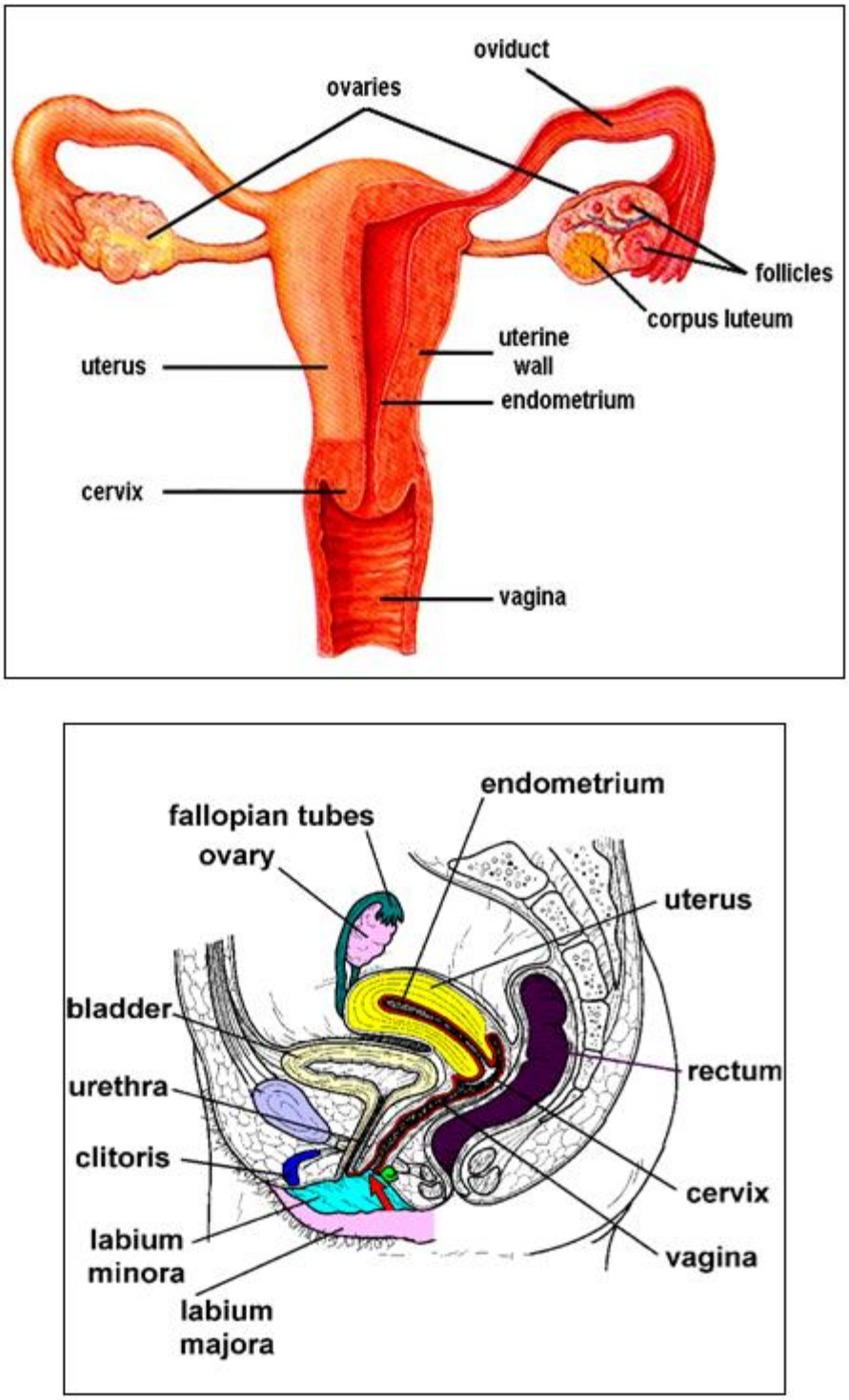


Figure 2.1: female reproductive system

Uterine anomalies

Uterine anomalies are often associated with vaginal maldevelopment.

Classification of Müllerian Anomalies (Fig.2.2)

Class I: Müllerian agenesis/Hypoplasia—segmental, Class II: Unicornuate uterus, Class III: Didelphys uterus, Class IV: Bicornuate uterus, Class V: Septate uterus, Class VI: Arcuate uterus, and Class VII: Diethylstilbestrol (DES)-related abnormality.

*Incidence of Müllerian abnormalities***:** It varies between 3 and 4%. The incidence is found to be high in women suffering from recurrent miscarriage or preterm deliveries (5–20%).

Failure of development of one or both Müllerian ducts: The absence of both ducts leads to absence of uterus, including oviducts. There is absence of vagina as well. Primary amenorrhea is the chief complaint. The absence of one duct leads to a unicornuate uterus with a single oviduct.

Failure of recanalization of the Müllerian ducts: Agenesis of the upper vagina or of the cervix—This may lead to hematometra as the uterus is functioning

Failure of fusion of Müllerian ducts: In majority, the presence of deformity escapes attention. In some, the detection is made accidentally during investigation of infertility or repeated pregnancy wastage. In others, the diagnosis is made during D + E operation, manual removal of placenta or during cesarean section.(J. A. Rock, S. M. Markhm et al, 2012)

2.2 Types of fusion anomalies

***Arcuate* (18%):** The cornual parts of the uterus remains separated. The uterine fundus looks concave with heart-shaped cavity outline .

***Uterus didelphys* (8%):** There is complete lack of fusion of the Müllerian ducts with a double uterus, double cervix and a double vagina

***Uterus bicornis* (26%):** There is varying degrees of fusion of the muscle walls of the two ducts.

Uterus bicornis bicollis: There are two uterine cavities with double cervix with or without vaginal septum.

Uterus bicornis unicollis: There are two uterine cavities with one cervix. The horns may be equal or one horn may be rudimentary and have no communication with the developed horn.

***Septate uterus* (35%):** The two Müllerian ducts are fused together but there is persistence of septum in between the two either partially (subseptate) or completely .

***Uterus unicornis* (10%):** Failure of development of one Müllerian duct .

***DES-related abnormality*:** It is due to DES exposure during intrauterine life. Varieties of malformations are included, e.g. **Vagina**: Adenosis, adenocarcinoma. **Cervix**: Cockscomb cervix, cervical collar. **Uterus**: Hypoplasia, T-shaped cavity, uterine synechiae. **Fallopian tube**: Cornual budding, abnormal fimbriae. Such cases are not seen now.(Konar, 2013)

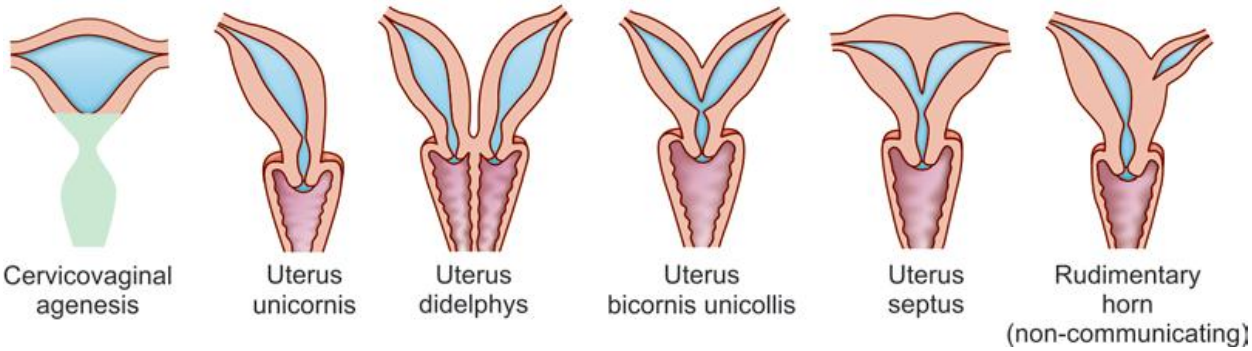


Figure 2.2: uterine anomalies

2.3 The Female Reproductive Cycle

The female reproductive cycle is a complex process that encompasses an intricate series of chemical secretions and reactions to produce the ultimate potential for fertility and birth. The female reproductive cycle is a general term encompassing the ovarian cycle, the endometrial cycle, the hormonal changes that regulate them, and the cyclical changes in the breasts. The endometrium, ovaries, pituitary gland, and hypothalamus are all involved in the cyclic changes that help to prepare the body for fertilization. Absence of fertilization results in menstruation, the monthly shedding of the uterine lining. Menstruation marks the beginning and end of each menstrual cycle. Menopause is the naturally occurring cessation of regular menstrual cycles.

2.3.1 Menstruation

Menstruation is the normal, predictable physiologic process whereby the inner lining of the uterus (endometrium) is expelled by the body. Typically, this occurs monthly. Menstruation has many effects on girls and women, including emotional and self-image issues. In the United States, the average age at menarche (the start of menstruation in females) is 12.8 years, with a range between 8 and 18. Genetics is the most important factor in determining the age at which menarche starts, but geographic location, nutrition, weight, general health, nutrition, and psychological factors are also important.

Pubertal events preceding the first menses have an orderly progression: the larche, the development of breast buds; adrenarche, the appearance of pubic and then axillary hair, followed by a growth spurt; and menarche (occurring about 2 years after the start of breast development). In healthy pubertal girls, the menstrual period varies in flow heaviness and may remain irregular in occurrence for up to 2 years following menarche.

After that time, the regular menstrual cycle should be established. experience 300 to 400 menstrual cycles within their lifetime. Normal, regular menstrual cycles vary in frequency from 21 to 36 days (with the average cycle lasting 28 days),bleeding lasts 3 to 7 days, and blood loss averages 20 to 80 ml. Irregular menses can be associated with irregular ovulation, stress, disease, and hormonal imbalances. Although menstruation is a normal process, various world cultures have taken a wide variety of attitudes toward it, seeing it as everything from a sacred time to an unclean time. In a society where menstruation is viewed negatively, nurses can help women develop a more positive image of this natural physiologic process.

2.3.2 Reproductive Cycle

The reproductive cycle, also referred to as the menstrual cycle, results from a functional hypothalamic–pituitary–ovarian axis and a precise sequencing of hormones that lead to ovulation. If conception doesn't occur, menses ensues. The ranges of normal menstrual cycles are as follows: cycle length: 21 to 36 days, duration of flow: 3 to 7 days and amount of flow: 20 to 80 mL

The female reproductive cycle involves two cycles that occur simultaneously: the ovarian cycle, during which ovulation occurs, and the endometrial cycle, during which menstruation occurs. Ovulation divides these two cycles at mid cycle. Ovulation occurs when the ovum is released from its follicle; after leaving the ovary, the ovum enters the fallopian tube and journeys toward the uterus. If sperm fertilizes the ovum during its journey, pregnancy occurs.

2.3.3 Ovarian Cycle

The ovarian cycle is the series of events associated with a developing oocyte (ovum or egg) within the ovaries. While men manufacture sperm daily, often into advanced age, women are born with a single lifetime supply of ova that are released from the ovaries gradually throughout the childbearing years. In the

female ovary, 2 million oocytesare present at birth and about 400,000 follicles are still present at puberty. The excess follicles are depleted during the childbearing years, with only 400 follicles ovulated during the reproductive period. The ovarian cycle begins when the follicular cells (ovum and surrounding cells) swell and the maturation process starts. The maturing follicle at this stage is called a graafian follicle. The ovary raises many follicles monthly, but usually only one follicle matures to reach ovulation. The ovarian cycle consists of three phases: the follicular phase, ovulation, and the luteal phase.

2.3.4 Follicular Phase

This phase is so named because it is when the follicles in the ovary grow and form a mature egg. This phase starts on day 1 of the menstrual cycle and continues until ovulation, approximately 10 to 14 days later. The follicular phase is not consistent in duration because of the time variations in follicular development. These variations account for the differences in menstrual cycle lengths. The hypothalamus is the initiator of this phase. Increasing levels of estrogen secreted from the maturing follicular cells and the continued growth of the dominant follicle cell induce proliferation of the endometrium and myometrium. This thickening of the uterine lining supports an implanted ovum if pregnancy occurs. Prompted by the hypothalamus, the pituitary gland releases follicle-stimulating hormone (FSH), which stimulates the ovary to produce 5 to 20 immature follicles. Each follicle houses an immature oocyte or egg. The follicle that is targeted to mature fully will soon rupture and expel a mature oocyte in the process of ovulation. A surge in luteinizing hormone (LH) from the anterior pituitary gland is actually responsible for affecting the final development and subsequent rupture of the mature follicle.

2.3.5 Ovulation

At ovulation, a mature follicle ruptures in response to a surge of LH, releasing a mature oocyte (ovum). This usually occurs on day 14 in a 28-day cycle. When

ovulation occurs, there is a drop in estrogen. Typically ovulation takes place approximately 10 to 12 hours after the LH peak and 24 to 36 hours after estrogen levels peak .The distal ends of the fallopian tubes become active near the time of ovulation and create currents that help carry the ovum into the uterus. The life span of the ovum is only about 24 hours; unless it meets a sperm on its journey within that time, it will die. During ovulation, the cervix produces thin, clear, stretchy, slippery mucus that is designed to help the sperm travel up through the cervix to meet the ovum for fertilization. The one constant, whether a women's cycle is 28 days or 120 days, is that ovulation takes place 14 days before menstruation.

2.3.6 Luteal Phase

The luteal phase begins at ovulation and lasts until the menstrual phase of the next cycle. It typically occurs day 15 through day 28 of a 28-day cycle. After the follicle ruptures as it releases the egg, it closes and forms a corpus luteum. The corpus luteum secretes increasing amounts of the hormone progesterone, which interacts with the endometrium to prepare it for implantation. At the beginning of the luteal phase, progesterone induces the endometrial glands to secrete glycogen, mucus, andother substances. These glands become tortuous and have large lumens due to increased secretory activity. The progesterone secreted by the corpus luteum causes the temperature of the body to rise slightly until the start of the next period. A significant increase in temperature, usually 0.5 to 1 degrees Fahrenheit, is generally seen within a day or two after ovulation has occurred; the temperature remains elevated for 12 to 16 days, until menstruation begins .This rise in temperature can be plotted on a graph and gives an indication of when ovulation has occurred. In the absence of fertilization, the corpus luteum begins to degenerate and consequently ovarian hormone levels decrease. As estrogen and progesterone levels decrease, the endometrium undergoes involution. In a 28-day cycle, menstruation then begins approximately 14 days after ovulation in the

absence of pregnancy. FSH and LH are generally at their lowest levels during the luteal phase and highest during the follicular phase.

2.3.7 Endometrial Cycle

The endometrial cycle occurs in response to cyclic hormonal changes. The four phases of the endometrial cycle are the proliferative phase, secretory phase, ischemic phase, and menstrual phase.

2.3.8 Proliferative Phase

The proliferative phase starts with enlargement of the endometrial glands in response to increasing amounts of estrogen. The blood vessels become dilated and the endometrium increases in thickness dramatically from 0.5 to 5 mm in height and increases eight-fold in thickness in preparation for implantation of the fertilized ovum. Cervical mucus becomes thin, clear, stretchy, and more alkaline, making it more favorable to sperm to enhance the opportunity for fertilization. The proliferative phase starts on about day 5 of the menstrual cycle and lasts to the time of ovulation. This phase depends on estrogen stimulation resulting from ovarian follicles, and this phase coincides with the follicular phase of the ovarian cycle.

2.3.9 Secretory Phase

The secretory phase begins at ovulation to about 3 days before the next menstrual period. Under the influence of progesterone released by the corpus luteum after ovulation, the endometrium becomes thickened and more vascular(growth of the spiral arteries) and glandular (secreting more glycogen and lipids). These dramatic changes are all in preparation for implantation, if it were to occur. This phase typically lasts from day 15 (after ovulation) today 28 and coincides with the luteal phase of the ovarian cycle. The secretory phase doesn’t take place if ovulation has not occurred.

2.3.10 Ischemic Phase

If fertilization does not occur, the ischemic phase begins. Estrogen and progesterone levels drop sharply during this phase as the corpus luteum starts to degenerate. Changes in the endometrium occur with spasm of the arterioles, resulting in ischemia of the basal layer. The ischemia leads to shedding of the endometrium down to the basal layer, and menstrual flow begins.

2.3.11 Menstrual Phase

The menstrual phase begins as the spiral arteries rupture secondary to ischemia, releasing blood into the uterus, and the sloughing of the endometrial lining begins. If fertilization does not take place, the corpus luteum degenerates. As a result, both estrogen and progesterone levels fall and the thickened endometrial lining sloughs away from the uterine wall and passes out via the vagina. The beginning of the menstrual flow marks the end of one menstrual cycle and the start of a new one. Most women report bleeding for an average of 3 to 7 days; the amount of menstrual flow varies, but approximately 6 to 8 ounces in volume per cycle is average.(Konar,2013)

2.3.12 Menstrual Cycle Hormones

The menstrual cycle involves a complex interaction of hormones. The predominant hormones include gonadotropin-releasing hormone, FSH, LH, estrogen, progesterone, and prostaglandins.

Gonadotropin-Releasing Hormone

Gonadotropin-releasing hormone (GnRH) is secreted from the hypothalamus in a pulsatile manner throughout the reproductive cycle. It pulsates slowly during the follicular phase and increases during the luteal phase. GnRH induces the release of FSH and LH to assist with ovulation.

Follicle-Stimulating Hormone

Follicle-stimulating hormone (FSH) is secreted by the anterior pituitary gland and is primarily responsible for the maturation of the ovarian follicle. FSH secretion is highest and most important during the first week of the follicular phase of the reproductive cycle.

Luteinizing Hormone

Luteinizing hormone (LH) is secreted by the anterior pituitary gland and is required for both the final maturation of pre-ovulatory follicles and luteinization of the ruptured follicle. As a result, estrogen production declines and progesterone secretion continues. Thus, estrogen levels fall a day before ovulation, and progesterone levels begin to rise.

Estrogen

Estrogen is secreted by the ovaries and is crucial for the development and maturation of the follicle. Estrogen is predominant at the end of the proliferative phase, directly preceding ovulation. After ovulation, estrogen levels drop sharply as progesterone dominates. In the endometrial cycle, estrogen induces proliferation of the endometrial glands. Estrogen also causes the uterus to increase in size and weight because of increased glycogen, amino acids, electrolytes, and water. Blood supply is expanded as well.

Progesterone

Progesterone is secreted by the corpus luteum. Progesterone levels increase just before ovulation and peak 5 to 7 days after ovulation. During the luteal phase, progesterone induces swelling and increased secretion of the endometrium. This hormone is often called the hormone of pregnancy because of its calming effect (reduces uterine contractions) on the uterus, allowing pregnancy to be maintained.

Prostaglandins

Prostaglandins are a closely related group of oxygenated fatty acids that are produced by the endometrium, with a variety of effects throughout the body. Although they have regulatory effects and are sometimes called hormones, prostaglandins are not technically hormones because they are produced by all tissues rather than by special glands.

Prostaglandins increase during follicular maturation and play a key role in ovulation by freeing the ovum inside the graafian follicle. Large amounts of prostaglandins are found in menstrual blood. Research is ongoing as to the various roles prostaglandins have on the menstrual cycle .

Menopause: Perimenopause and menopause are biologic markers of the transition from young adulthood to middle age. Neither of these are a symptom or disease, but rather a natural maturing of the reproductive system; during the perimenopausal years (2 to 8 years prior to menopause) women may experience physical changes associated with decreasing estrogen levels, which may include vasomotor symptoms of hot flashes, irregular menstrual cycles, sleep disruptions, forgetfulness, irritability, mood disturbances, decreased vaginal lubrication, fatigue, vaginal atrophy, and depression. Menopause refers to the cessation of regular menstrual cycles. This naturally occurring phase of every woman's life marks the end of menstruation and childbearing capacity. The average age of natural menopause—defined as1 year without a menstrual period—is 51. As the average life expectancy for women increases, the number of women reaching and living in menopausehas escalated. Most women can expect to spend more than one third of their lives beyond menopause. It is usually marked by atrophy of the breasts, uterus, fallopian tubes, and ovaries. Many women pass through menopause without untoward symptoms. These women remain active and in good health with little interruption of their daily routines. Other women experience vasomotor

symptoms, which give rise to sensations of heat, cold, sweating, headache, insomnia, and irritability.

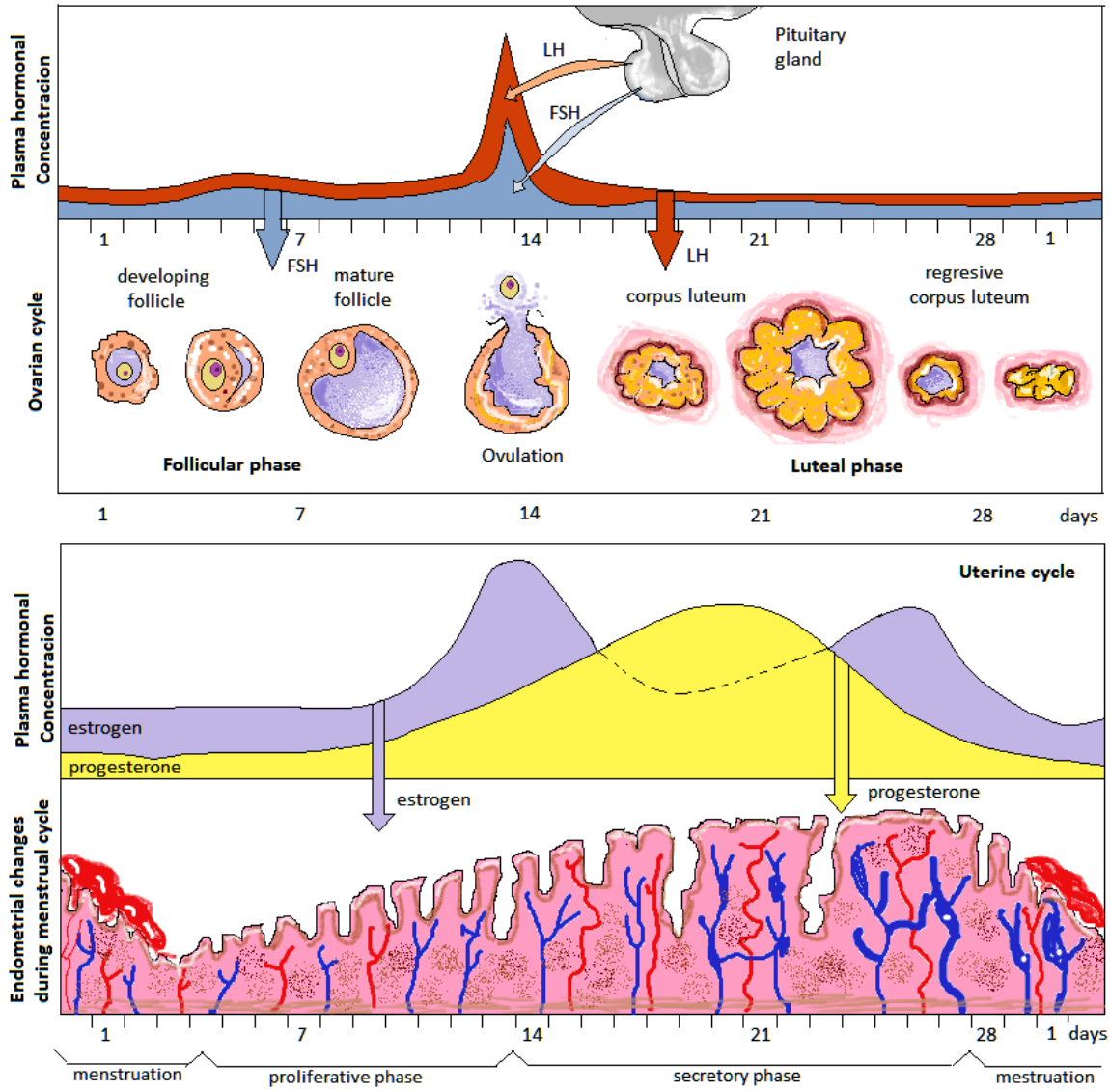


Figure 2.3 :menstrual cycle

2.4 Pathology

2.4.1 Menorrhagia:

is defined as cyclic bleeding at normal intervals; the bleeding is either excessive in amount (> 80 mL) or duration (>7 days) or both. The term menotaxis is often used to denote prolonged bleeding. ***Metrorrhagia*** is defined as irregular, acyclic bleeding from the uterus. ***Menometrorrhagia*** is the term applied when the bleeding is so irregular and excessive that the menses (periods) cannot be identified at all. ***Oligomenorrhea*** is a menstrual bleeding occurring more than 35 days apart and which remains constant at that frequency. ***hypomenorrhea*** is the term applied when the menstrual bleeding is unduly scanty and lasts for less than 2 days. ***Dysfunctional Uterine Bleeding (DUB)*** is defined as a state of abnormal uterine bleeding without any clinically detectable organic, systemic, and iatrogenic cause (Pelvic pathology, e.g. tumor, inflammation or pregnancy is excluded). ***Heavy menstrual bleeding (HMB)*** is defined as a bleeding that interferes with woman's physical, emotional, social and maternal quality of life. ***Abnormal Uterine Bleeding (AUB)*** Any uterine bleeding outside the normal volume, duration, regularity or frequency is considered abnormal uterine bleeding (AUB).(Mohan,2015)

2.4.2 Displacement of the Uterus

Retroversion (RV) is the term used when the long axes of the corpus and cervix are in line and the whole organ turns backwards in relation to the long axis of the birth canal. Retroflexion signifies a bending backwards of the corpus on the cervix at the level of internal os. *The two conditions are usually present together and are loosely called retroversion or retrodisplacement*

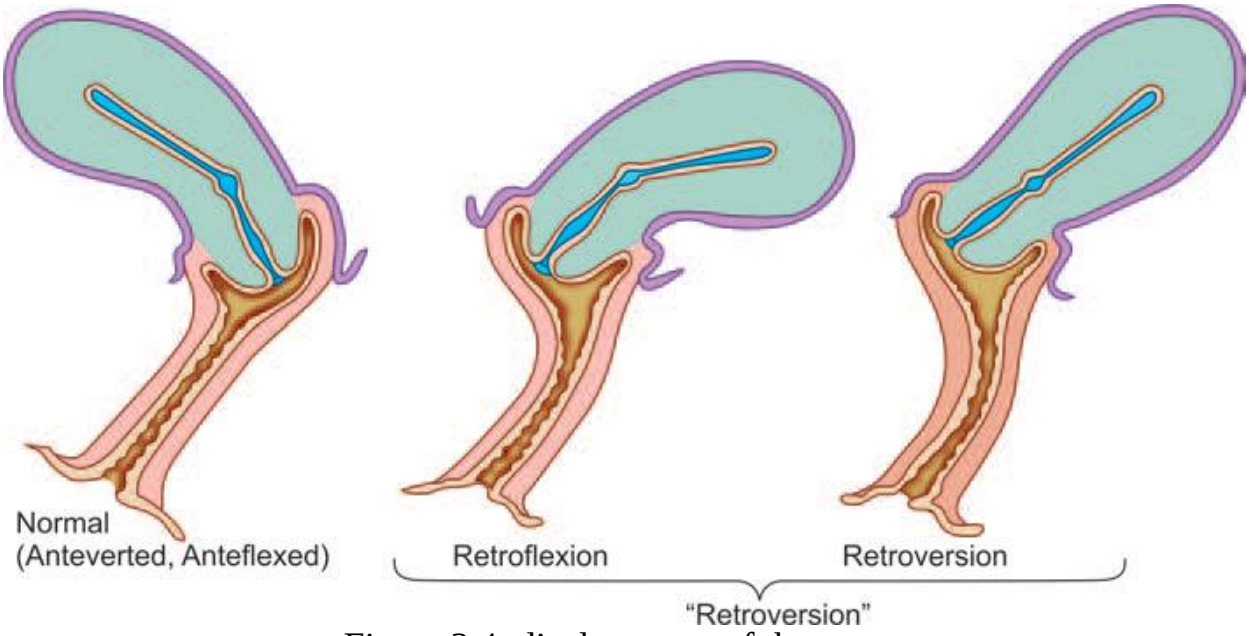


Figure 2.4: displacement of the uterus

Lesions of the cervix: include *Cervical carcinoma* and *cervical polyps* while ***lesion of the uterus*** include: *Fibroid is the commonest benign tumor of the uterus* and also the commonest benign solid tumor in female. Histologically, this tumor is composed of smooth muscle and fibrous connective tissue, so named as uterine *leiomyoma*, *myoma* or *fibromyoma*.

2.4.3 Types:

***Body*:** The fibroids are mostly located in the body of the uterus and are usually multiple

Intra mural: no bulging into the endometrium or the serosa.

Sub serosal: a significant portion of the leiomyoma is bulging into the serosal surface .

Pedunculated: the leiomyoma is exophytic and attached to the uterus by a pedicle

Sub mucosal: a significant portion is bulging into the endometrial cavity > < 50 % is important .

Intracavitary: the leiomyoma is within the endometrial cavity and it is attached to the myometrium by a pedicle.

Cervical: Cervical fibroid is rare (1–2 %).

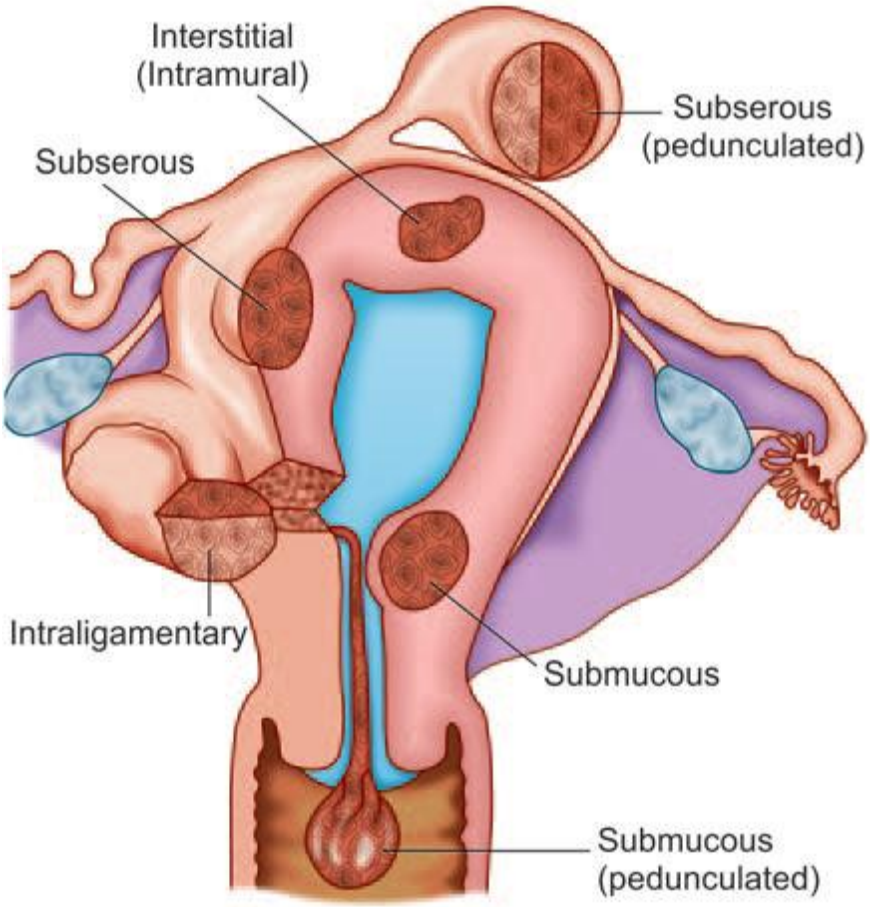


Figure 2.5 : location of fibroid

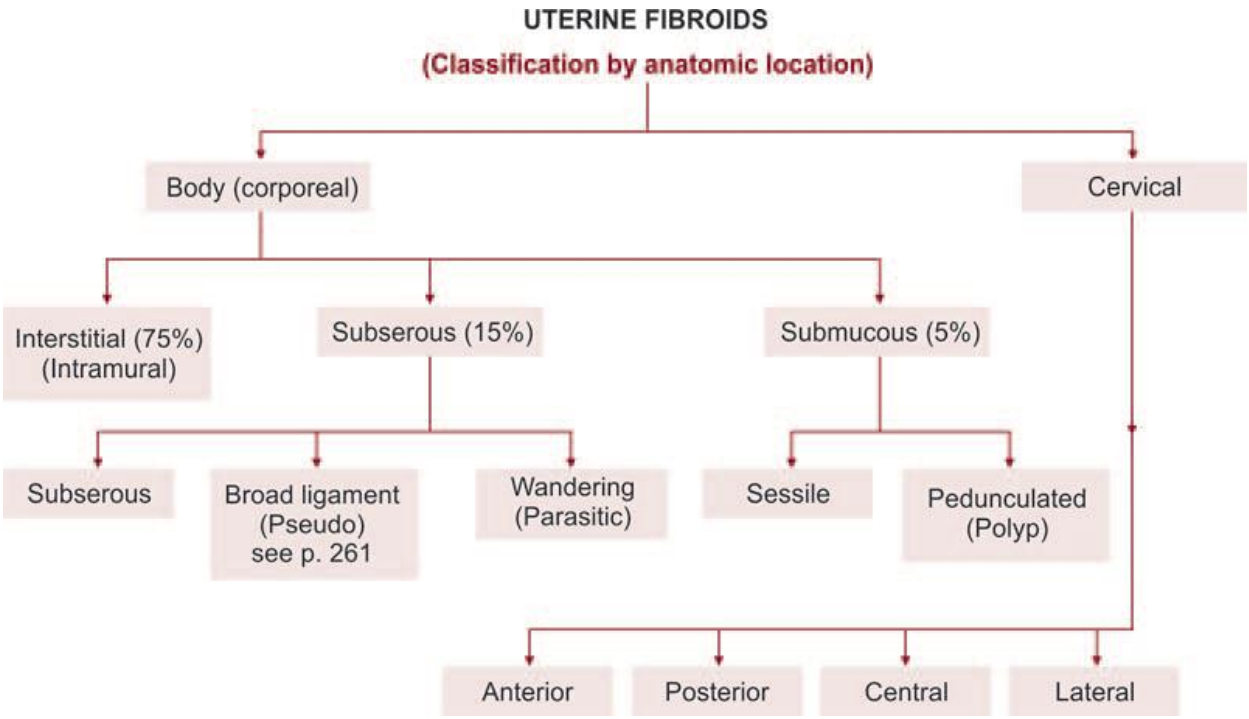


Figure 2.6 : uterine fibroid (classification by anatomic location)

***Symptoms of Fibroid Uterus*:** it include; asymptomatic-majority (75%), menstrual abnormality: menorrhagia, metrorrhagia, dysmenorrhea, dyspareunia, infertility, pressure symptoms, recurrent pregnancy loss (miscarriage, preterm labor), lower abdominal or pelvic pain and abdominal enlargement (Mohan,2015).

***Adenomyosis*:** Defined as the presence of ectopic endometrial glands within the myometrium and the presence of these glands induces a hypertrophic and hyperplastic reaction in the myometrial tissue; not always symptomatic (very very important when it comes to report) If symptomatic; dysmenorrhea, dyspareunia, chronic pelvic pain and menometrorrhgia; usually a diffuse disease but a focal variant can occasionally be seen.

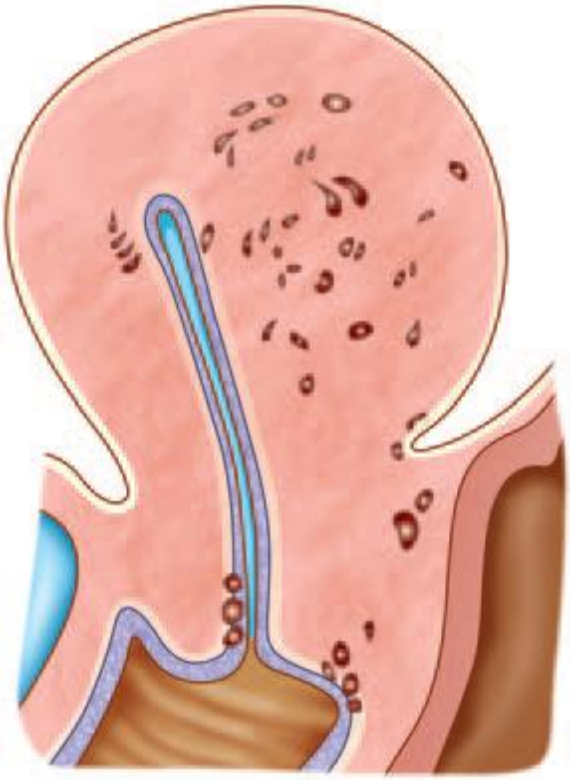


Figure 2.7: Adenomyosis. Note the absence of capsule and presence of dark blood spots

2.4.4 Polyps

***Benign*:** Polyp is a clinical entity referring a tumor attached by a pedicle. *Mucous*: The commonest type of benign uterine polyp is mucous one. It may arise from the body of the uterus or from the cervix

2.4.5 Endometrial hyperplasia

Endometrial hyperplasia is an abnormal proliferation of endometrial stroma and glands and represents a spectrum of endometrial changes

2.4.6 Endometrial carcinoma

Endometrial adenocarcinoma is the most common invasive gynaecologic malignancy, but thanks to early detection and treatment, it is not a leading cause of cancer deaths. .(J. A. Rock, S. M. Markhm et al, 2012)

2.4.7 Intra uterine fluid collections

Importance depends on the age of the patient in premenopausal patients, fluid collections are most commonly associated with: menstruation, early IUP, and the pseudogestational sac in an ectopic pregnancy. Other benign causes of obstruction leading to intrauterine fluid production include polyps, infection and submucosal fibroids.

2.4.8 Endometrial cavity fluid

A small amount of fluid in the endometrial canal is likely related to benign cervical stenosis. An intrauterine fluid collection in a postmenopausal patient, although possibly related to cervical stenosis, should raise concern for endometrial (or cervical) carcinoma. An obstructing tumour must be excluded even when cervical stenosis has been identified clinically. In prepubertal patients, fluid in the endometrial canal may be related to haematometrocolpos.

2.4.9 Uncommon Endometrial pathologies

Endometrial adhesions: Endometrial adhesions are posttraumatic or postsurgical in nature and can cause Asherman syndrome, which includes infertility, recurrent pregnancy loss, and amenorrhea.

AVM: These are actually very rare and typically arise following instrumentation of the endometrial cavity commonly in association with pregnancy loss or delivery

They can be associated with: malignancies, infections, RPOCS and molar gestations. They can be congenital and these are even less common and less symptomatic than acquired variety symptoms, heavy bleeding and pelvic pain and dyspareunia.

Osseous metaplasia: Endometrial ossification is a rare disease, and its aetiology and pathogenesis are controversial. Osseus metaplasia has been associated with secondary infertility and dysmenorrhea and has mimicked a retained intrauterine device. .(J. A. Rock, S. M. Markhm et al, 2012)

2.4.10 Lesions of the ovaries

It include ovarian enlargement which might be: non-neoplastic or neoplastic (Benign) as well as ovarian torsion and ovarian carcinoma and metastatic tumors of the ovary constitute about 5 percent of all ovarian tumors.

Non-neoplastic: The non-neoplastic enlargement of the ovary is usually due to accumulation of fluid inside the functional unit of the ovary.

The causes are: follicular cysts, corpus luteum cyst, theca lutein and granulosa lutein cysts, polycystic ovarian syndrome and endometrial cyst (chocolate cyst) ; Except the last one, all are functional cysts of the ovary and are loosely called cystic ovary.

Benign Ovarian Neoplasms: The incidence of ovarian tumor amongst gynecologic admission varies from 1–3%. About 75% of these are benign, they include: mucinous cyst adenoma, serous cyst adenoma, brenner tumor, dermoid cyst, endometrioid tumors and clear cell tumors.

Ovarian hyperstimulation syndrome (OHSS): The OHSS is characterized by multiple follicular development and ovarian enlargement following hCG stimulation. It occurs mostly with the conception cycle. The clinical features appear about 3–6 days after the ovulating dose of hCG is administered. It is an iatrogenic and potentially a life-threatening complication of superovulation.

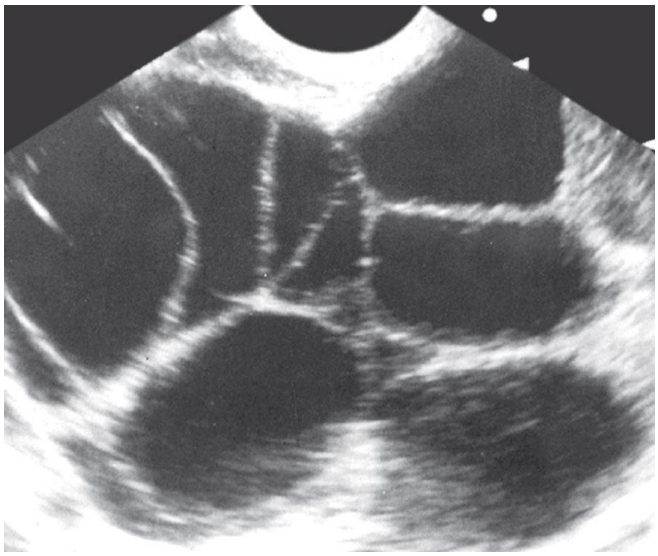


Figure 2.8 : Ultrasonographic view of ovarian hyperstimulation syndrome. Enlargement of the ovary with multiple follicles

Polycystic ovarian syndrome (PCOS): Polycystic ovarian syndrome (PCOS) was originally described in 1935 by Stein and Leventhal as a syndrome manifested by amenorrhea, hirsutism and obesity associated with enlarged polycystic ovaries. This heterogenous disorder is characterized by excessive androgen production by the ovaries mainly. PCOS is a multifactorial and polygenic condition. *Diagnosis is based upon the presence of any two of the following three criteria* (Asrm/Eshre, 2003); which include: oligo and/or anovulation, hyperandrogenism (clinical and/or biochemical) and polycystic ovaries. Other etiologies (CAH, thyroid dysfunction, hyperprolactinemia,Cushing syndrome) are to be excluded. The incidence varies between 0.5–4 percent, more common amongst infertile women. It is prevalent in young reproductive age group (20–30%). Polycystic ovary may be seen in about 20% of normal women.

2.4.11 Endometriosis

Presence of functioning endometrium (glands and stroma) in sites other than uterine mucosa is called endometriosis. It is not a neoplastic condition, although malignant transformation is possible.

Stromal Endometriosis: This is a rare condition where the endometrial stromal cells, without glandular components, are present in places other than uterine mucosa.

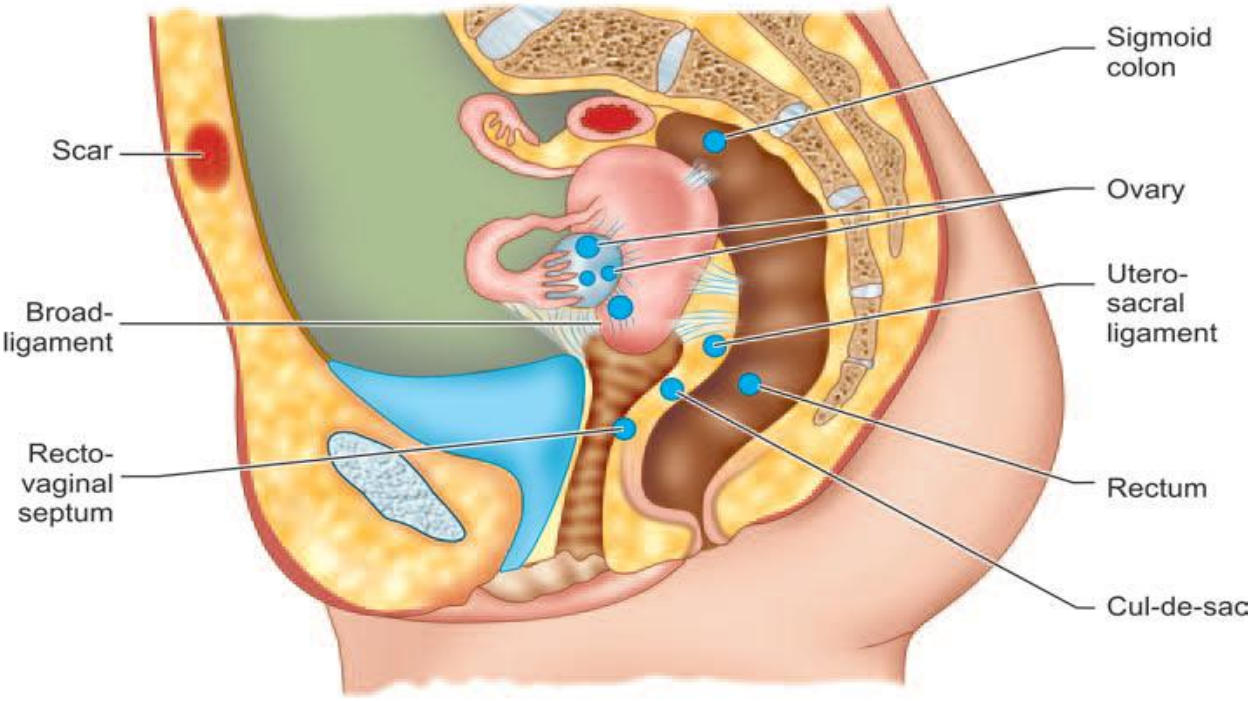


Fig (2.9) common sites of endometrosis

Endometrial carcinoma: *uterus Sarcoma* is rare and constitutes about 3 percent of uterine malignancy.

carcinoma fallopian tube: Primary carcinoma of the fallopian tube is very rare. The incidence of tubal carcinoma is less than 0.5 percent of gynecological malignancies.

2.4.12 Infertility

Infertility is defined as a failure to conceive within one or more years of regular unprotected coitus.

Primary infertility denotes those patients who have never conceived.

Secondary infertility indicates previous pregnancy but failure to conceive subsequently.

Fecundability is defined as the probability of achieving a pregnancy within one menstrual cycle. In a healthy young couple, it is 20 percent.

Fecundity is the probability of achieving a live birth within a single cycle.

Causes of infertility**:** Conception depends on the fertility potential of both the male and female partner. The male is directly responsible in about 30–40 percent, the female in about 40–55 percent and both are responsible in about 10 percent cases. The remaining 10 percent is unexplained, in spite of thorough investigations with modern technical knowhow. It is also strange that 4 out of 10 patients of unexplained category become pregnant within 3 years without having any specific treatment. It is also emphasized that the relative subfertility of one partner may sometimes be counter balanced by the high fertility of the other.

Causes of male infertility: The important causes of male infertility are: hypothalamic-pituitary disorders (1–2%), primary gonadal disorders (30–40%), disorders of sperm transport (10–20%) and idiopathic (40–50%). Where the *Congenital one includes: Undescended testes***:** the hormone secretion remains unaffected, but the spermatogenesis is depressed. Vas deferens is absent (bilateral) in about 1–2 percent of infertile males.

Kartagener syndrome (autosomal disease) there is loss of ciliary function and sperm motility and *Hypospadias* causes failure to deposit sperm high in vagina.

*Thermal Factor***:** The scrotal temperature is raised in conditions such as varicocele. Varicocele probably interferes with the cooling mechanism or increase scatecholamine concentration. However, no definite association between varicoceles and infertility has been established.

*Infection***:** Mumps orchitis after puberty may permanently damage spermatogenesis, the quality of the sperm is adversely affected by chronic systemic illness like bronchiectasis. Bacterial or viral infection of the seminal vesicle or prostate depresses the sperm count and T. mycoplasma or Chlamydia trachomatis infection is also implicated.

*General factors***:** Chronic debilitating diseases, malnutrition or heavy smoking reduce spermatogenesis. Alcohol inhibits spermatogenesis either by suppressing Leydig cell synthesis of testosterone or possibly by suppressing gonadotropin levels.

Endocrine: Testicular failure due to gonadotropin deficiency **(**Kallmann's syndrome**)** is rare. FSH level is raised in idiopathic testicular failure with germ cell hypoplasia **(**Sertoli-cell-only-syndrome**)**.Hyperprolactinemia is associated with impotence.

Genetic: Common chromosomal abnormality in azoospermic male is Klinefelter's syndrome (47 XXY). Gene deletion has been detected in the long-arm of Y chromosome (Yq) for patients with severe oligospermia and azoospermia.

Iatrogenic: Radiation, cytotoxic drugs, nitrofurantoin, cimetidine, b blockers, antihypertensive, anticonvulsant, and antidepressant drugs are likely to hinder spermatogenesis.

*Immunological factor***:** Antibodies against spermatozoa surface antigens may be the cause of infertility. This results in clumping of the spermatozoa after ejaculation.

Obstruction of the efferent ducts: The efferent ducts may be obstructed by infection like tubercular, gonococcal or by surgical trauma (herniorrhaphy)

following vasectomy. In Young's syndrome, there is epididymal obstruction and bronchiectasis.

Failure to Deposit Sperm High in the Vagina (Coital Problems): which might be due to**:** erectile dysfunction, ejaculatory defect-premature, retrograde or absence of ejaculation and hypospadias.

Sperm abnormality: Loss of sperm motility (asthenozoospermia), abnormal sperm morphology (roundheaded sperm, teratozoospermia) are the important factors.

Errors in the seminal fluid: it include; unusually high or low volume of ejaculate, low fructose content, high prostaglandin content and undue viscosity

Causes of female infertility: According to FIGO manual (1990) causes are: Tubal and peritoneal factors (25–35%), Ovulatory factor(30–40%) and Endometriosis (1–10%).

Ovarian factors: The ovulatory dysfunctions (dysovulatory) encompass: Anovulation or oligo-ovulation, decreased ovarian reserve, luteal phase defect (LPD) and luteinized unruptured follicle (LUF).

Anovulation or oligo-ovulation: The ovarian activity is totally dependent on the gonadotropins and the normal secretion of gonadotropins depends on the pulsatile release of GnRH from hypothalamus. As such, ovarian dysfunction is likely to be linked with disturbed hypothalamo-pituitary-ovarian axis either primary or secondary from thyroid or adrenal dysfunction. Thus, the disturbance may result not only in anovulation but may also produce oligomenorrhea or even amenorrhea. Anovulatory cycles usually represent a lesser degree of disturbance with these normal pathways than does amenorrhea. Possible causes of anovulation are given schematically. As there is no ovulation, there is no corpus luteum formation. In the absence of progesterone, there is no secretory endometrium in the second half of the cycle. The other features of ovulation are absent.

Luteal Phase Defect (LPD): In this condition, there is inadequate growth and function of the corpus luteum. There is in adequate progesterone secretion. The lifespan of corpus luteum is shortened to less than 10 days. As a result, there is inadequate secretory changes in the endometrium which hinder implantation. LPD is due to defective folliculogenesis which again may be due to varied reasons. Drug induced ovulation, decreased level of FSH and/or LH, elevated prolactin, subclinical hypothyroidism, older women, pelvic endometriosis, dysfunctional uterine bleeding are the important causes.

Luteinized Unruptured Follicular, Syndrome (Trapped Ovum): In this condition, the ovum is trapped inside the follicle, which gets luteinized. The cause is obscure but may be associated with pelvic endometriosis or with hyperprolactinemia.

Tubal and peritoneal factors: are responsible for about30–40 percent cases of female infertility. The obstruction of the tubes may be due to: pelvic infections causing: peritubal adhesions, endosalpingeal damage, and previous tubal surgery or sterilization, salpingitis is thmica nodosa, tubal endometriosis and others and polyps or mucous debris within the tubal lumen, or tubal spasm.

Peritoneal factors***:*** In addition to peritubal adhesions, even minimal endometriosis may produce infertility. Deep dyspareunia too often troubles the patient.

Uterine factors: The endometrium must be sufficiently receptive enough for effective nidation and growth of the fertilized ovum. The possible factors that hinder nidation are uterine hypoplasia, inadequate secretory endometrium, fibroid uterus, endometritis (tubercularin particular), uterine synechiae or congenital malformation of uterus.

Cervical factors: *Anatomic***:** Anatomic defects preventing sperm ascent may be due to congenital elongation of the cervix, second degree uterine prolapse and acute retroverted uterus. These conditions prevent the external os to bathe in the

seminal pool. Pinholeos may at times be implicated, or the cervical canal maybe occluded by a polyp.

*Physiologic***:** The fault lies in the composition of the cervical mucus, so much that the spermatozoa fail to penetrate the mucus. The mucus may be scanty following amputation, conization or deep cauterization of the cervix. The abnormal constituents include excessive, viscous or purulent dischargeas in chronic cervicitis. Presence of antisperm orsperm immobilizing antibodies may be implicated as immunological factor of infertility.

Vaginal factors: Atresia of vagina (partial or complete), transverse vaginal septum, septate vagina, or narrow introitus causing dyspareunia are included in the congenital group. Vaginitis and purulent discharge may at times be implicated but pregnancy too often occurs in presence of vaginitis, specific, or nonspecific. However, dyspareunia may be the real problem in such cases.

Combined factors: these include: these include the presence of factors both in the male and female partners causing infertility, general factors: Advanced age of the wife beyond 35 years is related but spermatogenesis continues throughout life although aging reduces the fertility in male also, infrequent intercourse, lack of knowledge of coital technique and timing of coitus to utilize the fertile period are very much common even amongst the literate couples, apareunia and dyspareunia, anxiety and apprehension, use of lubricants during intercourse, which maybe spermicidal and immunological factors.(Konar,2013)

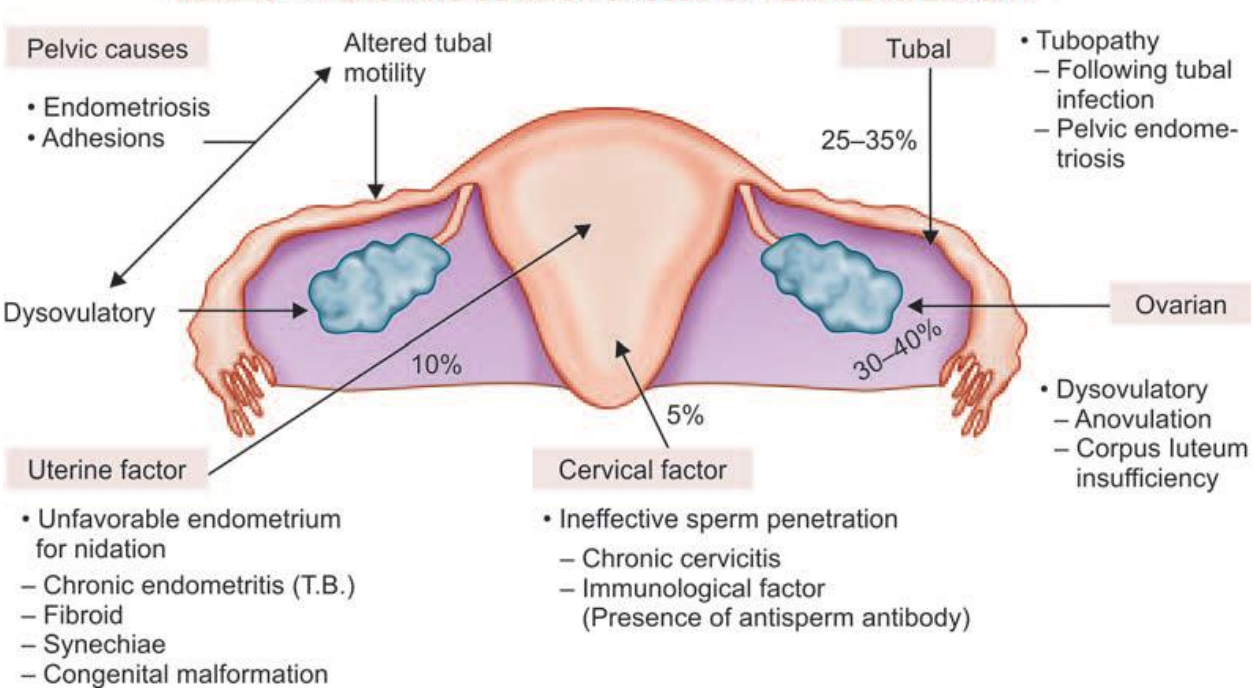


Fig (2.10) illustration of the common causes of female infertility

Previous studies :

Tochukwu et al. (2015) in a comprehensive review study the application of ultrasonography in female infertility; the quest for detailed evaluation of the uterus, fallopian tubes, and ovaries that is radiation free, inexpensive, readily available, non-invasive, relatively less time consuming and easily repeatable in female infertility has resulted in further studies. However, ultrasonography (US) remains the first line indispensable tool for gynecologic workup, monitoring and treating infertility. The aim is to review the current knowledge regarding the application of ultrasonography in female infertility. This was a descriptive review of ultrasonography in female infertility Several databases (Medline, Google scholar, PubMed) was searched with keywords “ultrasonography and female infertility”, “evaluation of female infertility”, “role of ultrasonography in female infertility:, and imaging in female infertility”. Female infertility is multifactorial in origin. Ultrasonography is the most widely used imaging in gynecology and has

revolutionized the management of female infertility worldwide. The recognition, evaluation and treatment of female infertility are complicated, complex, stressful and emotionally devastating for most couples. The couple's emotional state should be supportive, informative and well tolerated. Female infertility is an immense stress to couples, families and relatives worldwide. The causes are multifactorial in origin with both congenital and acquired problems of the uterus, fallopian tubes and ovaries. Ultrasound plays an important role in female infertility workup with hysterosalpingography (HSG), sonohysterography (Sono-HSG) and magnetic resonance imaging (MRI), each playing a complimentary role in the screening, diagnosis and/or management of female infertility.

Ali and Hisham studied the role of FSH, LH, and Prolactin Hormones in Female Infertility in order to determine the main hormonal disturbances in the hormones (FSH, LH. and prolactin) among infertile women where recently, a great attention has been paid to the role of hormones as a diagnostic tool in the evaluation of female infertility. The purpose of this study was to identify the association between female infertility and hormonal imbalance (FSH, LH and Prolactin) and what is the relationship between these hormones and the woman's socio-demographic and clinical characteristics. The study was carried out at the Fertility Center in Al-Sadr Medical City, which is located in Najaf province, Iraq, during the period from Dec, 2014 to Apr, 2015. The study involved (44) infertile women who attended the Fertility Center. In accordance to the socio-demographic data, the majority of the studies women were from urban regions (81.18%), while all them were housewives. The clinical history revealed a relatively high percentage (56.82%) of vaginitis, and UTI (50%) among the studies women, while most of them were either overweight (40.91%) or obese (22.73%). The results showed that the majority of studies women had normal hormonal levels according to the standard reference limits for FSH, LH and Prolactin. The study also

showed that there was a significant positive correlation between the level of FSH and the age of the studies infertile women. It was concluded that hormonal imbalance for (LH, FSH and prolactin) is just a minor suspected etiologic factor in causing infertility in the studies women the level of FSH increases with age, while the level of prolactin slightly decreases with age. It was recommended to achieve a comprehensive case-control study for evaluating hormonal imbalance of (FSH, LH, prolactin, estrogens, progesterone, thyroid and inhibit) hormones in the infertile women.

Shamsunnisa et al. (2009) studied the characteristics of infertile patients with ovulatory dysfunction and their relation to body mass index in order to describe the clinical and hormonal profile of subfertile women with ovulatory dysfunction in relation to their BMI. Ovulatory dysfunction is a group of disorders with variable clinical presentations occasionally having serious long-term adverse effects. It accounts for 30% of female fertility problems. Evidence suggests an association between an individual's weight and disorders of ovulation. This prospective, descriptive study was carried out in Mother and Child Health Centre, PIMS, Islamabad and Railway hospital, Rawalpindi from April 2001 to March 2007. One hundred & thirty eight infertile patients with ovulatory dysfunction were included. The clinical data including BMI of each patient was recorded in addition to reports of investigations comprised of cervical smear, pelvic ultrasound and hormonal profile. The results of their showed that the Primary infertility was found in 61% while secondary in 39% of the patients. The mean age was 29 years and mean duration of infertility was 6 years. Menstrual pattern was normal in 56.5%. BMI was normal in 30.4% while most patients were overweight and obese. Prolonged cycles, history of systemic endocrine disorders, abnormal vaginal discharge, hirsutism, polycystic ovarian morphology and hormonal abnormalities were more frequent in patients with increased BMI. During the study period, 21.7% of the

women conceived. Conclusion: Infertile patients with ovulatory dysfunction present more frequently with primary infertility. They usually have higher than required BMI. Oligomenorrhoea amenorrhoea, hirsutism and hormonal abnormalities are more frequent in overweight than infertile patients with ovulatory dysfunction having a normal BMI.

Sonal and Nagori (2015) investigate the application of ultrasound in infertility where evaluation of the complete cycle instead of only pre hCG scan is an essential for follicular monitoring. Using color Doppler in this assessment is mandatory because it allows to assess the functional status of follicle and endometrium. 3D ultrasound is useful for volume measurements, and 3D PD for assessment of global vascularity. Baseline scan is done to predict the ovarian reserve and response and decide the stimulation protocols for ARTs. Uterus is assessed for receptivity. But baseline scan also diagnoses PCOS. This is by counting antral follicles, stromal flows and stromal and ovarian volume. Ultrasound features of ovary on baseline scan can also be correlated closely with the baseline hormonal status of ovaries—LH, FSH and Androgen. Ultra- sound is a key tool to decide follicular maturity and endome- trial receptivity and to decide the time of hCG and time of IUI. Doppler plays a major role in correct decision making and 3D and 3D power Doppler add to the details and also improves the success rates of different ARTs. Luteal phase also can be better explained by the use of Doppler. Ultrasound to hormonal correlation in both preovulatory and luteal phase helps plan the ART for positivity.

Sheikh and Kupesic, (2014) studied the role of ultrasound in the assessment of female infertility. Ultrasound has made significant advancements in reproductive medicine, especially infertility of a female cause. It is a useful tool in the diagnosis and management of various disorders. Transvaginal ultrasonography in particular plays a vital role in infertility treatment as it allows for evaluation of normal and

stimulated ovarian cycles, aspiration of follicles, and subsequent transfer of embryos. The use of color Doppler permits visualization of endometrial and intraovarian vessels, facilitating an understanding of normal and abnormal physiology of the uterus and ovaries. This article reviews a variety of case scenarios regarding female infertility that may be encountered in the practice of reproductive endocrinology. Ovarian causes such as polycystic ovarian syndrome, luteinized unruptured follicle, luteal phase defect, premature ovarian failure, and endometriosis, are discussed together with tubal and uterine causes of infertility. By using illustrative images, the reader will be able to correlate findings on Bmode, color Doppler and 3D ultrasound with various causes of female infertility.

Chapter three

Material and Methods

3-1 Material

The data of this study was collected using ToshibaXario XG SSA-680A with convex 3.5 MHz endovaginal probs.

3-2 Design of the study

This study is a cross-sectional, descriptive study where the data collected prospectively

3-3 Population of the study

This study includes female complaining from primary infertility with different clinical symptoms and manifestation, visited the ultrasound clinic for examination.

3-4 Sample and size of the study

The data of this study collected from 180 patients selected conveniently

3-5 Place and duration of the Study:

This study carried out in Mohammed bin Naif Medical center in Saudi Arabia in the period from December 2017 to December 2018

3-6 Method of data collection

Techniques

A pelvic ultrasound is a noninvasive diagnostic exam that produces images that are used to assess organs and structures within the female pelvis. A pelvic ultrasound allows quick visualization of the female pelvic organs and structures including the uterus, cervix, vagina, fallopian tubes and ovaries.

An ultrasound gel is placed on the transducer and the skin to allow for smooth movement of the transducer over the skin and to eliminate air between the skin and the transducer for the best sound conduction.

Transvaginal ultrasound is a test used to look at a woman's reproductive organs, including the uterus, ovaries, and cervix.

Transvaginal means across or through the vagina. The ultrasound probe will be placed inside the vagina.

The women lie down on a table with her knees bent her feet may be held in stirrups. She will be given a probe, or transducer, to place into the vagina. The probe is covered with a condom and a gel.

The health care provider will move the probe around the area to see the pelvic organs.

She will be asked to undress, usually from the waist down. A transvaginal ultrasound is done with empty bladder or partly filled. The test is usually painless, although some women may have mild discomfort from the pressure of the probe. Only a small part of the probe is placed into the vagina. Transvaginal ultrasound may be done for the following problems: Abnormal findings on a physical exam, such as cysts, fibroid tumors, or other growths , Abnormal vaginal bleeding and menstrual problems , Certain types of infertility , Ectopic pregnancy , Pelvic pain and Transvaginal ultrasound is also used during pregnancy.

The pelvic structures or fetus is normal. An abnormal result may be due to many conditions. Some problems that may be seen include: Birth defects, Cancers of the uterus, ovaries, vagina, and other pelvic structures, Infection, including pelvic inflammatory disease , Growths in or around the uterus and ovaries (such as cysts or fibroids) and Twisting of the ovaries.

There are no known harmful effects of transvaginal ultrasound on humans.Unlike traditional x-rays, there is no radiation exposure with this test.

A special type of transvaginal ultrasound is called a saline infusion sonography (SIS). This procedure involves inserting sterile salt water into the uterus before the ultrasound to help identify any possible masses. The saline solution stretches the uterus slightly, providing a more detailed picture of the inside of the uterus than a conventional ultrasound.

3-7 Variables:

The data of this study will be collected using the following variables: Age, height, weight, echogenicity, texture, size, and level of female hormones.

3-8 Method of data analysis

The data analyzed by using Statistical Package for Social Studies (SPSS).

Chapter four
Results

Table 4-1 the mean and standard deviation of laboratory test results and ultrasound for fertile and infertile participant

Group Statistics				
Fertility		N	Mean	Std. Deviation
FSH	No	120	9.10	8.25
	Yes	60	13.29	9.03
T3	No	120	4.70	1.04
	Yes	60	4.56	0.89
T4	No	120	14.59	3.81
	Yes	60	14.35	2.01
LH	No	120	9.50	6.94
	Yes	60	9.06	6.91
PRL	No	120	22.76	14.73
	Yes	60	16.98	5.23
TEST	No	120	0.32	0.36
	Yes	60	0.26	0.21
TSH	No	120	3.59	2.50
	Yes	60	3.24	2.48
Uterus Length	No	120	49.93	9.92
	Yes	60	50.57	6.78
Uterus Width	No	120	42.39	7.96
	Yes	60	43.30	5.08
Rt ovary Length	No	120	34.38	7.35
	Yes	60	30.28	4.18
Rt ovary Width	No	120	29.85	6.78
	Yes	60	25.79	3.66
Lt ovary length	No	120	35.43	8.86
	Yes	60	29.66	3.17
Lt ovary Width	No	120	30.63	7.87
	Yes	60	25.54	3.03

Table 4-2 significance t-test for laboratory test results and ultrasound for fertile and infertile participant

Independent Samples Test between fertility and infertility results in table 4-1		
Parameters	t-test for Equality of Means	
	t	p-value
FSH	3.11	**0.00**
T3	0.93	0.35
T4	0.45	0.65
LH	0.40	0.69
PRL	2.94	**0.00**
TEST	1.22	0.22
TSH	0.90	0.37
Uterus Length	0.45	0.65
Uterus width	0.80	0.42
Rt ovary length	4.00	**0.00**
Rt ovary width	4.32	**0.00**
Lt ovary length	4.88	**0.00**
Lt ovary width	4.83	**0.00**

Table 4-3 Crosstabulation of ultrasound ovaries Findings with Fertility status (yes or no)

Ovaries Findings	Fertility		Total
	No	Yes	
Normal	55	58	113
PCO	42	0	42
Simple cyst	11	2	13
Heamorrhagic cyst	8	0	8
Endometrioma	2	0	2
Dermoid cyst	2	0	2
Total	120	60	180

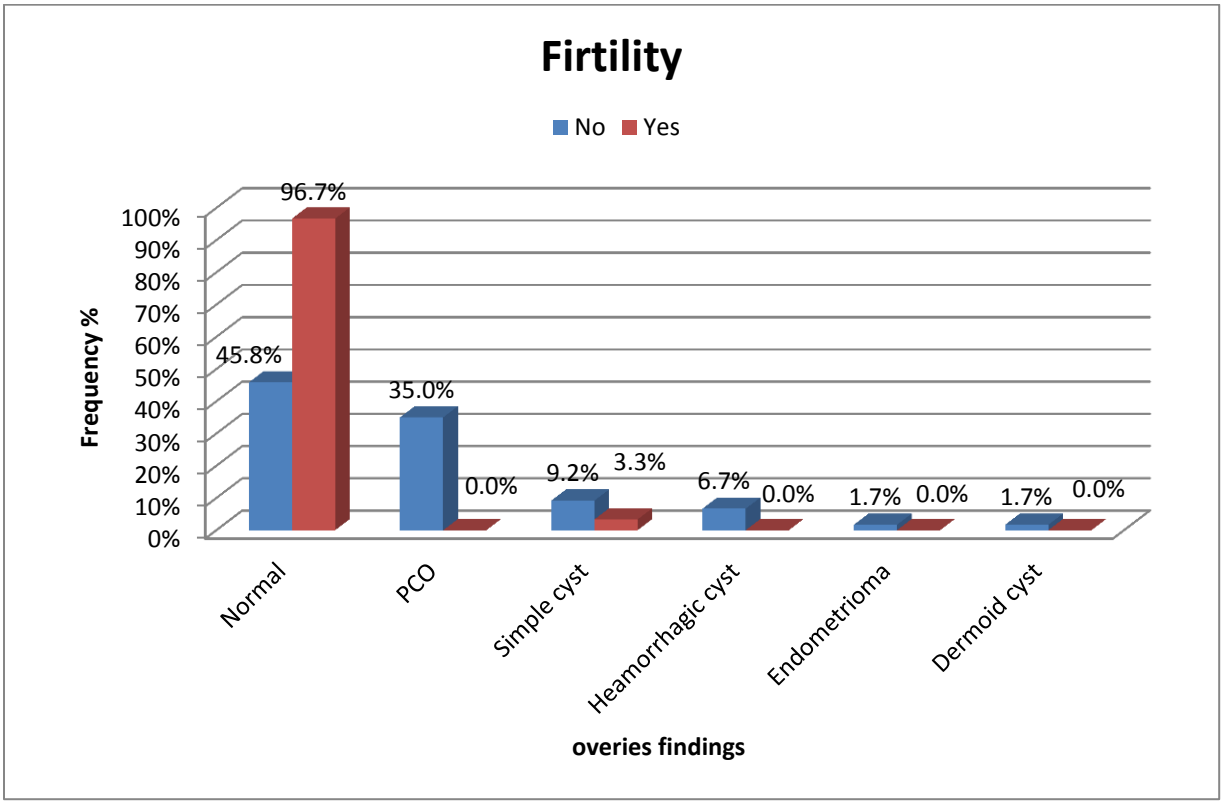


Figure 4-1 bar plot shows the percentage distribution of ultrasound ovaries finding in respect to fertility status

Table 4-4 Crosstabulation of ultrasound uterus findings with Fertility status

Uterus Findings	Fertility		Total
	No	Yes	
Normal	80	56	136
Subserous fibroma	3	1	4
Intramural fibroma	14	3	17
Submucous fibroma	5	0	5
Polyp	4	0	4
Bicornuate	1	0	1
Adenomyosis	2	0	2
Retroverted	11	0	11
Total	120	60	180

Bnn

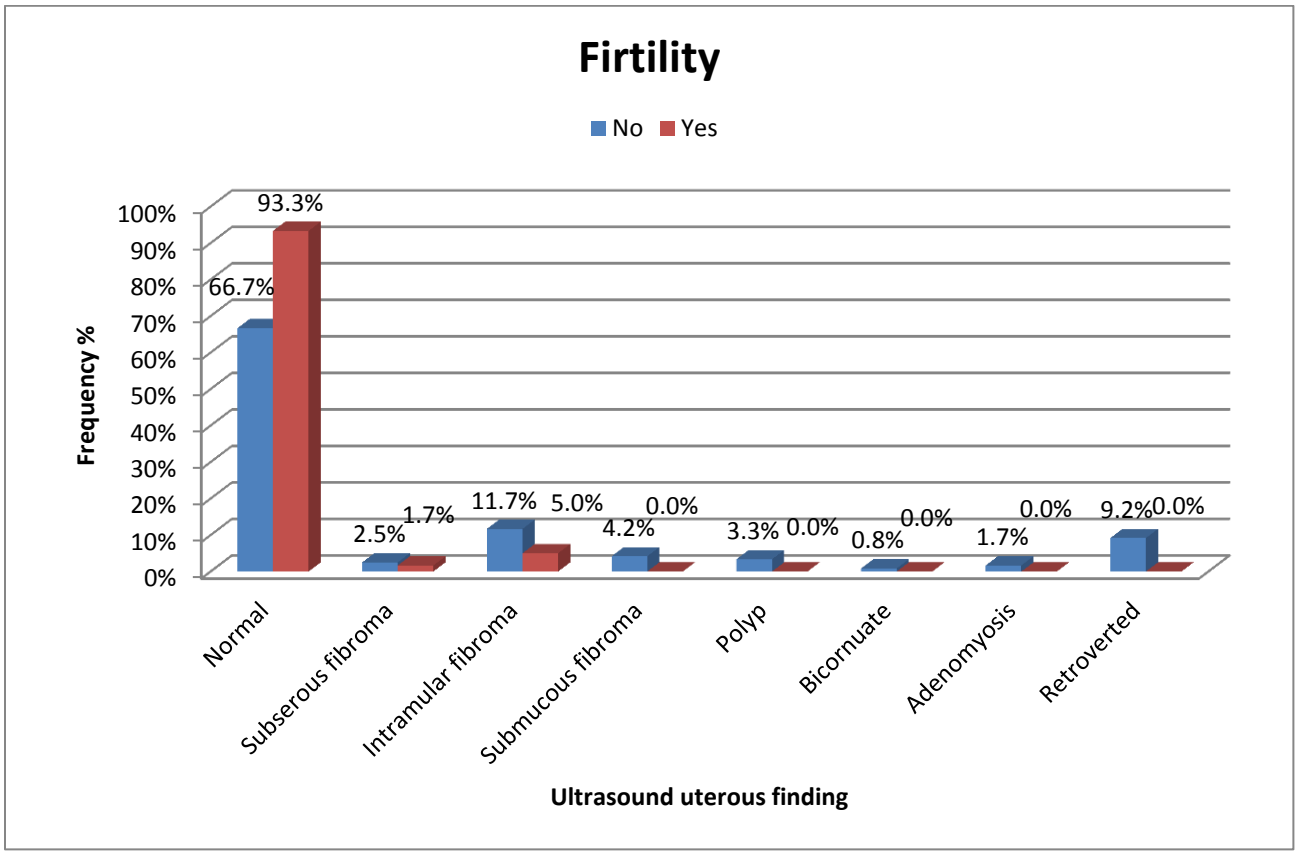


Figure 4-2 bar plot shows the percentage distribution of ultrasound uterus finding in respect to fertility status

Table 4-5 Summary of uterus and ovarian finding versus fertility status

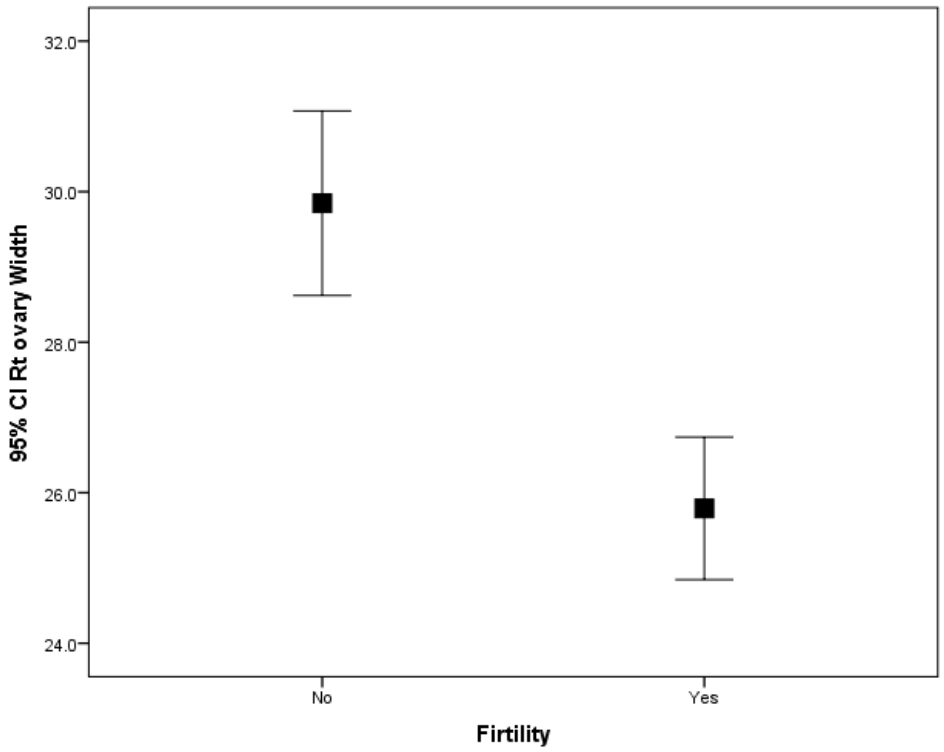
Uterus Findings * Ovaries Findings * Fertility Crosstabulation									
Fertility			Ovaries Findings						Total
			Normal	PCO	Simple cyst	Heamorrhagic cyst	Endometrioma	Dermoid cyst	
No	Uterus Findings	Normal	33	28	10	6	1	2	80
		Subserous fibroma	1	2	0	0	0	0	3
		Intramular fibroma	9	4	0	0	1	0	14
		Submucous fibroma	3	1	1	0	0	0	5
		Polyp	4	0	0	0	0	0	4
		Bicornuate	1	0	0	0	0	0	1
		Adenomyosis	2	0	0	0	0	0	2
		Retroverted	2	7	0	2	0	0	11
	Total		55	42	11	8	2	2	120
Yes	Uterus Findings	Normal	54		2				56
		Subserous fibroma	1		0				1
		Intramular fibroma	3		0				3
	Total		58		2				60
Total	Uterus Findings	Normal	87	28	12	6	1	2	136
		Subserous fibroma	2	2	0	0	0	0	4
		Intramular fibroma	12	4	0	0	1	0	17
		Submucous fibroma	3	1	1	0	0	0	5
		Polyp	4	0	0	0	0	0	4
		Bicornuate	1	0	0	0	0	0	1
		Adenomyosis	2	0	0	0	0	0	2
		Retroverted	2	7	0	2	0	0	11
	Total		113	42	13	8	2	2	180

Table 4-6 linear discriminant models using stepwise method for classification of women as fertile or infertile using two ultrasound parameters and two laboratory tests

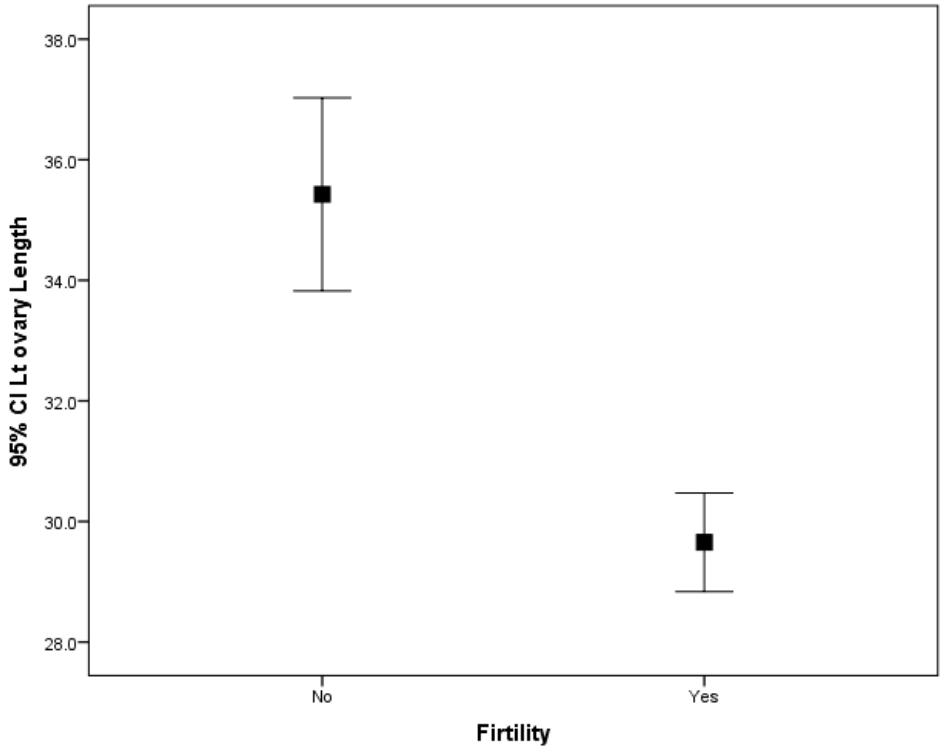
Variables	Fertility	
	Yes	No
FSH	0.190	.084
LH	-0.042	.040
Rt ovary width	0.597	.669
Lt ovary Length	0.378	.465
(Constant)	-15.072	-19.499
Fisher's linear discriminant functions		

Table 4-7 classification matrix show the sensitivity, specificity and accuracy of the model in classifying women as fertile and non-fertile using the variables in table 4-6

Fertility		Predicted Group Membership		Total
		No	Yes	
Original	No	**70.8%**	29.2%	100.0%
	Yes	5.0%	**95.0%**	100.0%
78.9% of original grouped cases correctly classified.				

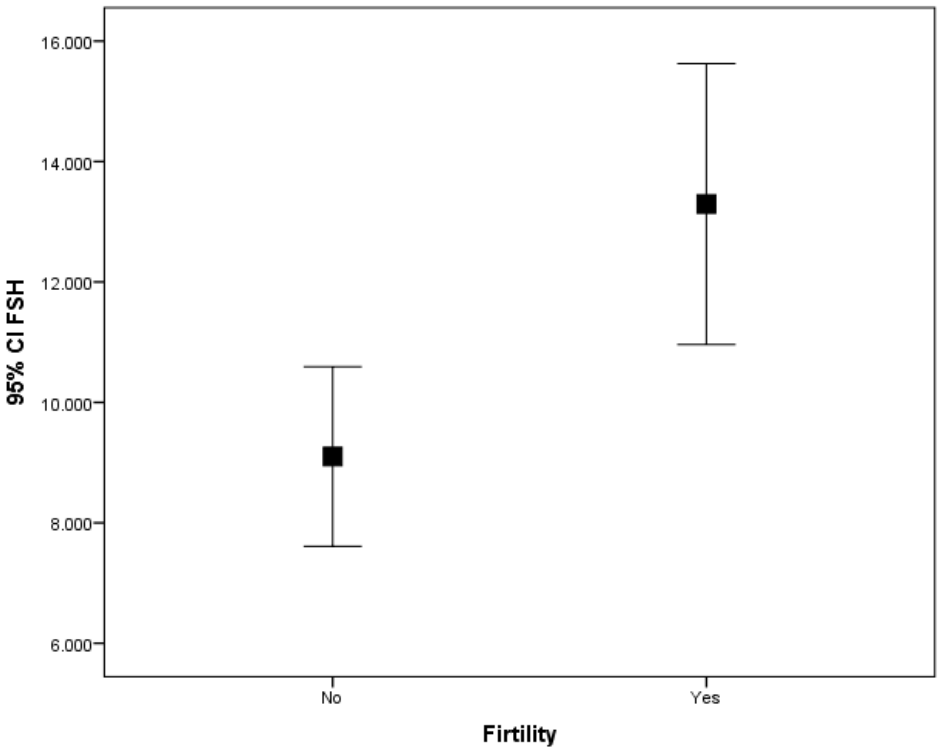


(A)

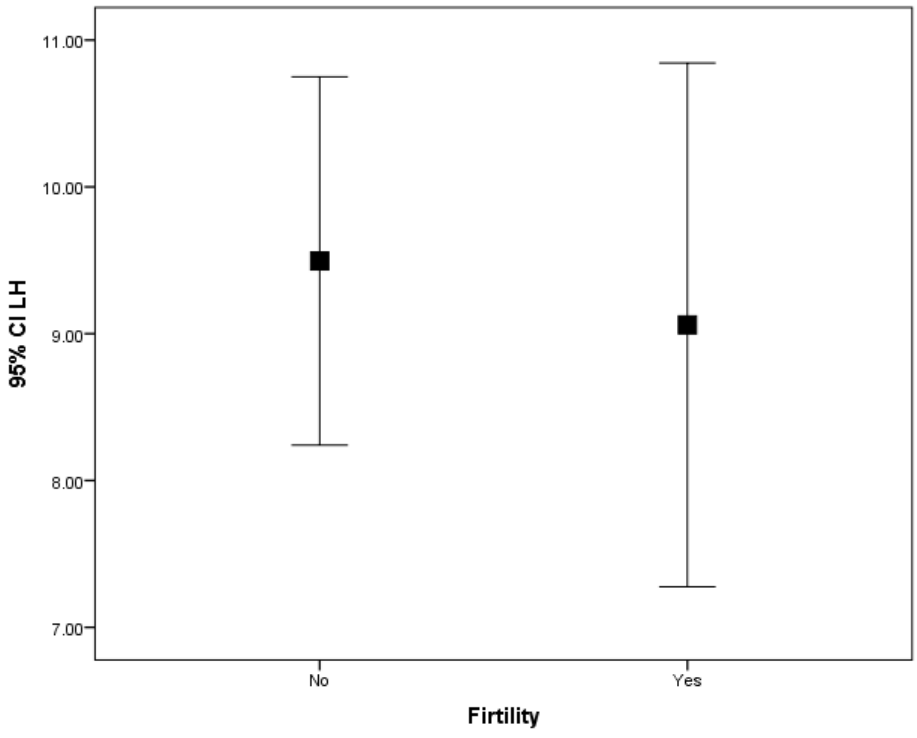


(B)

Figure 4-3 error bar blot show the discriminant power of (A) Rt ovary width and (B) Lt ovary length in discrimination between the fertile and non-fertile women using ultrasound caliber.



(A)



(B)

Figure 4-4 error bar blot show the discriminant power of (A) FSH and (B) LH discrimination between the fertile and non-fertile women using laboratory test in coordination with ultrasound caliber

Chapter five

Discussion, conclusion and Recommendation

5-1 Discussion

The main objective of this study was to characterize female infertility using vaginal ultrasonography in integration with laboratory test. The result of this study showed that there is a significance difference between the fertile and infertile; in respect to laboratory test two hormones (FSH and PRL) out of seven gives significance difference in means using independent *t*-test at $p = 0.05$; where t = 3.11 and 2.94 and $p < 0.001$. concerning ultrasonography measurement the uterus and ovary; uterus revealed inconclusive result while the length and width of the Rt and Lt ovary all of them gives significance difference using independence t-test with p for all was < 0.001 and above 4 (Table 4-1 and 4-2). This result dictates that; ultrasonography usually can highlight the status of fertility if the result integrated with the laboratory test and both formulated in linear model.

As mentioned earlier concerning ultrasound result; ovary plays an important role in discriminating the fertility status. The result for ovarian finding for 180 female showed that 113 female have normal ovary where 55 (48.7%) of them were infertile. Most commonly the infertile female were affected by PCO 42 females (35%) less frequently Endometrioma and Dermoid cyst (1.7%), while simple cyst can be found in both fertile and infertile but mostly affected infertile female (Table 4-3 and Figure 4-1).

Although uterus findings does not reveals significance differences concerning fertility status where 66.7% of infertile female showed normal result versus 93.3% of the fertile one. But the result showed that the most common finding was Intramural fibroma, where it found in both status but mostly in infertile female 11.7% as well as Retroverted uterus 9.2% (Table 4-4 and Figure 4-2).

To classify the female as fertile and infertile using linear discriminant analysis stepwise method, the programme chose four variable as the most discriminant one they include FSH, LH, Rt ovary width and Lt ovary length (Table 4-5). The overall classification accuracy was 78.9%, for infertile was 70.8% and 95.0% for the fertile one. The Rt ovary width value separate the fertile from the infertile significantly in average; where the width for the infertile were bigger than the fertile one (Figure 4-3 A), as well as the Lt ovary length, which show that the length of the infertile female were bigger than that of the fertile one (Figure 4-3 B). in case of hormones, FSH also discriminate between the fertile and infertile; where the values of this hormones were lower in infertile female in respect to fertile one (Figure 4-4 A), while LH showed wide variability for the fertile one as well as low value in average than the infertile one, but in coordination with the other variable it helps in the discrimination between the two status.

In summary differentiation between fertile and infertile female still an issue but in this study make it possible to classify them quantitatively by integrating the ultrasound results with laboratory one.

5-2 Conclusion

The main objective of this study was to characterize infertility in female using vaginal ultrasonography in order to make possible for classification. This study consisted of 180 female 120 infertile and 60 fertile carried out in Mohammed bin Naif Medical center in Saudi Arabia in the period from December 2017 to December 2018.

The result of this study showed that it is possible to classify female as fertile and infertile using ultrasound findings; mainly ovaries caliber (Rt ovary width and Lt ovary length) integrated with laboratory test (FSH, LH).

This study concluded that to identify that the women were fertile or not with 79% (although the main cause is unknown) you can use the following model:

Fertile = (0.19×FSH) + (-0.042 × LH) + (0.597 ×Rt ovary width) + (0.378 × Lt ovary length) -15.072

Infertile = (0.084×FSH) + (-0.04 × LH) + (0.669 × Rt ovary width) + (0.465 × Lt ovary length) -19.499

Where the vote will be to the higher values; i.e. the four values substituted in the two equations simultaneously and the bigger output define the fertility for the despondence.

5-3 Recommendations

- Infertility can be identified quantitatively by using ultrasound finding correlated with laboratory findings.
- In infertility cases more emphases should be attributed to ovaries ultrasound scanning.
- Further study could be used by including secondary infertility with the primary one with large control group.
- The obtained equation should be tested on a blind group in another thesis.

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Role of Ultrasound in the Assessment of Female Infertility

Appendix A

Data sheet

Age	Height	Weight	FSH	T3	T4	LH	PRL	TEST	TSH	Uterus Length	Uterus Width	Rt ovary Length	Rt ovary Width	Lt ovary Length	Lt ovary Width	Uterus US finding	Ovaries US finding
40	160	100	12.2	3.89	12.99	12.77	44.25	0.306	3.65	46	40.5	38.6	35.6	40	36.5	1	2
39	164	80	14.16	5.05	14.5	5.01	21.51	0.363	4.72	50.1	38	45.5	40.3	35.1	33.6	1	2
41	170	81	5.63	4.12	16.1	12.38	17.49	0.21	1.51	41.5	38.2	30.2	29.3	45.5	36.5	1	3
25	173	81	40.2	3.62	13.07	22.62	24.81	0.154	6.73	49.1	44.2	35.5	35	36.5	35.1	1	2
33	164	73	4.79	5.24	14.3	12.19	17.58	0.159	4.41	55	47.4	22.4	31.7	44	27.1	1	6
.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
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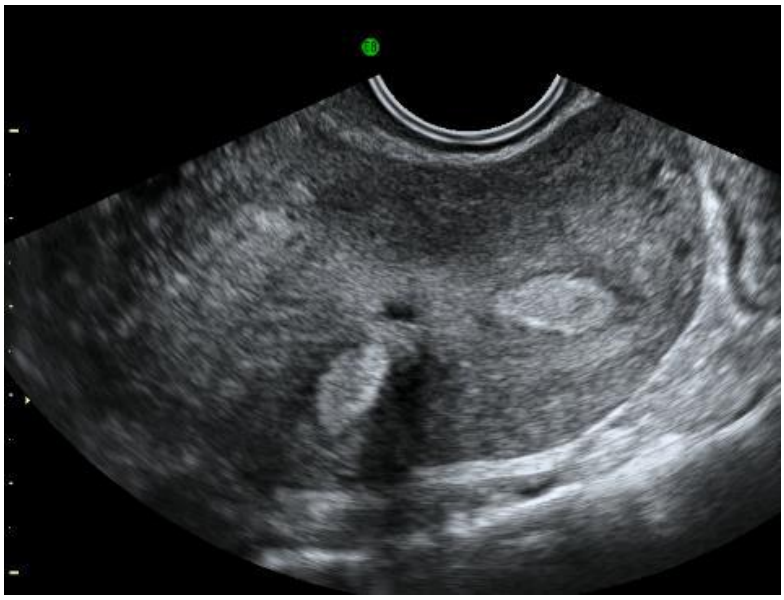
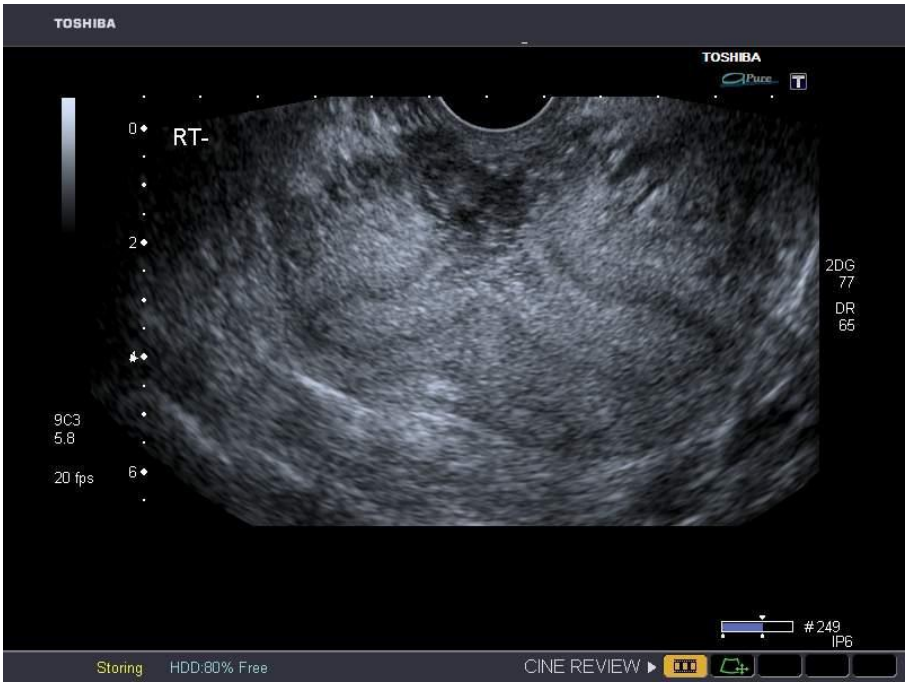
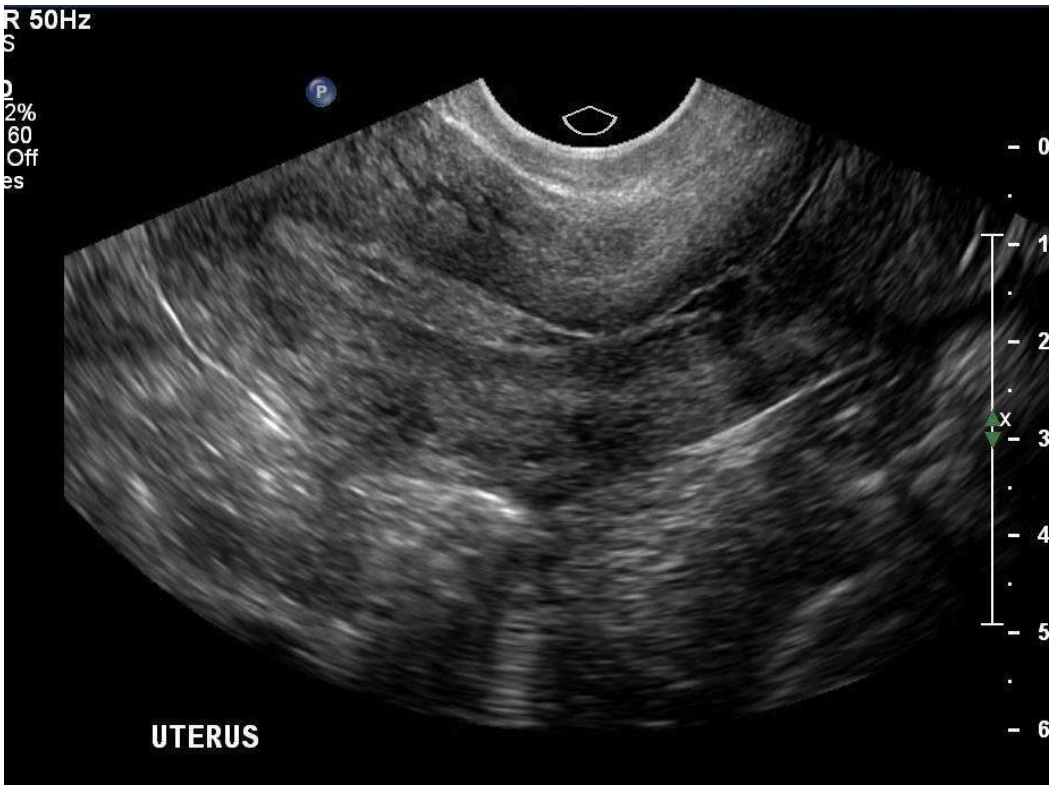
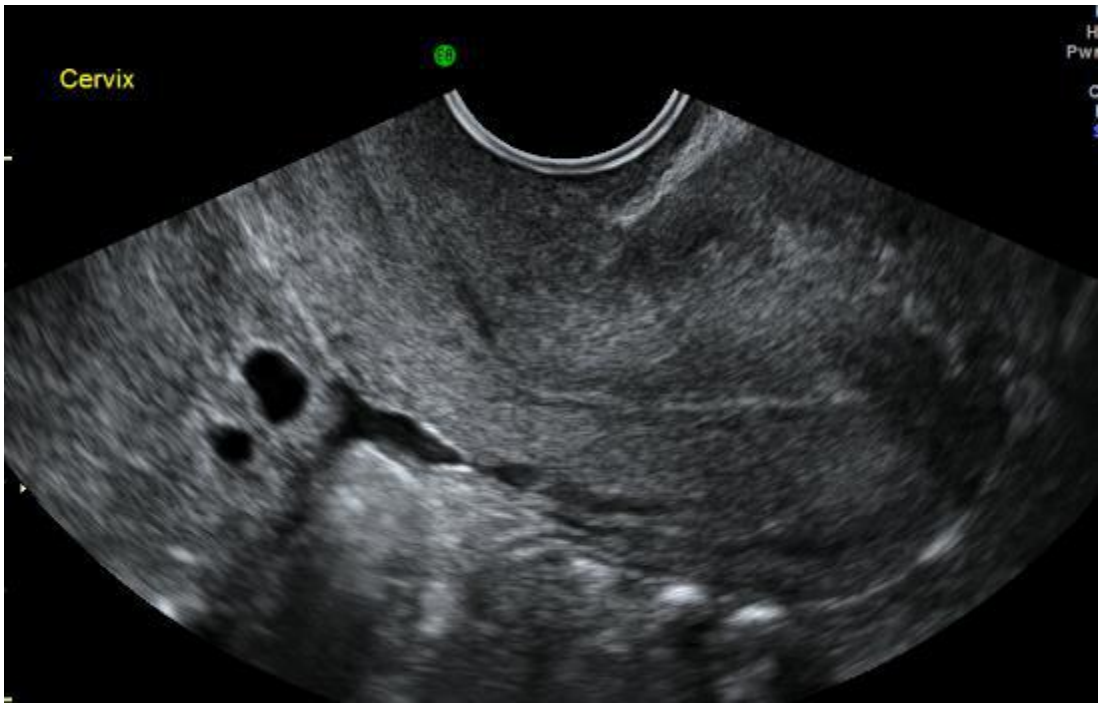
Appendix B
Ultrasound Images



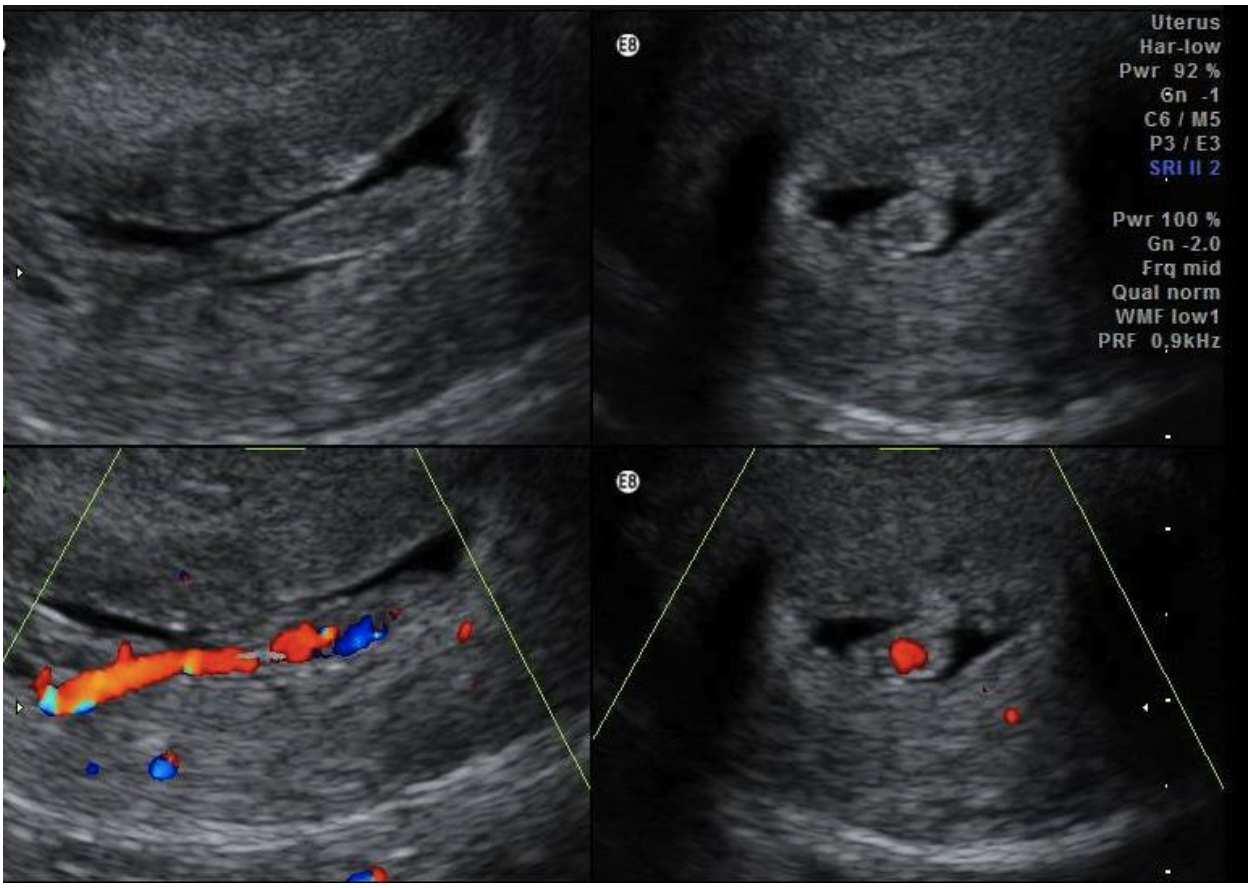




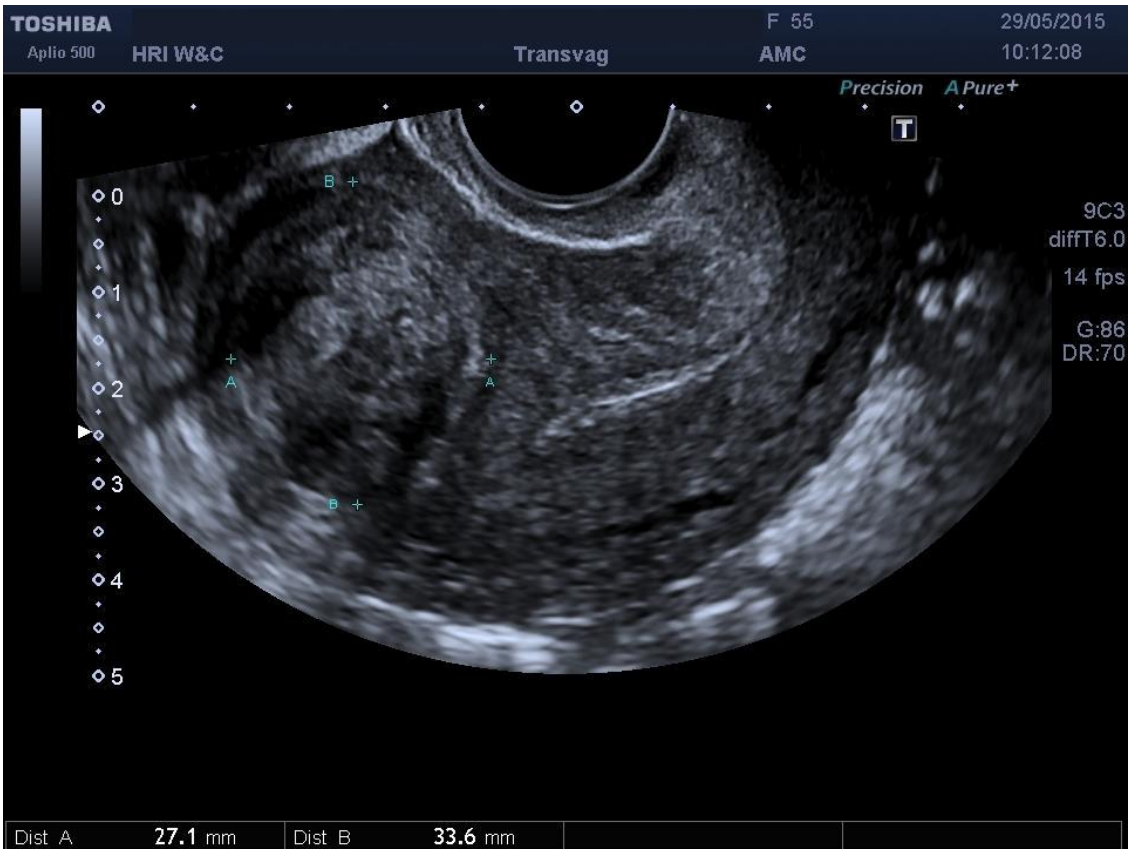
antiflexed



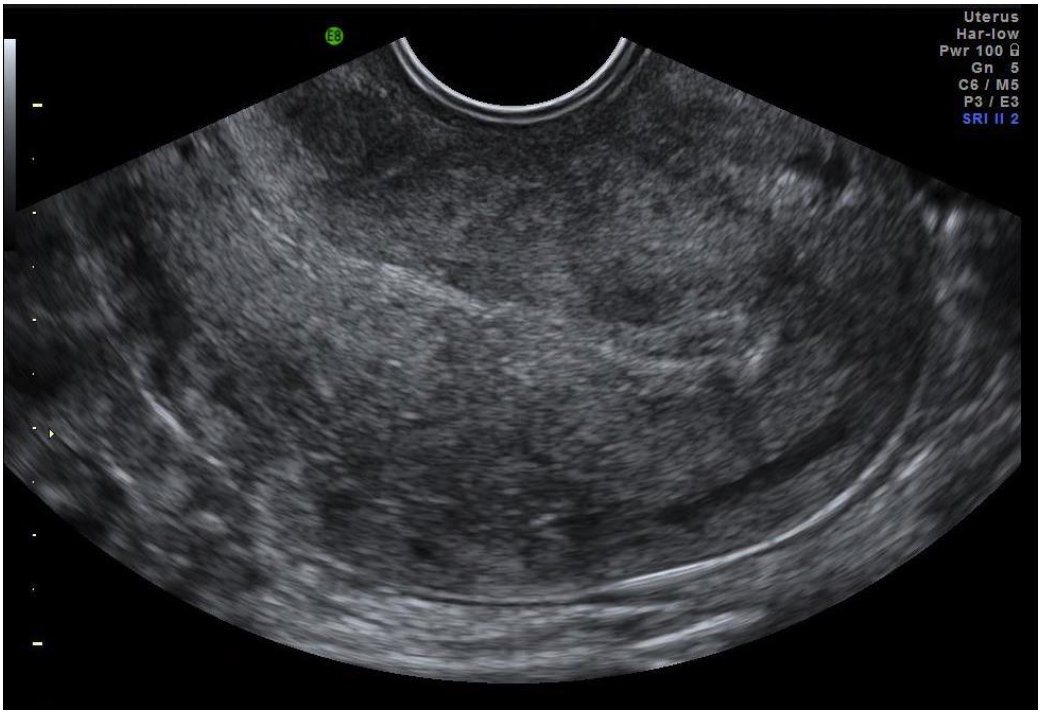
Retroflexed



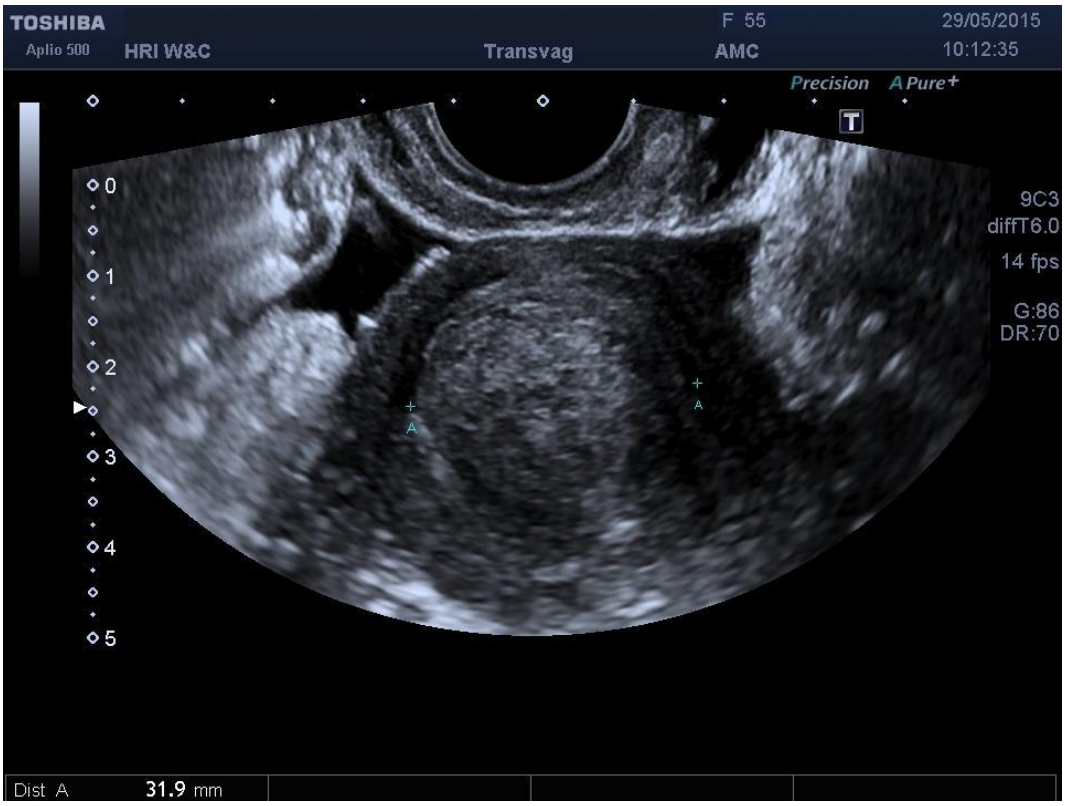
Cervical polyp



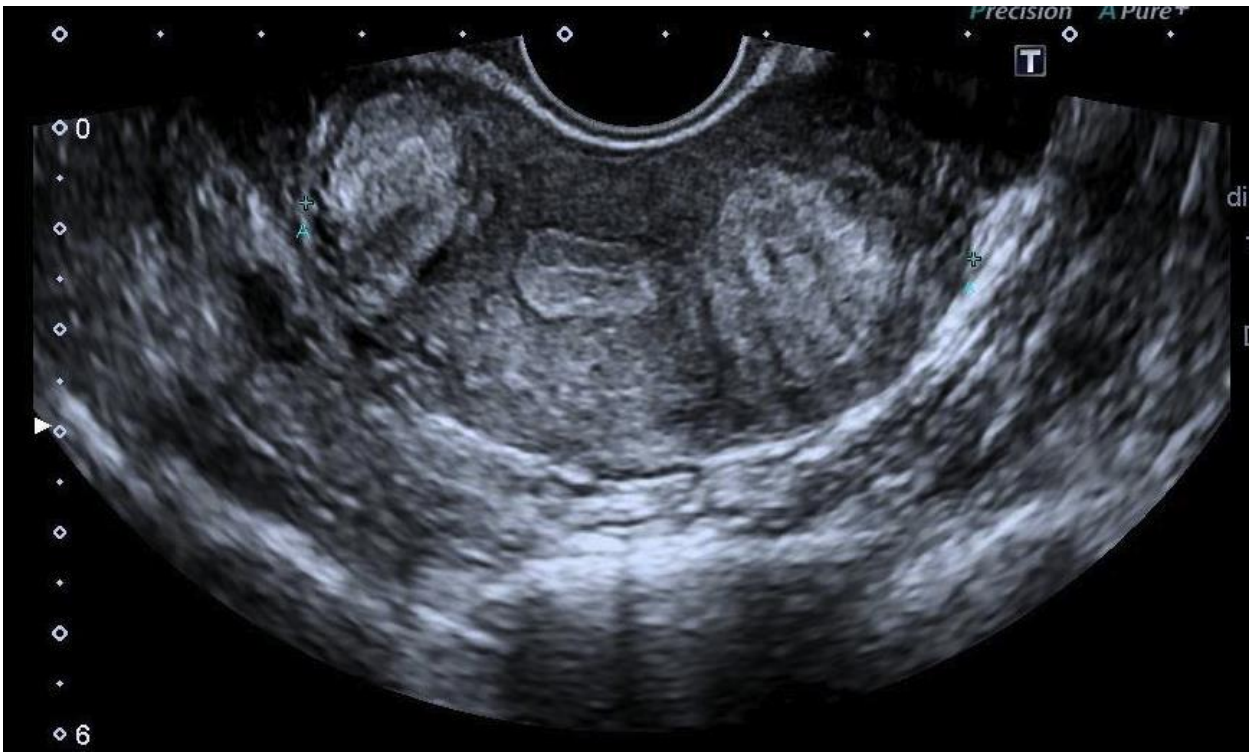
Fibroid



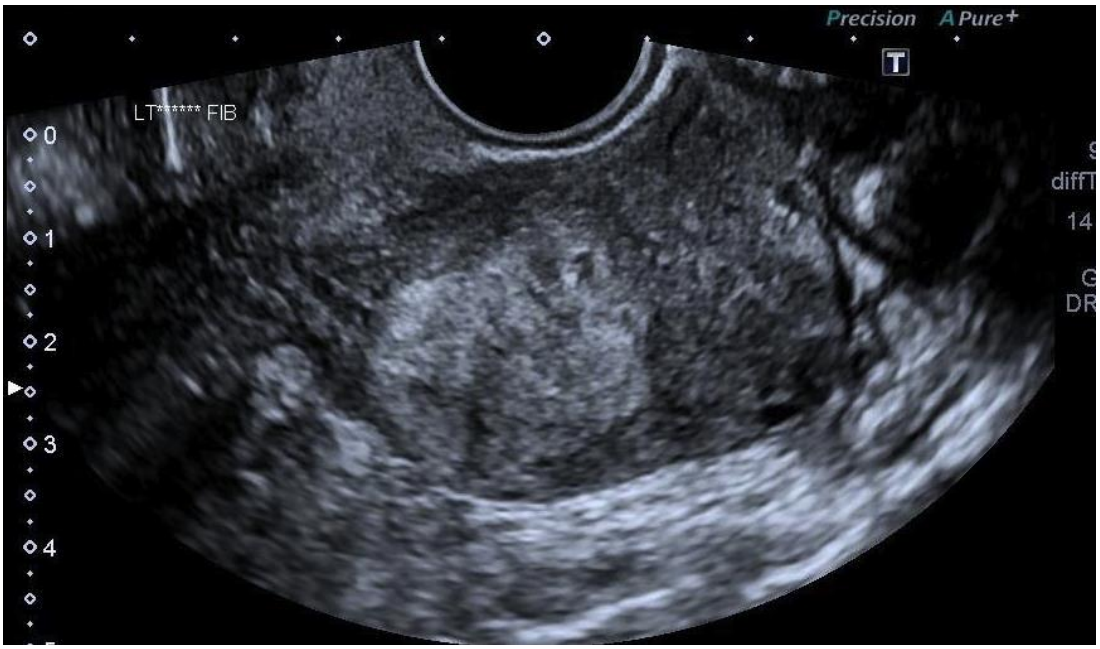
Enlarged uterus



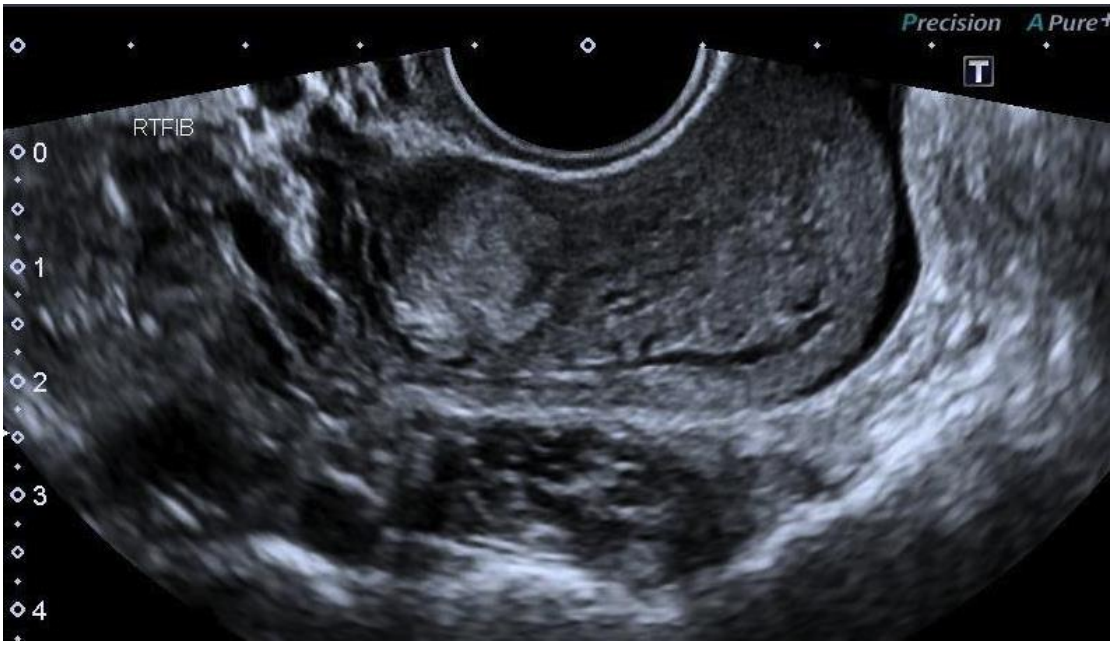
Fibroid



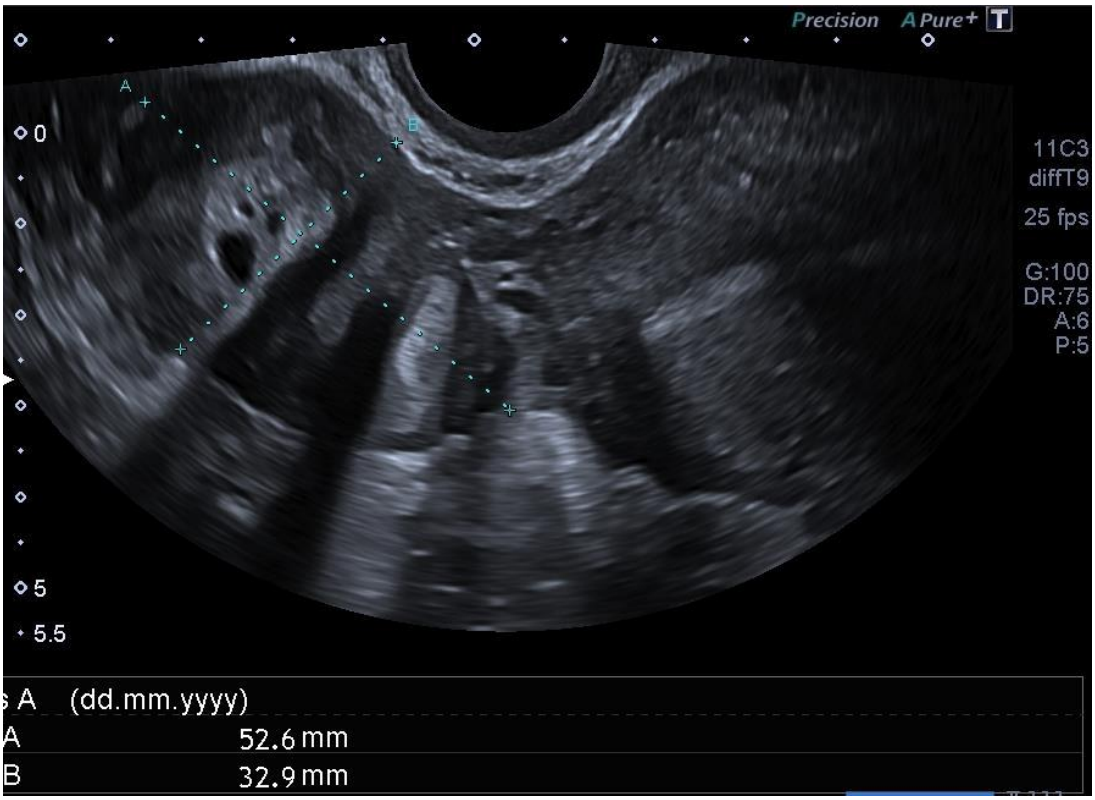
Intramural



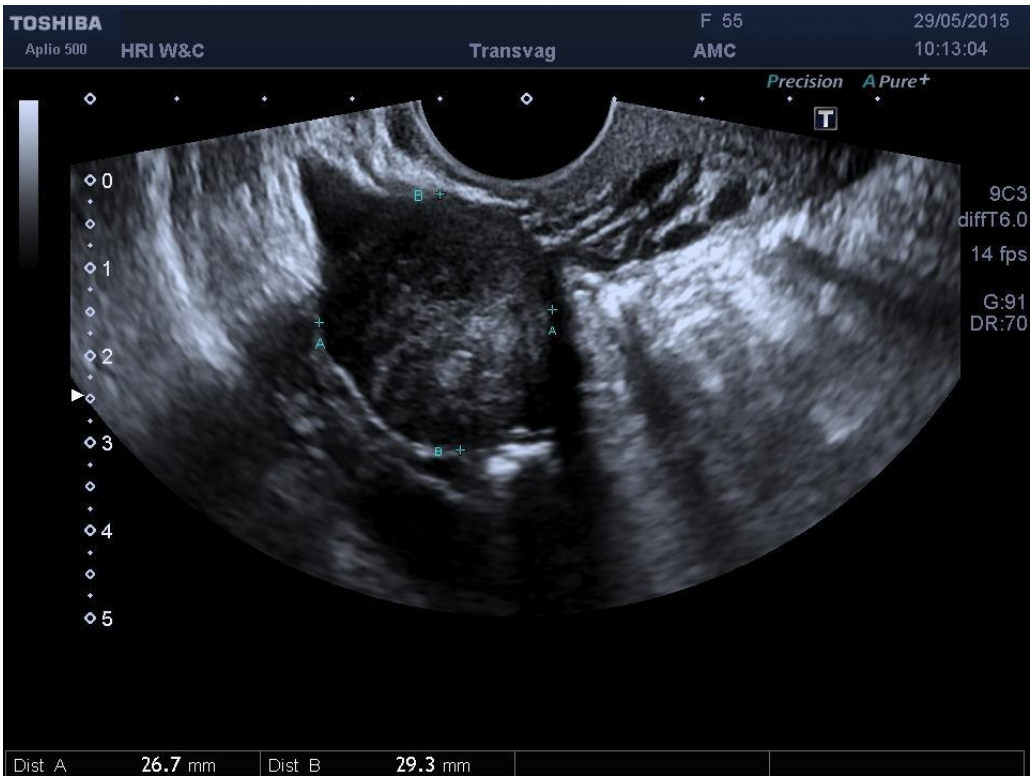
Intramural



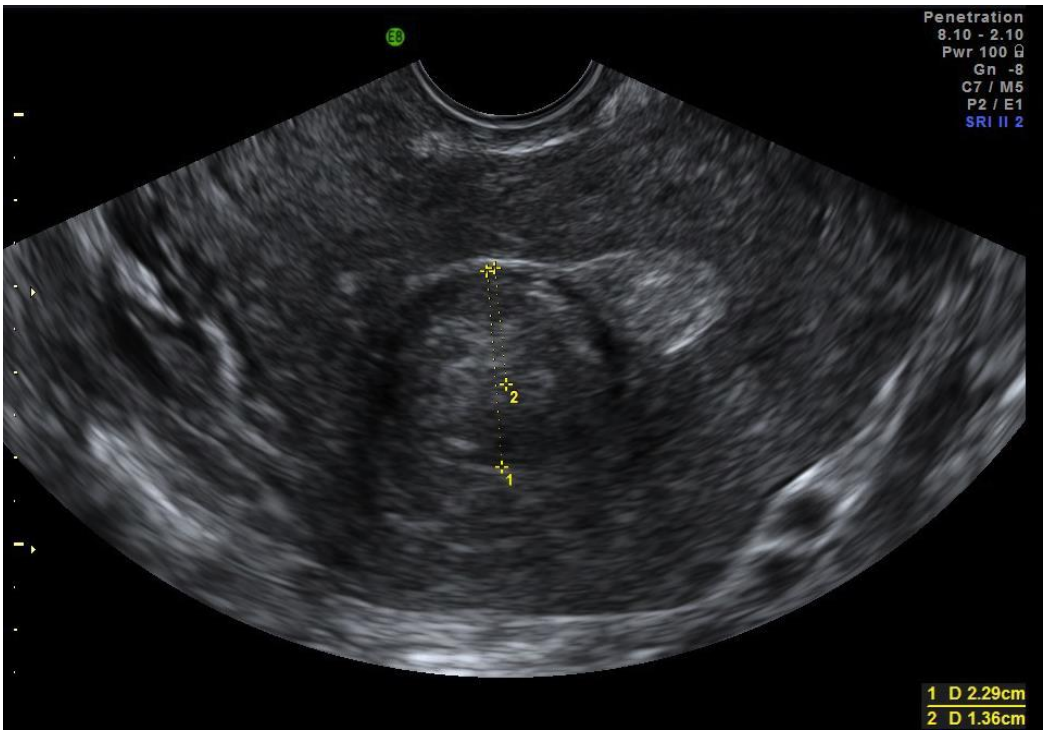
Subserosal



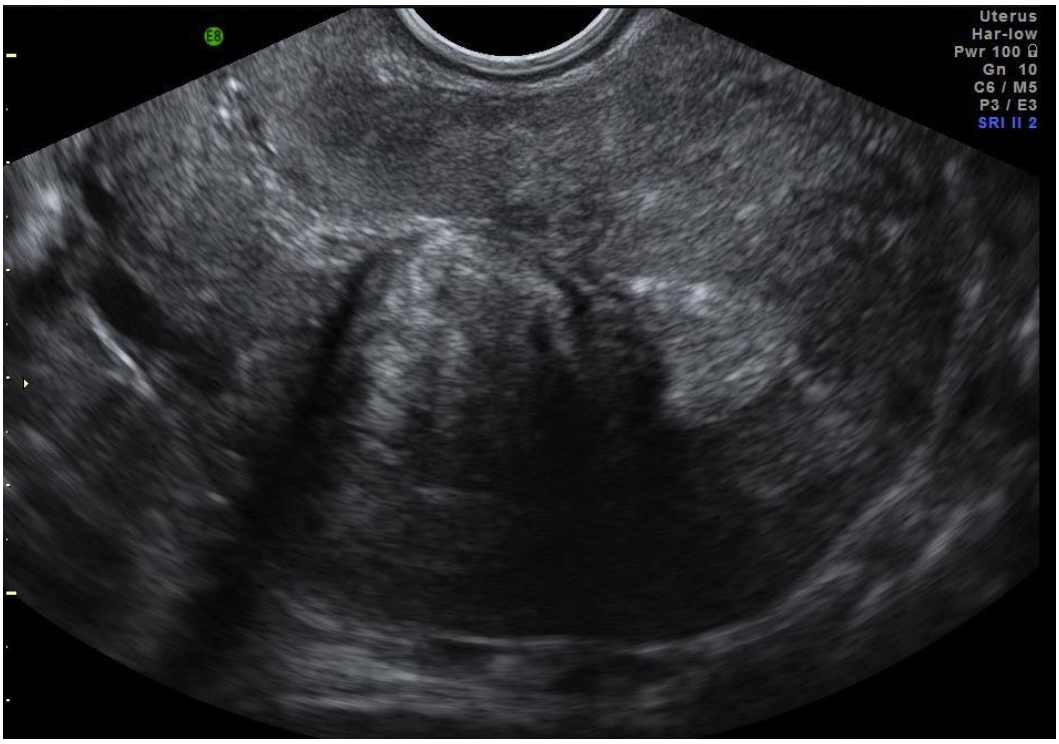
Pedunculated



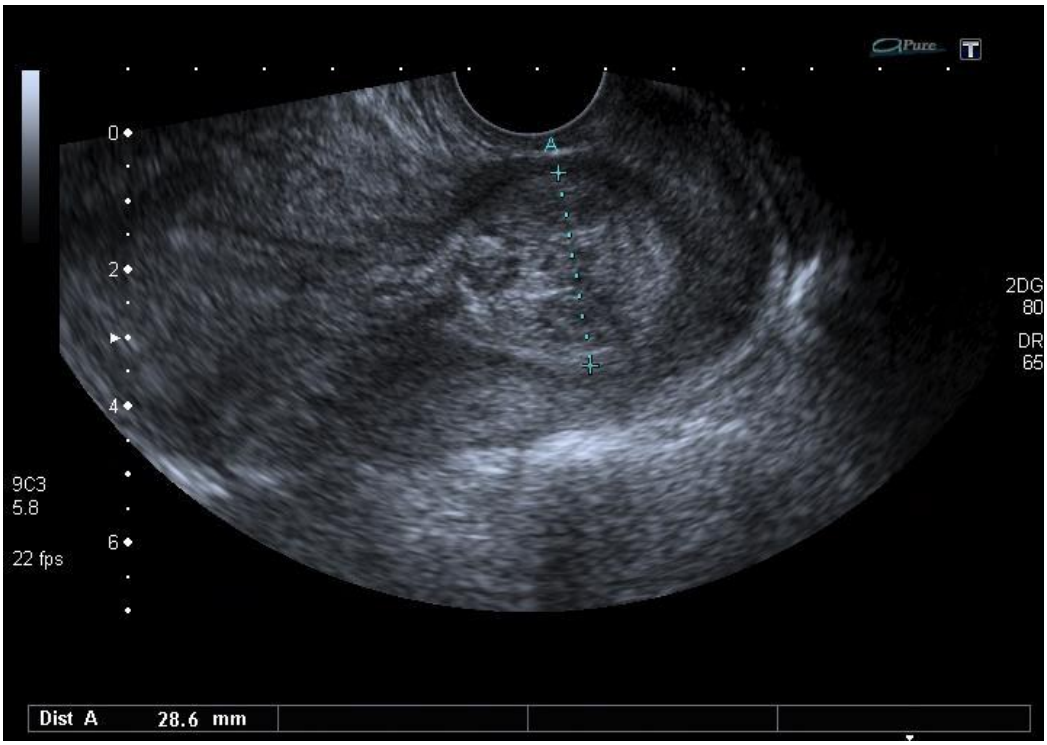
Fibroid



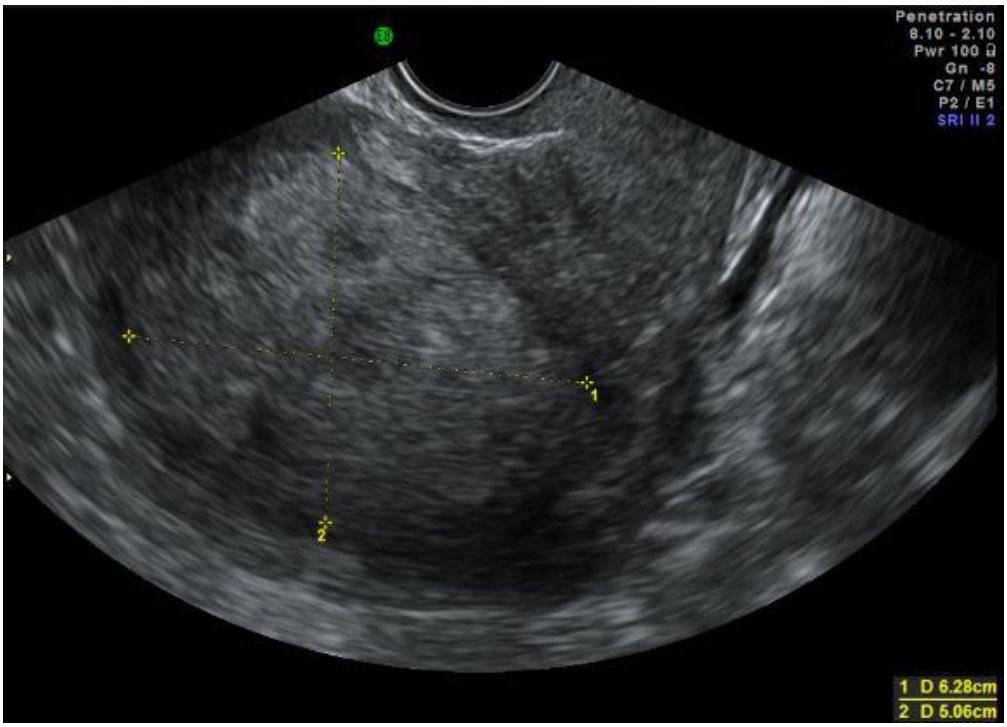
Submucosal



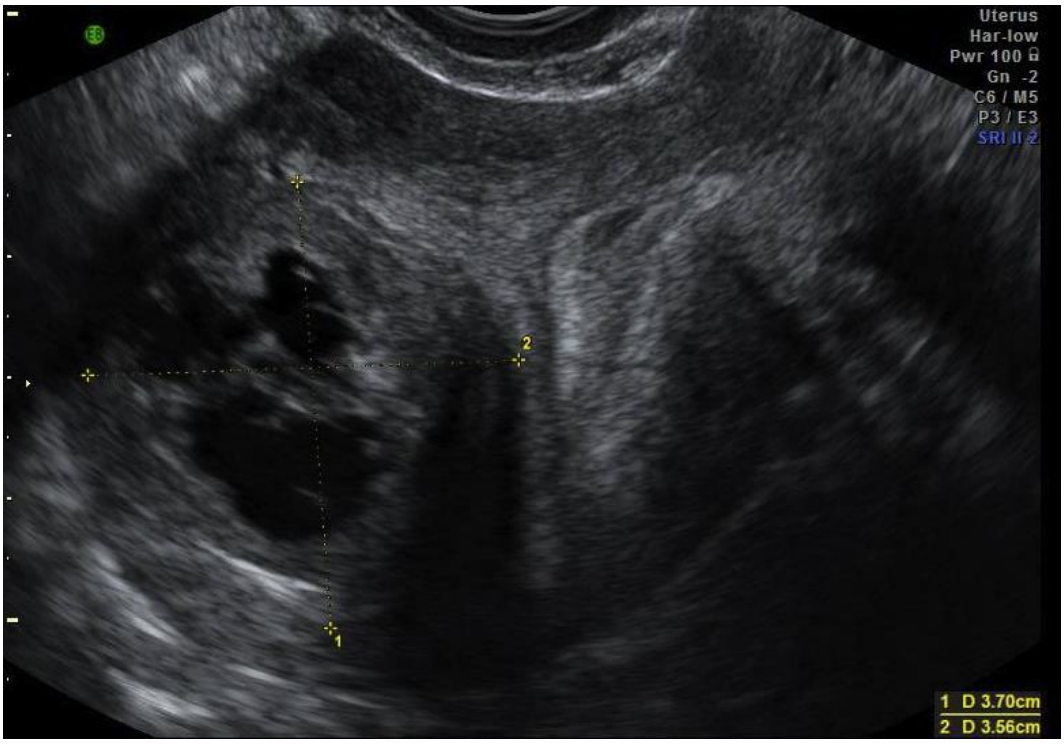
Submucosal



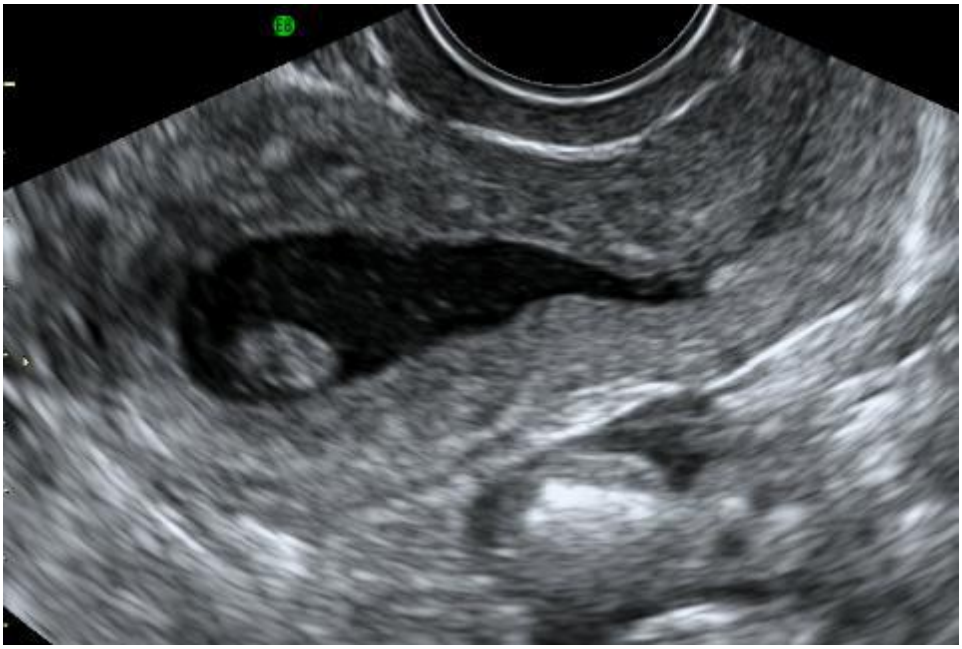
Intracavitary: the leiomyoma is within the endometrial cavity and it is attached to the myometrium by a pedicle

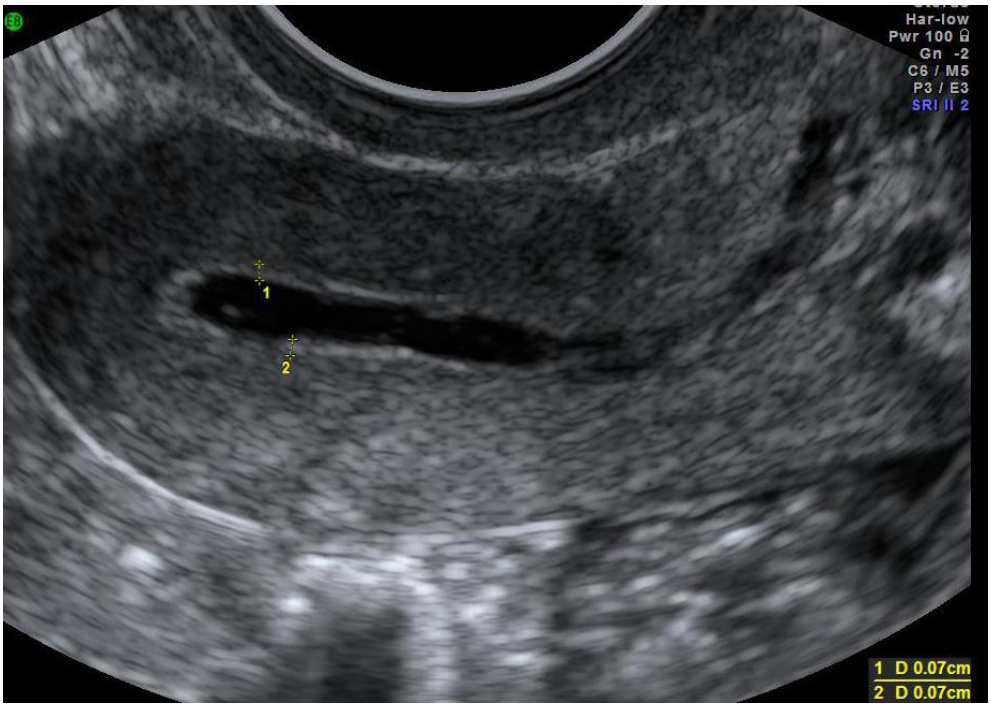


Fibroid

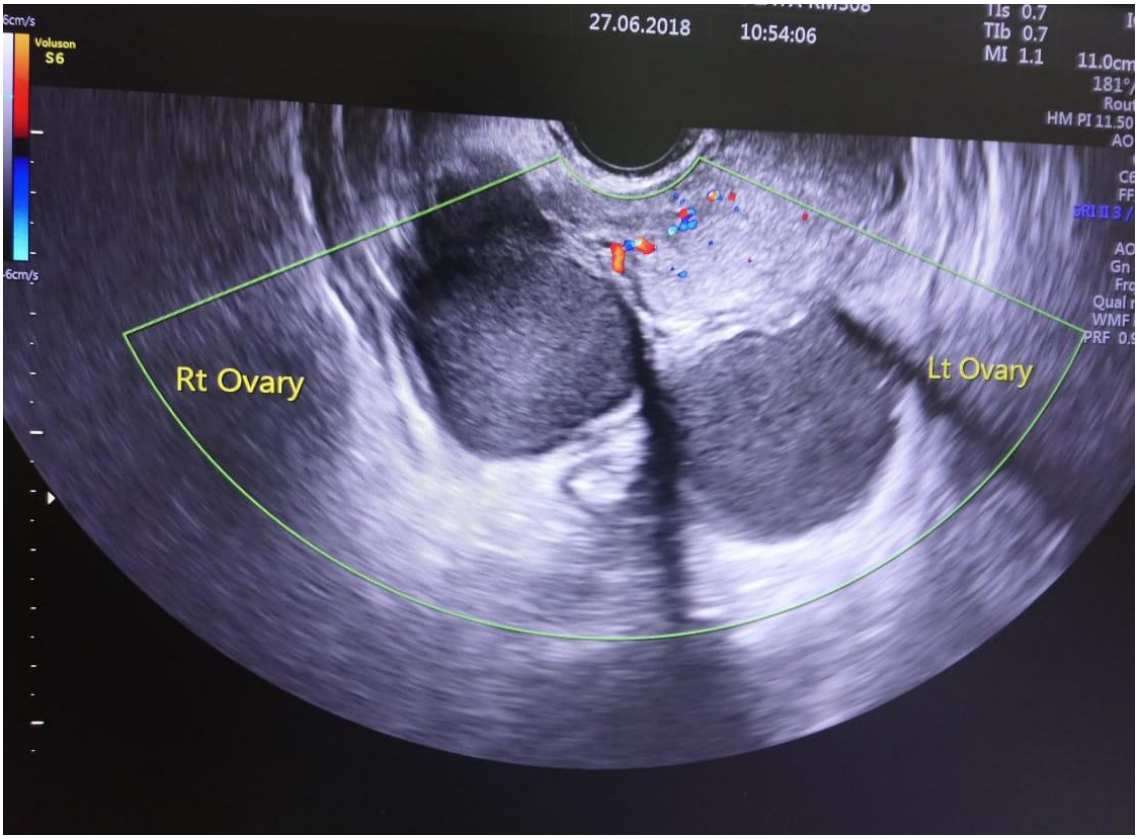


Fibroid with cystic changes


Endometrial polyp



Endometrial cavity fluid



Bilateral endometriosis