

Dedication

*This research is dedicated to
My beloved Parents for their patience and sacrifices.*

Acknowledgement

First of all my thanks and praise to Almighty Allah, beneficent, the merciful, for giving me health and strength to accomplish this work. I am and will remain very grateful to my supervisor Dr. Ahmed Mostafa who supported me with valuable help and encouragement throughout the period of this study my deepest gratitude to Dr. Khalid Hussein Bakheit Ahmed , Associate professor of biochemistry and consultant Obstetrician University of Khartoum, Faculty of Medicine his valuable help and encouragement .

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Abstract

A leiomyoma is a benign smooth muscle neoplasm that is not premalignant. Uterine myomas co-existing with pregnancy could cause obstetric complications.

The aim of this study was to define a diagnostic value of ultrasound examinations for uterine myomas assessment during pregnancy. 68 pregnant women were enrolled in the study, The entire abdomino-pelvic area was scanned in both longitudinal and transverse planes using transducer manipulations to assess fetal viability, presentation, gestational age (GA), and presence, location and size of co-existing myoma.

The result of the study revealed that Myoma coexisting with pregnancy was commoner in the older women. Uterine fibroids affect the population of study in the first ten year of marriage duration and it decrease with increased marriage duration. The most dominant anatomical locations of uterine fibroids are intramural (55.8%) ,followed by subserosal (22.6%). Furthermore, Obesity is known to increase the risk of uterine fibroid. Regarding the size of uterine fibroid, there was significant correlation established between the myoma size and GA.

Ultrasound scanning plays a central role in diagnosing and monitoring fibroids during pregnancy and in determining the relative position of the fibroids to the placenta. It is equally useful for detecting heterogeneous echo patterns associated with the appearance of pain in pregnancy.

الملخص

الورم الليفي للرحم من أورام العضلات الملساء وهي أورام حميدة لا تتطور الي سرطان . وجود هذه الاورام مع الحمل يمكن أن يسبب مضاعفات الولادة. وكان الهدف من هذه الدراسة هو تحديد القيمة التشخيصية لفحوصات الموجات فوق الصوتية لتقييم ورم الرحم أثناء الحمل. تم تسجيل 68 امرأة حامل في الدراسة، حيث تم فحص المنطقة البطنية-الحوضية بالكامل طوليا وعرضيا باستخدام مسبار الموجات فوق الصوتية لتقييم الجنين، عمر الحمل (GA)، وجود وموقع وحجم الورم الليفي.

كشفت نتائج الدراسة أن الورم مع الحمل كان عامة في النساء الأكبر سنا. الأورام الليفية في الرحم تؤثر على أول عشر سنوات من مدة الزواج تنخفض مع زيادة مدة الزواج. أكثر المواقع التشريحية التي توجد فيها الأورام الليفية الرحمية هي جدار الرحم (55.8٪)، تليها الطبقة تحت المضلية بنسبة (22.6)٪. علاوة على ذلك، ومن المعروف أن البدانة تزيد من خطر الورم الليفي في الرحم. وفيما يتعلق بحجم الورم الليفي في الرحم، كان هناك ارتباط كبير بين حجم الورم وعمر الجنين.

المسح بالموجات فوق الصوتية يلعب دورا محوريا في تشخيص ومتابعة الأورام الليفية أثناء الحمل وفي تحديد الوضع المشيمي للأورام. ومفيد أيضا للكشف عن أنماط صدى غير متجانسة مرتبطة مع ظهور آلام أثناء الحمل.

Chapter one

Introduction

1.1 Introduction

Benign diseases of the uterus are an important problem for many women and their gynecologists. The commonest condition in this category is fibroids but adenomyosis and uterine polyps are also of importance. Both fibroids and endometrial polyps are very common and although asymptomatic they can cause considerable morbidity for women's (Aboyaji and Ijaiya, 2002).

Leiomyoma (also known as fibroids or myomas) affect the reproductive health and well-being of approximately 25% of premenopausal women. A leiomyoma is a benign smooth muscle neoplasm that is not premalignant. Uterine leiomyoma originate from the myometrium and are classified according to their locations. They are monoclonal tumours derived from a single myometrial cell (Aboyaji and Ijaiya, 2002).

In symptomatic cases of uterine fibroids they can lead to multiple gynecologic problems, such as pelvic pain, infertility, menstrual abnormalities, and spontaneous abortion, significantly affecting the quality of life among women (Renée et.al, 200).

The most common clinical symptoms are associated with menstruation and include prolonged and/or heavy menstrual bleeding, which may lead to iron-deficiency anemia, and painful menstruation (Hirst et.al, 2008).

Uterine fibroids grow under the influence of the hormone estrogen and are most often seen after the menarche, and tend to shrink after the menopause. Typically the patient is nulliparous or of low parity and they are more commonly seen in women of African ancestry (Gross et al., 1983).

The postmenopausal incidence of leiomyomas was no lower than the premenopausal incidence, although postmenopausal leiomyomas were smaller and fewer.

According to the National Institute of Environmental Health Sciences (NIEHS), uterine fibroid study estimated that more than 80% of African-American women and about 70% of Caucasian women develop uterine fibroids by age 50 (Nakamura et al., 1991).

The incidence and natural history of uterine fibroids remain not fully understood. The prevalence varies with age, being increased in the late reproductive period and with ethnic origin. The reported frequency of the disease varies widely due to differences in study design (Nakamura et al., 1991)

Ultrasonography is the imaging modality of choice for the initial diagnosis and imaging workup of uterine leiomyoma and is also extremely helpful in determining the etiology of a broad range of pelvic symptoms in the female patient. Although the classic sonographic appearance of uterine leiomyomas is well established and easily recognizable, other pelvic masses may occasionally be confused with uterine leiomyomas, and the ability to distinguish between these entities is crucial in optimizing appropriate patient care (Early et al., 2016).

Ultrasound scanning plays a central role in diagnosing and monitoring fibroids during pregnancy and in determining the relative position of the fibroids to the placenta. It is equally useful for detecting heterogeneous echo patterns associated with the appearance of pain in pregnancy.

The aim of this study was to define a diagnostic value of ultrasound examinations for uterine myomas assessment during pregnancy.

1.2 Problem of the study:

Uterine fibroids have implications in pregnant and non-pregnant women of reproductive age. Based on risk factors for myoma development which include diet, race, geographical and socio-economic differences, our locality has a greater susceptibility of rapid myoma growth. Therefore, it is being advocated that routine ultrasound investigation should be encouraged in all pregnancies in order to detect myomas or any other lesions early enough for better obstetric management.

1.3 Objectives of the study

1.3.1 General objective:

The general objective of this study was to evaluate the uterine fibroid during pregnancy using ultrasonography.

1.3.2 Specific objectives:

- To measure the size of uterine fibroid
- To identify the anatomical location of uterine fibroid
- To correlate the size of uterine fibroid to anatomical location
- To correlate the size of uterine fibroid to gestational age.

Chapter 2

2. Literature Review and theoretical background

2.1 Anatomy of the uterus:

The female reproductive system consists of two ovaries, two oviducts (uterine tubes), the uterus, the vagina, and the external genitalia. Its functions are to produce female gametes (oocytes) and to hold a fertilized oocyte. During its complete development through embryonic and fetal stages until birth. The system also produces sexual hormones that control organs of the reproductive system and influence other organs of the body. The reproductive system undergoes cyclic changes in structure and functional activity at menarche, when the first menses occurs. These modifications are controlled by neurohumoral mechanisms. Menopause is a variable period during which the cyclic changes become irregular and eventually disappear. In the postmenopausal period there is a slow involution of the reproductive system (Renner-Martin et al., 2009).

The uterus (womb) is a thick-walled, pear-shaped, hollow muscular organ. The embryo and fetus develop in the uterus, its muscular walls adapting to the growth of the fetus and then providing the power for its expulsion during childbirth. The non-gravid (non-pregnant) uterus usually lies in the lesser pelvis, with its body lying on the urinary bladder and its cervix between the urinary bladder and the rectum. The adult uterus is usually anteverted (tipped anterosuperiorly relative to the axis of the vagina) and anteflexed (flexed or bent anteriorly relative to the cervix) so that its mass lies over the bladder. The position of the uterus changes with the degree of fullness of the bladder and rectum. Although its size varies considerably, the uterus is approximately 7.5 cm long, 5 cm wide and 2 cm thick and weighs approximately 90 g. The uterus is divisible into two main parts the body and cervix (Renner-Martin et al., 2009).

The body of the uterus, forming the superior two thirds of the organ, includes the funds of the uterus, the rounded part that lies superior to the orifices of the uterine tubes. The body lies between the layers of the broad ligament and is freely movable. It has two surfaces: vesical (related to the bladder) and intestinal. The body is demarcated from the cervix by the isthmus of the uterus, a relatively constricted segment, approximately 1cm long.

The cervix of the uterus is the cylindrical, relatively narrow inferior third of the uterus, approximately 2.5 cm long in an adult non-pregnant woman. Described into two parts : a supravaginal part between the isthmus and the vagina, and a vaginal part, which protrudes into the vagina. The rounded vaginal part surrounds the external os of the uterus and is surrounded in turn by a narrow space, the vaginal fornix. The supra-vaginal part is separated from the bladder anteriorly by loose connective tissue and from the rectum posteriorly by the rectouterine pouch. The uterine horns (L. cornua) are the superolateral regions of the uterine cavity, where the uterine tubes enter (Perez et al., 2013).

The uterine cavity continues inferiorly as the fusiform cervical canal. The canal extends from the anatomical internal os, through the supravaginal and vaginal parts of the cervix, communicating with the lumen of the vagina through the external os .The uterine cavity (in particular, the cervical canal) and the lumen of the vagina together constitutes the birth canal through which the fetus passes at the end of gestation.

2.2 Ligaments of the Uterus

Externally, the ligament of the ovary attaches to the uterus posteroinferior to the uterotubal junction. The round ligament of the uterus attaches anteroinferiorly to this junction. These two ligaments are vestiges of the ovarian gubernaculum, related to the descent of the gonad from its developmental position on the posterior abdominal wall.

The broad ligament of the uterus is a double layer of peritoneum (mesentery) that extends from the sides of the uterus to the lateral walls and floor of the pelvis. This ligament assists in keeping the uterus in position. The two layers of the broad ligament are continuous with each other at a free edge that surrounds the uterine tube. Laterally, the peritoneum of the broad ligament is prolonged superiorly over the vessels as the suspensory ligament of the ovary. Between the layers of the broad ligament on each side of the uterus, the ligament of the ovary lies posterosuperiorly and the round ligament of the uterus lies anteroinferiorly. The uterine tube lies in the anterosuperior free border of the broad ligament, within a small mesentery called the mesosalpinx. Similarly, the ovary lies within a small mesentery called the mesovarium on the posterior aspect of the broad ligament. The principal supports of the uterus holding it in this position are both passive and active or dynamic (Perez et al., 2013).

Passive support of the uterus is provided by its position, the way in which the normally anteverted and anteflexed uterus rests on top of the bladder. When intra-abdominal pressure is increased, the uterus is pressed against the urinary bladder. The cervix is the least mobile part of the uterus because of the passive support provided by attached condensations of endopelvic fascia (ligaments), which may also contain smooth muscle.

Transverse cervical (cardinal) ligaments extend from the cervix and lateral parts of the fornix of the vagina to the lateral walls of the pelvis. Uterosacral ligaments pass superiorly and slightly posteriorly from the sides of the cervix to the middle of the sacrum; they are palpable during a rectal examination.

2.3 Relations of the Uterus

Anteriorly (anteroinferiorly in its normal anteverted position): the vesicouterine pouch and superior surface of the urinary bladder; the supravaginal part of the cervix is related to the bladder and is separated from it by only fibrous connective tissue.

Posteriorly; the rectouterine pouch containing loops of small intestine and the anterior surface of rectum; only the visceral pelvic fascia uniting the rectum and uterus here resists increased intra-abdominal pressure.

Laterally; the peritoneal broad ligament flanking the uterine body and the facial transverse cervical ligaments on each side of the cervix and vagina; in the transition between the two ligaments, the ureters run anteriorly slightly superior to the lateral part of the vaginal fornix and inferior to the uterine arteries, usually approximately 2 cm lateral to the supravaginal part of the cervix (Cicinelli et al., 2004).

2.4 Arterial Supply of the Uterus

The blood supply of the uterus derives mainly from the uterine arteries, with potential collateral supply from the ovarian arteries. Venous drainage of the Uterus; The uterine veins enter the broad ligaments with the arteries and form a uterine venous plexus on each side of the cervix. Veins from the uterine plexus drain into the internal iliac veins.

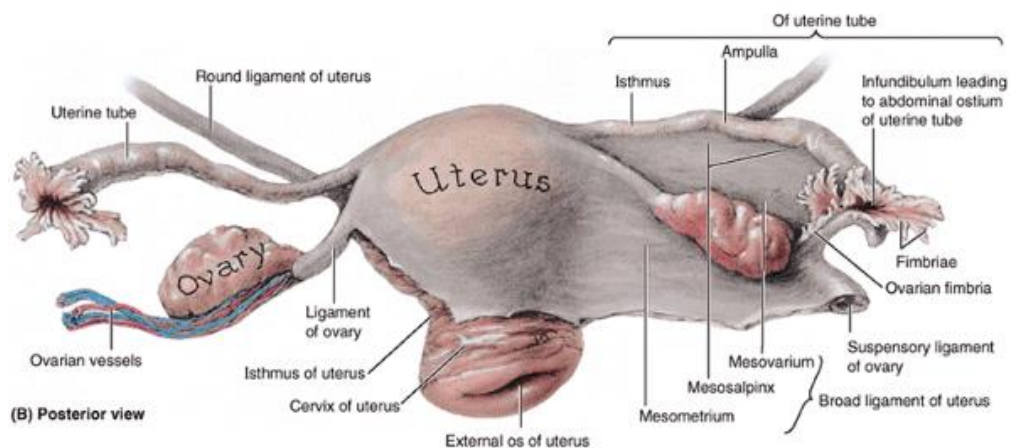
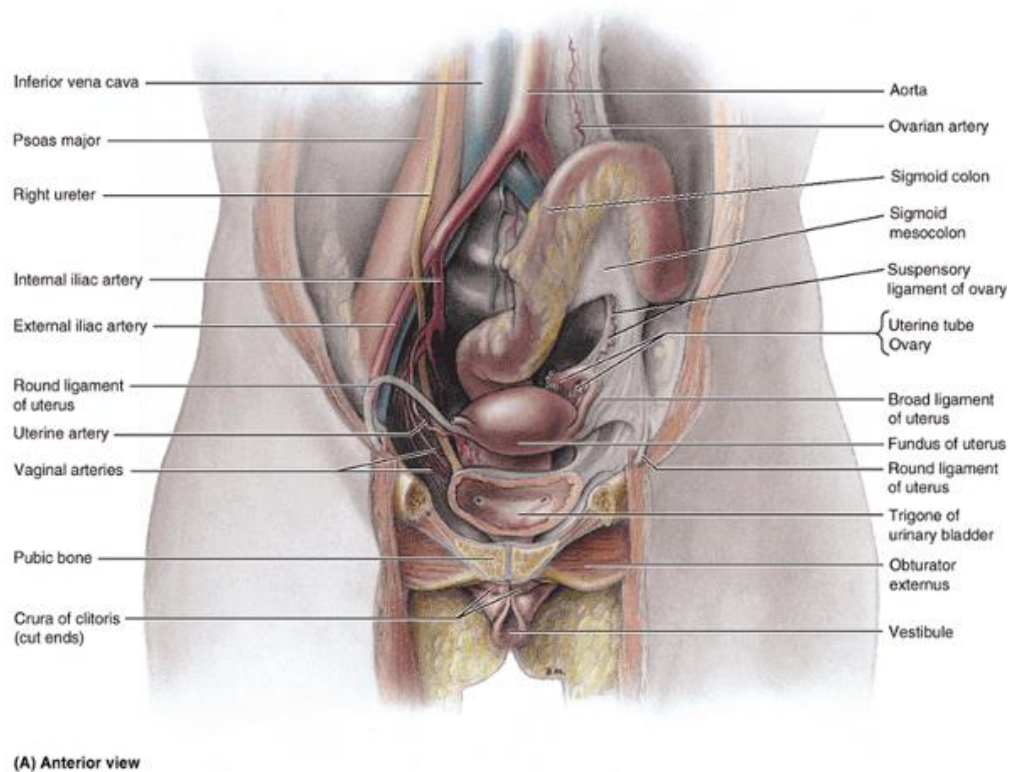


Figure: Shows the Female pelvic viscera. A. In this dissection of the female genital organs, the bladder and adjacent anterior pelvis (superior ramus and bodies of pubic bones) have been coronally sectioned and the anterior segment has been removed. On the right side, the uterine tube, ovary, broad ligament, and peritoneum covering the lateral wall of the pelvis have been removed to display the ureter and branches of the internal iliac artery. B. This dissection reveals the uterus, ovaries, uterine tubes, and related structures. The broad ligament is removed on the right side.

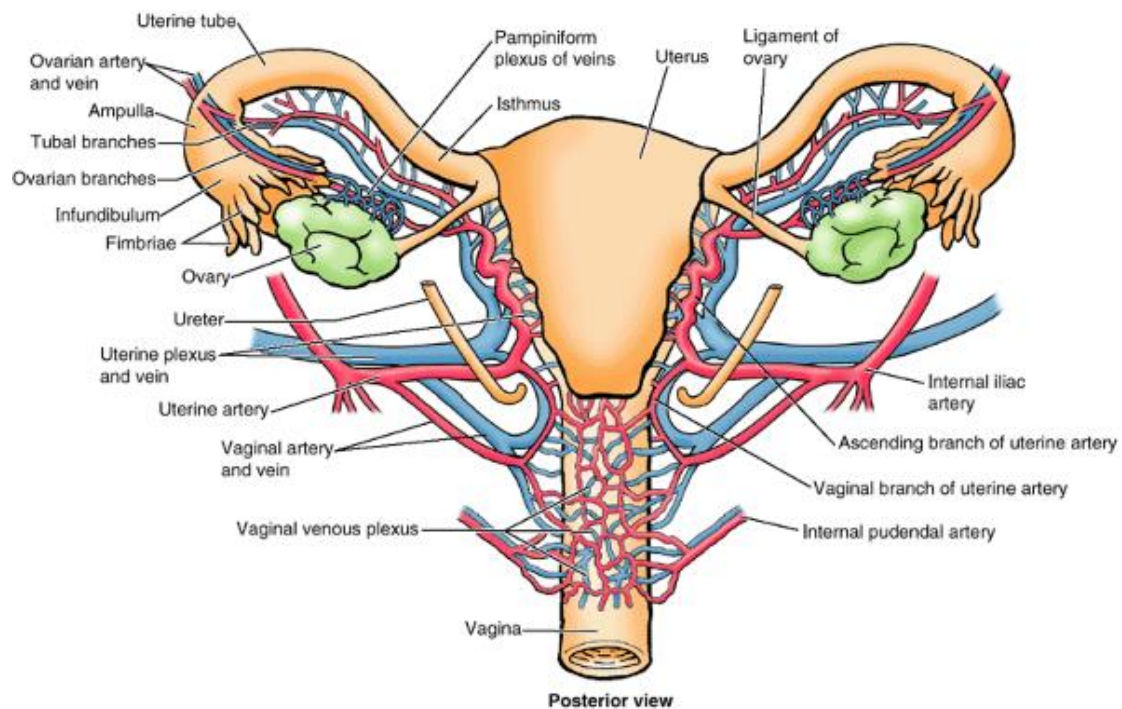


Figure: Show Blood supply and venous drainage of uterus, vagina, and ovaries.

The broad ligament of the uterus is removed to show the anastomosing branches of the ovarian artery from the aorta and the uterine artery from the internal iliac artery supplying the ovary, uterine tube, and uterus. The veins follow a similar pattern, flowing retrograde to the arteries, but are more plexiform, including a pampiniform plexus related to the ovary and continuous uterine and vaginal plexuses (collectively, the uterovaginal plexus) (Cicinelli et al., 2004).

2.5 Lymphatic drainage of the uterus:

Lymphatic vessels from the uterus drain in many directions, coursing along the blood vessels that supply it as well as the ligaments attached to it. Most lymphatic vessels from the fundus and superior uterine body pass along the ovarian vessels to the lumbar lymph nodes; but some vessels from the fundus, particularly those near the entrance of the uterine tubes

and attachments of the round ligaments, run along the round ligament of the uterus to the superficial inguinal lymph nodes.

Vessels from most of the uterine body and some from the cervix pass within the broad ligament to the external iliac lymph nodes.

Vessels from the uterine cervix also pass along the uterine vessels, within the transverse cervical ligaments, to the internal iliac lymph nodes, and along uterosacral (sacrogenital) ligaments to the sacral lymph nodes (Cicinelli et al., 2004).

2.6 Innervation of the Uterus

Afferent nerves supplying uterus are T11 and T12. Sympathetic supply is from hypogastric plexus and ovarian plexus. Parasympathetic supply is from second, third and fourth sacral nerves.

2.7 Uterine Tubes

The uterine tubes (oviducts; formerly called fallopian tubes) conduct the oocyte (ovum), discharged monthly from an ovary during child-bearing years, from the periovarian peritoneal cavity to the uterine cavity. They also provide the usual site of fertilization. They extend laterally from the uterine horns and open into the peritoneal cavity near the ovaries. The uterine tubes (approximately 10 cm long) lie in the mesosalpinx in the free edges of the broad ligaments. the tubes extend symmetrically posterolaterally to the lateral pelvic walls, where they arch anterior and superior to the ovaries in the horizontally disposed broad ligament.

The uterine tubes are divisible into four parts, from lateral to medial
Infundibulum: the funnel-shaped distal end of the tube that opens into the peritoneal cavity through the abdominal ostium; the finger-like processes of the fimbriated end of the infundibulum (the fimbriae) spread over the medial surface of the ovary; one large ovarian fimbria is attached to the superior pole of the ovary.

Ampulla: the widest and longest part of the tube, which begins at the medial end of the infundibulum; fertilization of the oocyte usually occurs in the ampulla.

Isthmus: the thick-walled part of the tube, which enters the uterine horn (Cicinelli et al., 2004).

2.8 Myometrium

The myometrium (Gr. mys, muscle, + metra, uterus), the thickest tunic of the uterus, is composed of bundles of smooth muscle fibers separated by connective tissue. The bundles of smooth muscle form four poorly defined layers. The middle layers contain the larger blood vessels. During pregnancy, the myometrium goes through a period of great growth as a result of both hyperplasia (an increase in the number of smooth muscle cells) and hypertrophy (an increase in cell size).

2.9 Endometrium

The endometrium consists of epithelium and a lamina propria containing simple tubular glands that sometimes branch in their deeper portions (near the myometrium). Its covering epithelial cells are a mixture of ciliated and secretory simple columnar cells. The epithelium of the uterine glands is similar to the superficial epithelium, but ciliated cells are rare within the glands. The connective tissue of the lamina propria is rich in fibroblasts and contains abundant ground substance.

Connective tissue fibers are mostly made of collagen type III. The endometrial layer can be subdivided into two zones:

The basalis is the deepest one, adjacent to the myometrium; it contains lamina propria and the closed tips of the uterine glands. The functionalis contains the remainder of the lamina propria and the glands, as well as the surface epithelium. Whereas the functionalis undergoes profound changes during the menstrual cycles, the basalis remains mostly unchanged. The

blood vessels supplying the endometrium are of special significance in the periodic sloughing of most of this layer. Arcuate arteries are circumferentially oriented in the middle layers of the myometrium. From these vessels, two sets of arteries arise to supply blood to the endometrium: straight arteries, which supply the basalis, and spiral arteries, which bring blood to the functionalis (Cicinelli et al., 2004).

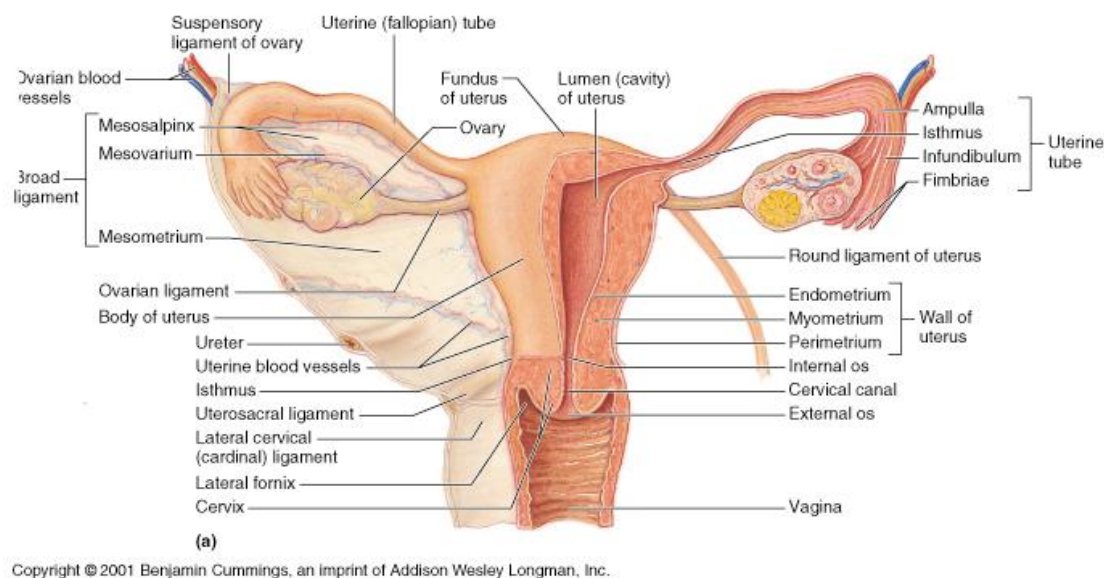


Figure 4 :Shows uterine wall layers & uterine tube

2.10 Uterine Cervix

The cervix is the lower, cylindrical part of the uterus (Figure 1), and it differs in histological structure from the rest of the uterus. The lining consists of a mucus-secreting simple columnar epithelium. The cervix has few smooth muscle fibers and consists mainly (85%) of dense connective tissue. The external aspect of the cervix that bulges into the lumen of the vagina is covered with stratified squamous epithelium. The mucosa of the cervix contains the mucous cervical glands, which are extensively branched. This mucosa does not undergo remarkable changes during the

menstrual cycle and does not desquamate during menstruation (Dall'Asta et al., 2014).

2.11 The Menstrual Cycle

The menstrual cycle includes the activity of the hormones of the ovaries and anterior pituitary gland and the resultant changes in the ovaries (ovarian cycle) and uterus (uterine cycle). There are four hormones involved, FSH and LH from the anterior pituitary gland, estrogen from the ovarian follicle, and progesterone from the corpus luteum . The fluctuations of these hormones are shown as they would occur in an average 28-day cycle. A cycle may be described in following three phases:

2.11. 1 Menstrual phase

The loss of the functional layer of the endometrium is called menstruation or the menses. Although this is actually the end of a menstrual cycle, the onset of menstruation is easily pinpointed and is, therefore, a useful starting point. Menstruation may last 2 to 8 days, with an average of 3 to 6 days. At this time, secretion of FSH is increasing, and several ovarian follicles begin to develop (Dall'Asta et al., 2014).

2.11.2 Follicular phase

Follicular stimulating hormone (FSH) stimulates growth of ovarian follicles and secretion of estrogen by the follicle cells. The secretion of Luteinizing hormone (LH) is also increasing, but more slowly. FSH and estrogen promote the growth and maturation of the ovum, and estrogen stimulates the growth of blood vessels in the endometrium to regenerate the functional layer. This phase ends with ovulation, when a sharp increase in LH causes rupture of a mature ovarian follicle.

2.11.3 Luteal phase

Under the influence of LH, the ruptured follicle becomes the corpus luteum and begins to secrete progesterone as well as estrogen. Progesterone stimulates further growth of blood vessels in the functional layer of the endometrium and promotes the storage of nutrients such as glycogen. As progesterone secretion increases, LH secretion

decreases, and if the ovum is not fertilized, the secretion of progesterone also begins to decrease. Without progesterone, the endometrium cannot be maintained and begins to slough off in menstruation. FSH secretion begins to increase (as estrogen and progesterone decrease), and the cycle begins again. The corpus luteum during the cycle secretes the hormones inhibin and relaxin. Inhibin inhibits the secretion of FSH, and perhaps LH as well, from the anterior pituitary gland. Relaxin is believed to inhibit contractions of the myometrium (as does progesterone), which would help make implantation of the early embryo successful. Women may have cycles of anywhere from 23 to 35 days, the normal range. Women who engage in strenuous exercise over prolonged periods of time may experience amenorrhea, that is, cessation of menses (Dall'Asta et al., 2014).

2.12 Infantile uterus

Some adults may have an infantile uterus, a condition in which the uterus is much smaller than normal and resembles that present before puberty. Amenorrhea is present, but the vagina and ovaries may be normal.

2.13 The Uterus in pregnancy

During the pregnancy, the uterus becomes greatly enlarged as a result of the increasing production of estrogens and progesterone, first by the corpus luteum of the ovary and later by the placenta. At first it remains as

a pelvic organ, but by the third month the fundus rises out of the pelvis, and by the ninth month it has reached the xiphoid process (Cicinelli et al., 2004).

2.14 Pathophysiology Of Uterine Fibroids:

National Institute of Child Health and human development (NICHD), part of the national institute of Health (NIH) within the US Department of health and Human service (DHHS), is trying to learn more about uterine fibroid, through research into their causes and treatments. NICHD scientists are exploring genetics, hormones, the immune system and environmental factors that may play a role in starting the growth of fibroids and or in continuing the growths, this information could lead to a cure for uterine as a consequence of interference with implantation, fibroids that does not involve taking out of uterus.

Family history is a key factor, since there is often a history of fibroid developing in women of the same family. Estrogen receptors on fibroid cause them to respond to estrogen stimulation during the reproductive years. During hypoestrogenic states such as after menopause, leiomyoma are expected to shrink. Leiomyoma are more common in overweight women because of increased estrogen from adipose aromatase activity.(Nivethithai P, Nikhat SR et al 2010)

Uterine leiomyomas are monoclonal tumors. However, the factors involved in their initiation and growth remain poorly understood. The neoplastic transformation of myometrium to leiomyoma likely involves somatic mutations of normal myometrium and the complex interactions of sex steroids and local growth factors. Traditionally, estrogen has been considered the major promoter of myoma growth. Biochemical studies suggest that progesterone, progestins, and the progesterone receptor modulate myoma mitotic activity (Rutgers, 2015)

2.15 Anatomical Locations Of Uterine Fibroids:

Fibroids are often multiple and are solitary in only 2% of cases. Based on their location within the uterus, fibroids are divided into three types: submucosal, intramural and subserosal. Submucosal fibroids are the least common (5%) and are commonly symptomatic, associated with dysmenorrhea, menorrhagia and infertility . Intramural fibroids are the most common and are mostly asymptomatic. Subserosal fibroids are also usually asymptomatic but large pedunculated fibroids may undergo torsion and cause abdominal pain. These can mimic ovarian or adnexal masses on imaging. 8% of fibroids occur in the cervix (Rutgers, 2015)

Leiomyomas are classified by their location in the uterus, so they mentioned as follows , subserosal leiomyomas are located just under the uterine serosa and may be pedunculated (attached to the corpus by a narrow stalk) or sessile (broad-based). Intramural leiomyomas are found predominantly within the thickness of myometrium but may distort the uterine cavity or cause an irregular external uterine contour. Submucousal leiomyomas are located just under the uterine mucosa (endometrium) and, like subserosal leiomyomas, may be either pedunculated or sessile. Tumors in sub-serosal and intramural locations comprise the majority (95%) of all leiomyomas; submucousleiomyomas make up the remaining 5% (Rutgers, 2015)

Uterine fibroids vary in size from grain sized to large uterine growth. They can be solitary or multiple, and they are clinically characterized as intra cavity, submucosal, intramural and subserosal, depending on their location within the uterus. The final diagnoses in the 44 patients were based on pathologic findings (35 cases), radiographic findings (four cases), and clinical and/or sonographic follow-up (five cases). The gross features of the tumours included pedunculated (17), pedunculated and

degenerate six), pedunculated and Calcified (two), degenerated or without hemorrhage (six),)intrauterine with,solid intrauterine calcified (seven), and solid intrauterine noncalcified fibroids (six).

Uterine leiomyoma constituted 117 of the 1094 gynecological admissions during this study period (10.7%, 117/1094). The mean age of presentation was 35.7 (6.1) years. Most of the patients were nulliparous (76.7%, 79/103) and 51.5% (53/103) were married. The commonest mode of presentation was lower abdominal mass (66.9%, 67/103) and the least was recurrent abortion (1%, 1/103). Surgery was employed in all cases, with myomectomy being the commonest modality used in 90.3% (93/103) of cases. The common postoperative complications were prolonged pain (49.5%, 51/103) and postoperative pyrexia (34.9%, 36/103) (Rollestad et al.).

The size, number and location of fibroids undoubtedly determine their clinical behaviour, but research has yet to correlate these parameters with clinical presentation of the fibroids.

their decision to performed a myomectomy during pregnancy was based on the fibroid size, the rapid growth, and the retroplacental location.

Uterine myomas may be classified in subserosal, intramural or submucosal or peduculated. In the current study, subserosalmyomas had the heighest incidence (54%) as reported by other authors. Several authors have also recommended the optimal type of uterine myomas which could be treated by cesarean myomectomy. Others concluded that intramural myomas in the fundus, myomas located proximal to the fallopian tubes and myomas located in the cornua should be avoided. In the current study, cesarean myomectomies were performed with no restriction based on location. We performed cesarean myomectomy without damaging the fallopian tubes, ever in cases in which the myomas were located in the

fundus or proximal to the fallopian tubes (Rutgers, 2015)

Neiger R, Sonek JD et al 2006 evaluated 137 leiomyomas in 72 women (average, 2.3 +/- 1.8 per woman). Each underwent an average of 3.7 +/- 2.1 scans. The average gestational age at the time of first assessment was 14.4 +/- 5.4 weeks. The average diameter of the leiomyomas at the first study was 34.2 +/- 23 mm. On average, there was no significant change in the size of leiomyomas during pregnancy. They found that the size, location and our ability to visualize leiomyomas varied significantly during pregnancy. Four of the 72 women had obstetric complications related to the presence of leiomyomas.

2.16 Risk Factor associated with Uterine Fibroids:

The risk factors of uterine fibroids include nulliparity, obesity, family history, black race, and hypertension. Also it includes the age, familial history, ethnic origin (African-American women are more likely to develop uterine fibroids than Caucasian women).

A retrospective study to determine the incidence, clinical presentation and management of uterine fibromyoma at the University of Ilorin Teaching Hospital in Nigeria, Five hundred and sixty-nine consecutive cases of histologically confirmed uterine fibroid over a ten-year period were reviewed. Uterine fibromyoma constituted 13.4% of gynaecological admission and was responsible for 26.2% of major gynaecological surgery. Majority of the patients (78.4%) were aged between 30 and 44 years and 60.8% were of low parity (0-2). The common presentations were menstrual disorders (64.3%), infertility (56.2%) and lower abdominal swelling (35.5%). Hypertension was present in 26.5% and 42% were obese. Pelvic adhesion was noted in 58.9% of patients. Total abdominal hysterectomy was the surgical procedure in 52% of cases. Pyrexia (32.5%), Anaemia (29.3%), Prolonged hospital stay (24.1%) and

Wound infection (20.2%) were the common postoperative morbidities. Fibromyoma at the University of Ilorin Teaching Hospital follows a pattern similar to other parts of the world (Aboyeji and Ijaiya, 2002).

Nulliparity, hereditary, black race, obesity, polycystic ovary syndrome, hypertension and diabetes mellitus are associated with increased risk of uterine fibroids. Most frequently myomatosis affects nulliparous, obese, black women, or those with family history of myomatosis or hyperestrogenic syndrome.

A study analyzed the associations of uterine leiomyoma with atherogenic risk factors and potential sources of uterine irritation. The study included 318 case women with uterine leiomyoma that was first confirmed between 1990 and 1993 in the Baltimore, Maryland, area and 394 controls selected from women visiting the same gynecologists' offices for routine reasons. Telephone interviews were conducted with 77.8% of eligible cases and 78.0% of eligible controls. Compared with participants with no hypertension history, increased risks were observed among participants with any history of hypertension (odds ratio (OR) = 1.7; 95% confidence interval (CI): 1.0, 2.8), hypertension requiring medication (OR = 2.1; 95% CI: 1.1, 4.1), hypertension diagnosed at ages less than 35 years (for hypertension requiring medication, OR = 2.7; 95% CI: 1.0, 7.6), and hypertension of 5 or more years' duration (for hypertension requiring medication, OR = 3.1; 95% CI: 1.2, 8.2). Risk of uterine leiomyoma was also associated in a graded fashion with frequency of perineal talc use (daily use vs. no use: OR = 2.2; 95% CI: 1.4, 3.1). It was concluded that nonhormonal factors may influence risk of uterine leiomyoma. (Eduardo et.al 2001)

(Wise LA, Palmer JR et al 2005) investigated the risk of self-reported

uterine leiomyomata in relation to body mass index (BMI), weight change, height, waist and hip circumferences, and waist-to-hip ratio in a large cohort of U.S black women. BMI and weight gain exhibited a complex relation with risk of uterine leiomyomata in the Black Women's Health Study. The BMI association was inverse J-shaped and findings were stronger in parous women. Weight gain was positively associated with risk among parous women only. Risk factors associated with uterine fibroids include obesity, early menarche, low parity, late age of first pregnancy, and long interval since last pregnancy.

The decreased risk of uterine fibroids is associated with cigarette smoking, pregnancy, use of oral contraceptives, pre-menarche and postmenopause. The sex steroid hypothesis is the dominant incumbent framework to explain these associations. However, the data on progesterone and estrogen remain inconclusive . Furthermore, the weakness of the sex steroid hypothesis is evident in the myriad of other factors well known to be associated with fibroids that cannot be easily explained. Hypertension requiring medication was found to have a positive association with uterine fibroids. (Anthony et.al, 2005).

Both uterine leiomyoma (UL) and cardiovascular disease are public health problems affecting women at different age ranges. Smoking, obesity, and hypertension have been shown to be associated with UL in different random studies. However cardiovascular risk factors have not been evaluated systematically in patients with UL. Accordingly Nasir Sivri, Tulin Yalta et al 2012 study aimed to evaluate the cardiovascular risk factors and their relation with the presence of UL in one hundred and eighty nine patients with the pathological diagnosis of UL and one hundred and eighty nine age matched control . The following clinical and demographic parameters were recorded; age, sex, hypertension, diabetes

mellitus, and hypercholesterolemia. Current cigarette smoking was defined as active smoking within the past 12 months. Comparison of cardiovascular risk factors between with and without UL revealed that the presence of hypertension (80 (42.3%) vs 53 (28%) $p=0.004$) diabetes mellitus (33 (17.4%) vs. 16 (8.4%) $p=0.009$), smoking (31 (16.4%) vs. 11 (5.8%) $p=0.001$), were significantly higher in patients with UL than in control subjects.

Black race, heredity, nulliparity, obesity, polycystic ovary syndrome, diabetes and hypertension are associated with increased risk of fibroids, and there is emerging evidence that familial predisposition to fibroids is associated with a distinct pattern of clinical and molecular features compared with fibroids in families without this prevalence.(Okolo2008)

A Study done by UL. Karen L., Carolien I.M et al 2008) to identify risk factors for uterine leiomyomata (UL) in a racially diverse population of women with a family history of UL and to evaluate their contribution to disease severity and age at diagnosis. They collected and analyzed epidemiological data from 285 sister pairs diagnosed with UL. It was concluded that Self-reported race is a significant factor in the severity of UL among women with a family history of UL.

Race and ethnicity are also associated with hysterectomy rate, route, and complications. Overall, the current literature has significant deficits in the identification of racial and ethnic disparities in the incidence of fibroid tumors, endometriosis, and hysterectomy. (Jacoby et.al, 2010)

2.17 Impact Of Uterine Fibroids On The Reproductive Outcome:

Ferenc Bánhidý, NándorÁcs et al 2010 evaluate the recent progress in the treatment of these pregnant women on the basis of the association of leiomyoma in pregnancy (LP) with pregnancy complications and birth outcomes including structural birth defects(congenital abnormalities).

They found that Women with of leiomyoma in pregnancy have a higher risk of threatened abortion, placental disorders and anaemia, but a higher rate of adverse birth outcomes including congenital abnormalities was not found in their offspring.

Uterine fibroids are often found in women of reproductive age. Different types of fibroids may affect reproductive outcome to a different extent, with submucous, intramural and subserosal fibroids being a cause of infertility and pregnancy wastage. Fibroids may also produce a number of complications during pregnancy. Women who are scheduled for assisted conception should be advised to have submucous and possibly intramural fibroids removed prior to IVF. Large fibroids (>5 cm), wherever their location, should be considered individually, with the reproductive history being an important consideration. Miscarriage rates are significantly reduced following myomectomy (Rutgers, 2015)

Submucosal fibroid is one of the most recognised causes of infertility and habitual abortion. Uterine peristaltic movements were partly interrupted by submucosal fibroids, but not by myometrial or subserosal fibroids. These findings are considered to represent dysfunctional contractility, and may be related with pregnancy loss. Uterine fibroids 5 Cm or larger are independently associated with caesarean delivery performed before labour, and the risk increases with the size of the fibroids (Rutgers, 2015). This descriptive study was conducted in the Department of Obstetrics and Gynaecology, Ayub Teaching Hospital Abbottabad from March 2009 to March 2010. Thirty patients were included in this study who had pregnancy with fibroid. Normal delivery was achieved in 14 (46.66%) patients. Eight (26.67%) patients had caesarean section and eight (26.67%) had miscarriages. Seven (23.33%) patients had no complications while 8 (26.67%) had miscarriages, 8 (26.67%) had postpartum

haemorrhage, 10 (33.33%) had preterm delivery, and 3 patients had ante-partum haemorrhage. Two (10%) patients had premature rupture of membranes and 1 patient (3.33%) had pain abdomen and technical difficulty during caesarean section. There were 12 (40%) healthy babies. Five (16.67%) babies delivered with morbidity but recovered. There were 4 (13.33%) intrauterine deaths and one early neonatal death. It was concluded that Fibroid in pregnancy, especially multiple intramural fibroids and fibroids larger than 10 cm, cause miscarriage and preterm labour. Uterine peristaltic movements were partly interrupted by submucosal leiomyomas, but not by myometrial or subserosal leiomyomas. Loss of peristalsis and focal myometrial movements was noted only adjacent to submucosal leiomyomas. These findings are considered to represent dysfunctional contractility, and may be related with pregnancy loss. (Mizuki et.al, 2005)

At present, it is estimated that fibroids may be associated with infertility in 5 to 10% and are possibly the sole cause of infertility in 1 to 3%. Their effects on fertility remain debated. The aim of this review of published studies between January 1990 and November 2010 was to clarify the relation between myoma and fertility, and to assess the role of myomectomy in infertile patients. In assisted reproduction technology and spontaneous conception, hysteroscopic sub-mucous myoma resection increased pregnancy rates. Intramural fibroids appear to decrease fertility, but the myomectomy does not improve assisted reproduction technology and spontaneous fertility. Subserosal fibroids do not affect fertility outcomes, and removal does not confer benefit. (Bendifallah et al, 2011). Cohort study held in Wad Medeni City, Gazera state aimed to identify the etiology of Sudanese infertility in period between June 2001 to June 2002 the study sample size was 200 infertile couples the study found that

uterine fibroids was presents in 11 women (5.5) five of them had secondary infertility.(Osman, 2010)

This study linked two data sets: Taiwan's birth certificate registry and its National Health Insurance Research Data set. A total of 5627 mothers with uterine leiomyoma and 28 135 unaffected mothers were included for analysis. It was concluded that after adjusting for potential confounders, women with uterine leiomyoma experience a small yet significant increased risk of preterm and small for gestational age infants. It suggested that clinicians intensively monitor women with uterine leiomyoma during pregnancy (Yi-Hua et.al, 2009).

(Peter C. Klatsky et al2008) were examined the relationship between uterine fibroids and reproductive outcomes. Submucosal fibroids had the strongest association with lower ongoing pregnancy rates, odds ratio, 0.5; 95% confidence interval, 0.3-0.8, primarily through decrease. Cumulative pregnancy rates appeared slightly lower in patients with intramural fibroids 36.9% vs 41.1%, which may reflect biases in the literature; however, patients with intramural fibroids also experienced more miscarriages, 20.4% vs 12.9%. Adverse obstetric outcomes are rare and may reflect age or other differences in fibroid populations. Increased risk of malpresentation (odds ratio, 2.9; 2.6-3.2), cesarean (odds ratio, 3.7; 3.5-3.9), and preterm delivery (odds ratio, 1.5; 1.3-1.7) are reported; however, the incidence of labor dystocia was low (7.5%). There was no conclusive evidence that intramural or subserosal fibroids adversely affect fecundity. Major complications of pregnancy appear to be related to whether the placenta and the myoma are in contact. The location and number of myomas, especially in the lower uterine segment, increases the likelihood of cesarean birth and malpresentation.

Comprehensive study examined the relationship between age at menarche,

fibroid characteristics, and race. Fibroid presence, number, type, volume, and diameter were recorded through Endovaginal ultrasounds to estimate associations between age at menarche and fibroid status and to test for interactions with race. Of 5,023 participants, 11% had a fibroid, it was concluded that early age at menarche had a similar positive association in individual analyses with fibroid size, type, and location but was stronger for multiple fibroids. The findings confirmed other reports of an association between age at menarche and fibroid, explain no effect modification by race, and suggest a stronger association for women with multiple fibroids (Velez Edwards et al., 2013).

The prevalence of uterine fibroids among reproductive age women is high and the associated morbidity can cause declines in overall quality of life by causing fertility problems, affecting work and social activities because of pain and heavy bleeding, and leading to mental distress related to the management of the disease symptoms.(VINES, 2010)

(T.C. Li1, R. Mortimer et al 1999) studied the impact of myomectomy on pregnancy outcome with particular reference to its effect on the incidence of pregnancy loss. Myomectomy was performed using microsurgical procedures upon 51 women who had intramural or subserosal fibroids and wished to conceive. There was no instance of premature labour or scar rupture among 25 live births. They suggested that myomectomy for intramural and subserosal fibroids may significantly improve the reproductive performance of women presenting with infertility or pregnancy loss.

Sato F,Find all citations by this author (default) Or filter your current search Nishi M et al 1998 investigate the etiological relationship between body fat and uterine leiomyomas.A study was done Japan, 100 Japanese women with uterine leiomyomas (pathologically diagnosed) and 200

controls who were confirmed to have no uterine leiomyomas by clinical examination. They concluded that occult obesity and upper body fat distribution may lead to the development of uterine leiomyomas.

Chapter three

Materials and Method

3.3 Materials

3.3.1 Subjects:

The study was carried out at departments of Radiology, and Obstetrics and Gynecology, Mohammed Ali Fadul Hospital, Omdurman, from January, 2016 to August, 2016. Ethical approval was obtained from the Research Ethics Committee of the hospital before commencement of the study. A convenience sample of 68 consecutive consenting pregnant women who met the inclusion criteria was evaluated during routine prenatal ultrasound scan. The women were attending antenatal clinic in the hospital and were referred to have prenatal sonography.

Inclusion criterion was singleton pregnancy of between 6 weeks and 40 weeks gestational age. Exclusion criteria were non gravid women with myoma, ectopic pregnancy and multiple pregnancies. Multiple pregnancies are known to be high-risk pregnancies with a number of complications developing which may not be necessarily associated with co-existing myoma.

3.3.2 Machine used:

GE Ultrasound machine (General Electric Company, USA) real time ultrasound machines with 3.5MHz, 5.0MHz and 7.5MHz curvilinear and linear transducers respectively. The choice of these probes was based on varying degrees of penetration needed. Validity and reliability of the equipment were tested prior to the study through pilot study and quality assurance.

3.4 Method

3.4.1 Technique used:

The entire abdomino-pelvic area was scanned in both longitudinal and transverse planes using transducer manipulations⁴ to assess fetal viability, presentation, gestational age (GA), expected date of delivery (EDD), and presence, location and size of co-existing myoma. Myomas were measured in three dimensions in millimeter (height, width and length) to determine the mean size. Also location/type of myoma was determined in each subject and documented.

3.4.2 Image interpretation:

Identification of myomas was firstly done by obstetrician, then the follow up and measurements were performed by the researcher and other colleagues in the duty.

3.4.3 Data analysis

Data collected were analyzed using the Statistical Package for Social Sciences (SPSS) version 19.0 (Chicago, Illinois, USA). Both descriptive and inferential statistics were carried out. Statistical significance was considered at $p < 0.05$. Incidence of myoma co-existing with pregnancy was expressed as percentage of total number of subjects evaluated

Chapter four

Results

Table 4 -1: Frequency distribution of patients according to age group

Age group	Frequency	%
20 – 25	4	4.7
26 – 30	14	20.7
31 – 35	16	23.6
36 – 40	17	25
41 – 45	13	19.2
46 – 50	4	5.8
Total	68	100

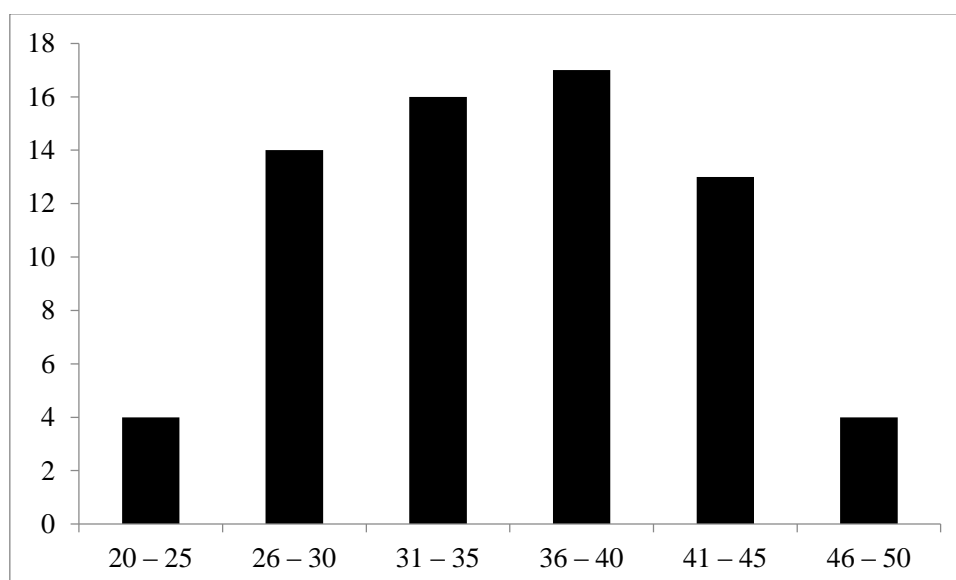


Figure 4.1: Age group

Table 4-2: Frequency distribution of patients according to the duration of marriage:

Duration	Frequency	%
1 – 10	44	64.7
11 - 20	14	20.6
21 - 30	10	14.7
Total	68	100

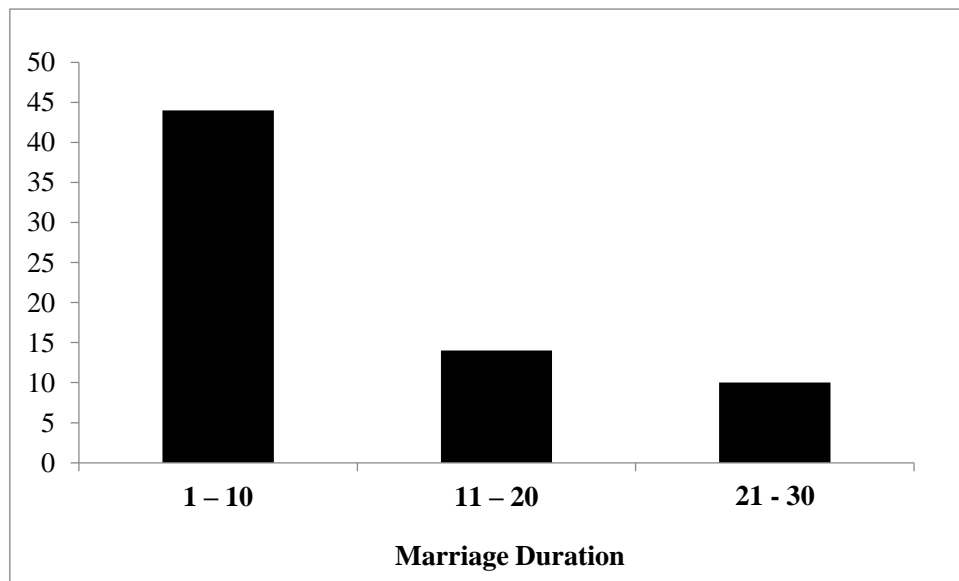


Figure 4.2: duration of Marriage

Table 4-3: Frequency distribution of patients according to the weight:

Weight / kg	Frequency	%
50 – 60	11	16.2
61 – 70	22	32.3
71 – 80	13	19.1
81 – 90	10	12.2
>90	12	20.2
Total	68	100

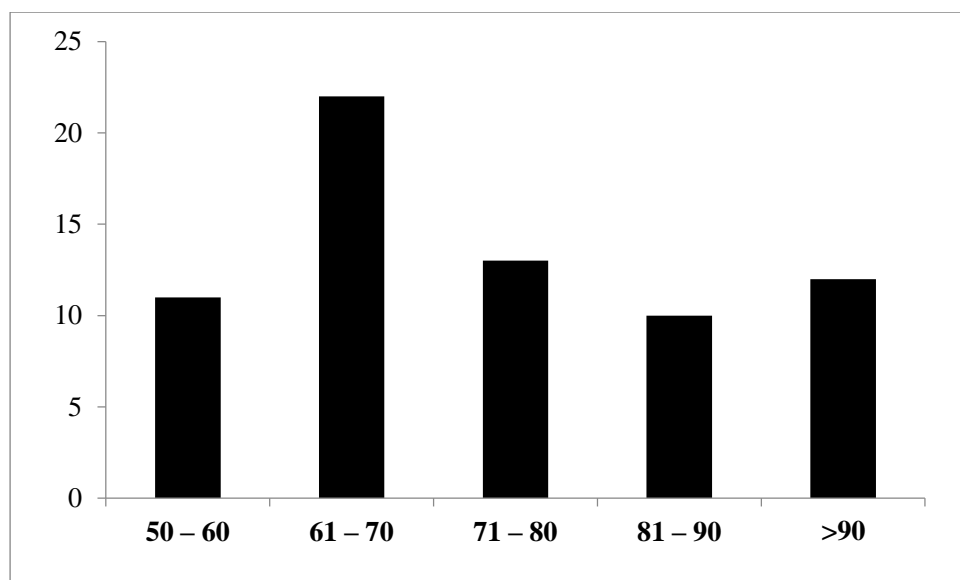


Figure 4.3 Weight distribution

Table 4-4 uterine fibroids anatomical locations

Types	Frequency	%
Intramural	38	55.8
Subserosal	14	20.6
Submucosal	8	11.8
Pedunculated Subserosal	5	7.4
Cervical	3	4.4
Total	68	100

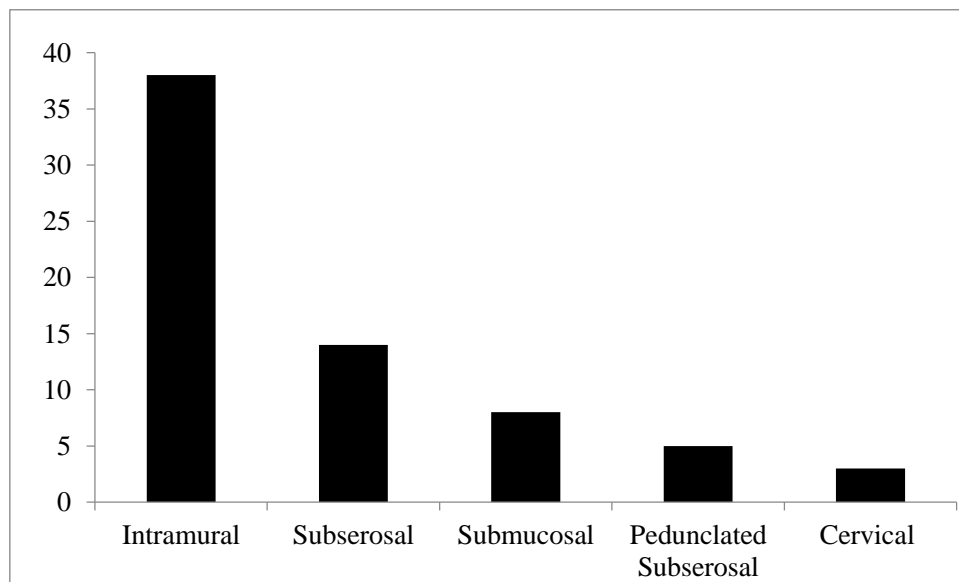


Figure 4-4: Fibroids Anatomical Locations

Table 4-5 uterine Fibroids size

Fibroid size (mm)	Frequency	%
<2.0	3	4.4
2.0-4.9	33	48.5
5.0-7.9	21	30.9
8.0-9.9	6	8.8
10>	5	7.4
Total	68	100

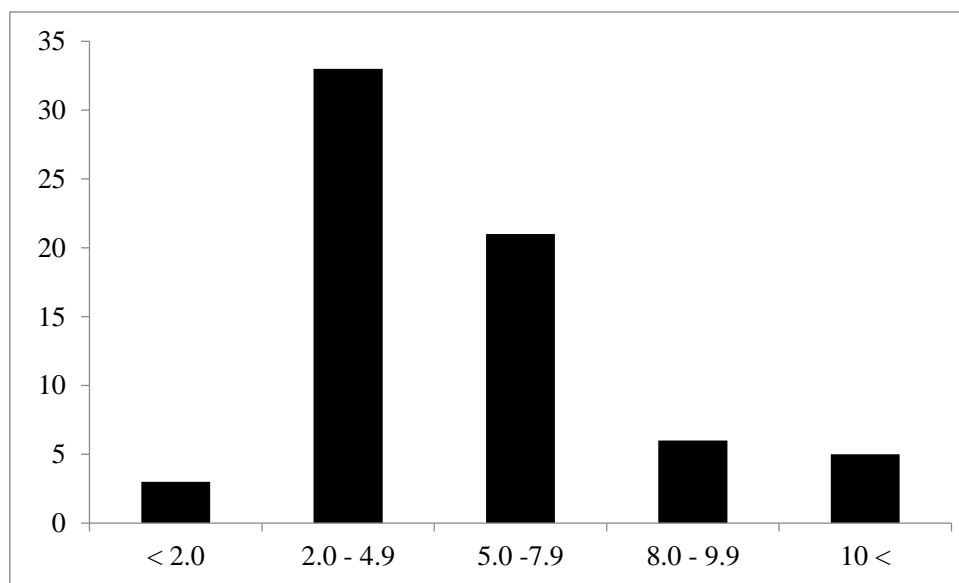


Figure 4-5 Fibroid size

Table 4-6: calcification of uterine fibroids:

Calcification of mass	Frequency	%
Calcified	19	27.8
Non-calcified	49	72.2
Total	68	100

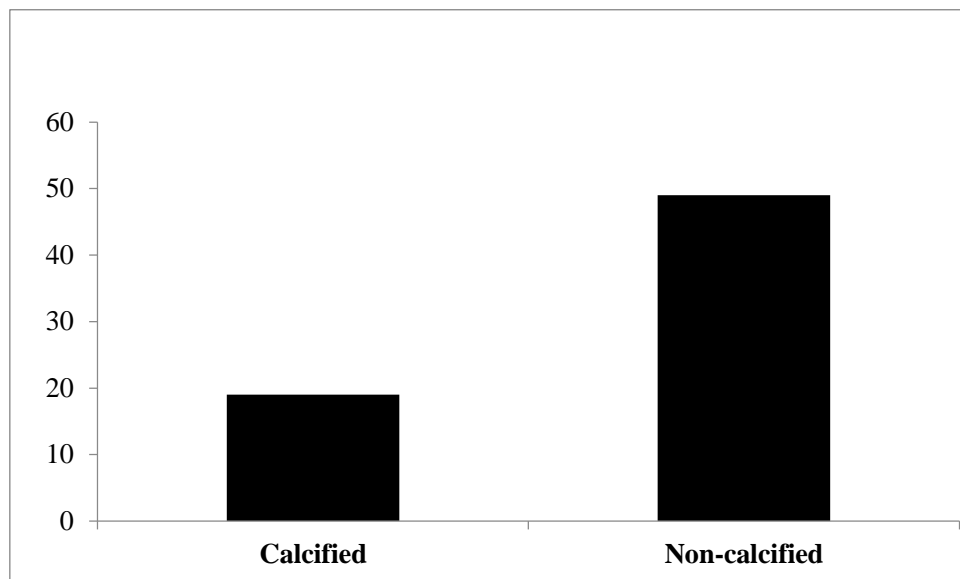


Figure 4-6: Calcification of uterine Fibroid

Table 4-7 Correlation between the Uterine Fibroids Anatomical Locations and the uterine fibroids size:

Uterine Fibroids Anatomical Locations Types		Fibroids Size					Total
		< 2	2 - 4.9	5 - 7.9	8 - 9.9	>10	
Intramural	Count	2	22	7	3	4	38
Subserosal	Count	1	9	3	1	0	14
Submucosal	Count	0	4	2	0	2	8
Peduncled Subserosal	Count	0	2	3	0	0	5
Cervical	Count	0	1	2	0	0	3

		Mean size of fibroid
GA	Pearson Correlation	0.205*
	Sig. (2-tailed)	.0340
	N	68

* Correlation is significant at the 0.05 level (2-tailed)

Chapter 5

Discussion, Conclusion and Recommendation

5.4 Discussion:

Myoma coexisting with pregnancy was commoner in the older women. The majority of subjects with fibroid fall in the age group (26 – 45) years the highest incidence in age group (36-40) years, it was found that the incidence increase steadily and then decrease over 50 years. This result was in line with previous studies which stated that increasing age is a risk factor for fibroid growth (Vollenhoven et al., 1990)

Uterine fibroids affect the population of study in the first ten year of marriage duration (64.7%) and it decrease with increased marriage duration (14.7 %) as shown in Table (4-2).

The patients in this study had a tendency to be obese having a weight of more than 60 kg. Obesity is known to increase the risk of uterine fibroid as shown in Table (4-3).

Myomas classified into types based on their location within the uterus and found that intramural myomas account for about 70% of all the types (Aboyaji and Ijaiya, 2002). Gross and Fleischer¹⁸ found 10% of myomas in their study to be submucous and less than 10% to be cervical, while Tsuda and Gross found the occurrence of subserous myomas to be as high as 20% and retroplacental myomas to be less than 5%. In this study Intramural fibroid had the highest incidence amongst other types/location. The study revealed that Intramural and subserosal are dominants locations. These finding agree with (Vergani et al., 2007) they mentioned that subserosal and intramural anatomical locations represents the majority of all uterine fibroids. The location of myoma in relation to the uterus and placenta has a lot of implications and may serve as a pointer to obstetric management and mode of delivery.

The present study reveals changes in size of myoma during pregnancy. This finding agrees with that studied by (Bogani et al., 2016) who stated that changes in the myoma size during pregnancy in the first, second and third trimesters. There was significant correlation established between the myoma size and GA in present study but no relationship with maternal age. This implies greater risk of complications as pregnancy advances. Several studies (Gross et al., 1983) opined that myoma cell hypertrophies during pregnancy and later shrinks in late pregnancy and this probably explains the observed fibroid growth trend in our study. The cells in small fibroids enlarge during pregnancy and shrink in late pregnancy. The decrease in size observed in late pregnancy, by some studies, could be explained in part by the decrease in cell size. Myoma cells have a greater number of estrogen receptors than surrounding normal myometrial cells³. Therefore, these cells are more responsive to the increased concentration of estrogen during pregnancy and exceed the growth of the surrounding myometrium.

This study met with some difficulties while being conducted. Difficulty was encountered during measurement of very large fibroids in the third trimester. Measurement of fibroids in the same plane in subsequent scans was a challenge. The findings in this study should be considered with these imposed limitations and difficulties taken into consideration.

5.5 Conclusion:

Uterine fibroids are common benign tumor. Myoma coexisting with pregnancy was commoner in the older women. Uterine fibroids affect the population of study in the first ten year of marriage duration and it decrease with increased marriage duration.

The most dominant anatomical locations of uterine fibroids are intramural (55.8%) ,followed by subserosal (22.6%). Furthermore, Obesity is known to increase the risk of uterine fibroid. Regarding the size of uterine fibroid, there was significant correlation established between the myoma size and GA.

Ultrasound scanning plays a central role in diagnosing and monitoring fibroids during pregnancy and in determining the relative position of the fibroids to the placenta. It is equally useful for detecting heterogeneous echo patterns associated with the appearance of pain in pregnancy.

5.6 Recommendations:

- Routine ultrasound scan is recommended to all pregnant women and should be performed carefully between 18 to 22 weeks gestation. Sonography of pregnant patients with co-existing myomas should aim at:
 - Confirming presence of myoma.
 - Location of myoma in the uterus and relationship with the placenta.
 - Number and size of the myomas.
 - Scanning of the entire abdomen/pelvis for any associated lesions.
- Follow-up scans are recommended to determine any change in size of myoma as the pregnancy progresses.
- Diffuse uterine fibroids not recognized by ultrasound machine so Future studies should use method of assessments like MRI.

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