بسم الله الرحمن الرحيم

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Assessment of Endometrial Thickness in Postmenopausal Women Using Ultrasonography

تقييم سمك بطانة الرحم للنساء بعد سن الإنجاب بإستخدام التصوير بالموجات فوق الصوتية

A thesis submitted in Partial Fulfillment for the Requirements of MSc Degree in Medical Diagnostic Ultrasound

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قال تعالى:

{وَقُل رَّبِّ زِدْنِي عِلْمًا}

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Dedication

To my parents for their everlasting love and support.

To my small family (husband & kids) who suffered a lot, with all love.

To my brothers and sisters.

Acknowledgement

I would like to expressing my thank and gratitude to my supervisor thank Dr. Ahmed Mostafa Abukonna, Radiologist, for his invaluable guidance with his super talent, professional expertise and immense patience; showing great care and attention to details and without his guidance this study would have been impossible.

I am also extremely indebted and will remain grateful to my teachers in Medical Diagnostic Ultrasound, who guided me throughout my training course, prepared me and led me to this run on the ladder.

My thanks extended to postmenopausal women who included in this study, for their cooperation.

My deep gratitude is extended to all those who made this effort successful.

I would like to convey my thanks to all my family members, especially my husband, for all goodwill during difficult times and urging me to keep fighting.

LIST OF ABBREVIATIONS

D & C	Dilatation &curettage
TVUS	Transvaginal ultrasonography
HRT	Hormone replacement therapy

Abstract

Background: Endometrial abnormalities pose diagnostic challenges for radiologists and gynecologists. The endometrial appearance is influenced by several factors, such as age, menstrual status, pregnancy and hormonal therapy. Amongst these, menstrual status is potentially the most influential factor affecting endometrial thickness.

Methodology: This is a prospective, descriptive case study, conducted to assess the endometrium thickness in postmenopausal Sudanese women. The study was carried out in the period from October 2016 to April 2017 in different hospitals and clinics in Khartoum State. The study was conducted on (50) postmenopausal Sudanese women, their age 45 years and above, and they had amenorrhea for 6 month. The study subjects were scanned twice in international scanning guideline protocols by transvaginal scan, endometrial thickness was measured at the thickest part of the endometrium in the longitudinal plane.

Results: The mean of endometrium thickness was 7.57 ± 3.480 mm in age group (45-50) years, the mean of endometrium thickness was 4.60 ± 2.927 mm in age group (51-60) years, while the mean of endometrium thickness was 1.88 ± 0.619 mm in age group > 60 years. The endometrial thickness of more than 5mm was observed in age group (45-50) and starts to decrease with increasing age.

Conclusion : Transvaginal ultrasonography is of great value as a screening test for abnormal endometrium in patients with postmenopausal bleeding, endometrial thickness of 5 mm or more should be considered for further investigation.

المستخلص

الخلفية : تشوهات بطانة الرحم تشكل تحديات التشخيص لأطباء الأشعة وأمراض النساء. ويتأثر مظهر بطانة الرحم بعدة عوامل، مثل العمر، وحالة الحيض والحمل والعلاج الهرموني. من بين هذه العوامل حالة الحيض هي الأكثر تأثيرا على سمك بطانة الرحم.

الاهداف : هذه دراسة وصفية، أجريت لتقييم سماكة بطانة الرحم في النساء بعد سن اليأس. أجريت الدراسة في الفترة من أكتوبر 2016 إلى أبريل 2017 في مختلف المستشفيات والعيادات في ولاية الخرطوم.

النتائج: أجريت الدراسة على (50) امرأة بعد سن اليأس، سنهن 45 سنة فأكثر، وانقطع الطمث لديهن لمدة 6 أشهر. تم مسحهن مرتين علي حسب البروتوكول الدولي للموجات فوق الصوتية عن طريق المسح المهبلي، تم قياس سمك بطانة الرحم في أسمك جزء من بطانة الرحم في المقطع الطولي.كان متوسط سماكة بطانة الرحم 7.57 ± 3.480 مم في الفئة العمرية (45-50) سنة، وكان متوسط سماكة بطانة الرحم 4.60 ± 2.927 مم في الفئة العمرية (51-60) سنة، في حين كان متوسط سماكة بطانة الرحم 1.88 ± 0.619 مم في الفئة العمرية أكثر من 60 عاما. لوحظ سمك بطانة الرحم أكثر من 5مم في الفئة العمرية (45-50) ويبدأ في الانخفاض مع زيادة العمر.

خلاصة: مسح الموجات فوق الصوتية عن طريق المهبل طريقة ذات قيمة كبيرة في اختبار بطانة الرحم غير الطبيعي في المرضى الذين يعانون من نزيف بعد سن اليأس، وينبغي النظر في سمك بطانة الرحم الأكثر من 5 ملم لمزيد من التحقيق.

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CHAPTER ONE

1.1. INTRODUCTION

Endometrial abnormalities cause diagnostic challenges for radiologists and gynecologists. The endometrial appearance is influenced by several factors, such as age, menstrual status, pregnancy and hormonal therapy. Amongst these, menstrual status is potentially the most influential factor affecting endometrial thickness (Gambacciani et al., 2004). Although the accepted normal value for endometrial thickness is < 5 mm, endometrium ≥ 5 mm on transvaginal ultrasonography (TVUS) imaging in a postmenopausal woman is considered asymptomatic endometrial thickening. Current literature concerning TVUS imaging suggests that asymptomatic endometrial thickness of 8 mm – 11 mm in a postmenopausal woman may be normal (Smith-Bindman et al., 2004).

In 2009, the American College of Obstetricians and Gynecologists stated that there was no evidence to recommend routine investigations for asymptomatic endometrial thickening (Obstetricians and Gynecologists, 2009). Despite this recommendation, clinicians are concerned when the ultrasound report states that endometrial cancer cannot be ruled out because of endometrial thickening found in an asymptomatic postmenopausal woman. Goldstein, in 2010, recommended postmenopausal asymptomatic endometrial thickening is evaluated on a case-by-case basis. The clinician must consider risk factors for endometrial cancer including obesity, polycystic ovary syndrome, and diabetes mellitus in their decision making. Goldstein19 emphasized that it is inappropriate to investigate every asymptomatic patient with thickened endometrium>5mm (Goldstein, 2010).

Transvaginal scan has become an examination technique that is accepted by postmenopausal women in particular and which gives the less experienced examiner an overall view of the internal genital tract in the female. Recent advantages of transvaginal color Doppler and three-dimensional ultrasound enables the more experienced examiner to visualize even the smallest vessels and investigate blood flow characteristics in the poorly perfused small pelvis in the postmenopausal, what helps to differentiate between the normal, suspicious and pathologic variations of the structures or detect and follow the effects the hormone replacement therapy on the perfusion of genital tract (Kasraeian et al., 2011).

The aim of this study was to assess the normal range of the endometrium thickness in symptomatic postmenopausal Sudanese women so as to know the cutoff point above which we can investigate.

1.2. Problem of the study:

Endometrial cancer is the most common gynaecologic malignancy, approximately 80% of endometrial cancers occur in postmenopausal women.

1.3. Objective of the study:

1.3.1. General objectives:

To evaluate the endometrial thickness in asymptomatic postmenopausal Sudanese women.

2.3.2 Specific objectives:

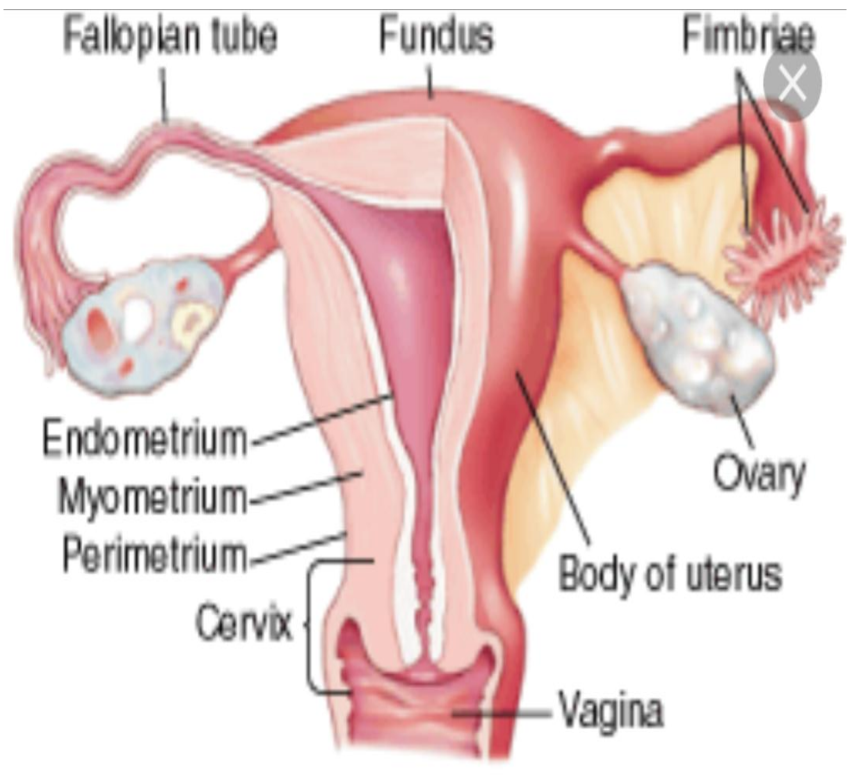
1- To estimate the average thickness of endometrium in asymptomatic post-menopausal women.
2- To study the relation between age group, parity and endometrium thickness.
3- To study the relationship between pelvic pathology, and endometrial thickness.

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Pelvic anatomy:

Pelvic bones form firm hoop where uterus, ovaries, Fallopian tubes, vagina, urinary bladder, ureters and part of the colon are placed.



Layers of Uterine wall

Uterus is a pear-like organ positioned between the urinary bladder in front and the rectum behind it. Uterus has its corpus (body of the uterus) and cervix, having a 2:1 length ratio. Dimensions of the body are commonly 7.5–9 cm length, 4.5–6 cm, width 2.5-4 cm thickness. Normal uterine size varies with parity, but after postpartum involution, it stabilizes at an increase of approximately 1.5 cm in all directions (Standring, 2015).

Dimensions of the cervix are 2.5 cm length and 2.5 cm diameter. Cervix presents uterine communication with outer world. The cervix is a cylinder-like structure that consists of a fibrous and elastic connective tissue and smooth muscle. It constitutes a lower third of the uterus in an adult, while in childhood cervix accounts for two-thirds of the uterine length. Since cervix connects upper part of the vagina with the uterine cavity, it serves as a depot for spermatozoa, allowing their migration towards the uterine ostia. After rupture of the follicle and due to the drop of the estrogen level, the cervical canal is closed again (Marieb and Hoehn, 2007).

The entire uterus (its long axis) is bent by three-quarter of women towards the symphysis (anteversion) and in relation to cervix closes angle 90°135° towards symphysis (anteflexion). On contrary, when the uterus is bent towards the rectum, it is named retroversion and in relation to the cervix, uterus closes angle 90°-135° towards the sacrum (retroflexion).

Uterus has a thick muscular-walled body (myometrium) lined internally with columnar epithelium (endometrium) that undergoes changes in addition to the part of the menstrual cycle and age of the female patient. Uterus is supported by uterosacral ligament and the peritoneum is draped over the uterus (Marieb and Hoehn, 2007).

The space formed between the uterus and the rectum is the rectovaginal pouch of Douglas. The fold of peritoneum laterally from the uterus in which Fallopian tubes are positioned is known as broad ligament.

Uterine vascularization is complex. The main uterine arteries, originate from the internal iliac arteries, and they give off branches, which penetrate in outer third of the myometrium thickness without significant branching. Further, they subdivide into an arcuate wreath encircling the uterus. From this network, smaller branches, called the radial arteries, arise, directed towards the uterine lumen. The radial arteries branch into basal arteries and endometrial spiral arteries as they pass the myometrial-endometrial border (Marieb and Hoehn, 2007).

Basal arteries, that are relatively short, terminate in the capillary bed that serves the basal layer of the endometrium. The spiral arteries project further into the endometrium and terminate in a vast capillary network that serves the functional layer of the endometrium (Hall, 2015).

Only spiral arteries undergo substantial anatomical changes during the menstrual cycle. At the time of menstruation, probably because of decreasing estrogen and progesterone levels, the spiral arteries constrict.

Fallopian tubes are tube-shaped organs that origin from the lateral uterine angles toward the corresponding ovary. The Fallopian tubes are approximately 10 to 12 cm long and few millimeters wide. Fallopian tubes consist from dilated part with fimbria positioned most laterally to the ovary (infundibulum), ampular part (5 cm long, meandering with thin walls, varying in diameter), isthmic part (2 cm long) and intramural part (passing through myometrium).

Ovaries present pair of endocrine female sex glands in which follicles develop during the reproductive age. Ovaries are positioned on each side of the cervix, close to the lateral wall of the pelvis in fossa Waldeyer (delimited with ureter and internal iliac vessels). Ovaries are connected with peritoneal leaf - mesovarium with the backside of the broad ligament. In the direction to the uterus, ovaries are connected with ligamentum ovarian proprium, and ligamentum suspensorium ovary connects them with the Fallopian tubes.

Normal ovaries are ellipsoid in shape, with dimensions approximately 3 × 2 × 2 cm in reproductive age. The number of primordial follicles present in the ovaries is inversely proportional to the woman's age. Approaching the menopause, the supply of endocrine responsive follicles becomes depleted causing cycle irregularities. About 7 million of the follicles containing oocytes are present in a female fetus at about 20 weeks gestation (Hall, 2015).

These follicles, called primordial, are microscopic in size and metabolically quiescent. Later in childhood, reproductive age or during oral contraception therapy, they grow from primordial to primary, secondary and tertiary follicles (microscopic in size) forming a fluid-filled antrum. In adequate hormonal conditions (increased local follicle stimulating hormone-FSH levels), follicles continue to grow. Only 100 to 1000 follicles are left until the menopausal period. Most of them are going through the process of atresia, and only some of them ovulate. The small and transient rise in FSH serum levels at the end of each ovarian cycle affects the small antral follicles (size of 1 or 2 mm). These follicles have apotential to grow further instead to become atretic. During the early follicular phase of the ovarian cycle, hypophyseal FSH affects follicular cells to secrete estradiol and eptide hormone inhibin (reduces FSH production as the follicular phase progresses). The smaller follicles go to regression with the drop in FSH levels, while the larger ones grow regardless. Sometimes two follicles become dominant, producing the substantial amount of estradiol as they grow, while the others become atretic. This turnover happens by the end of the first week of the follicular phase. Atretic follicles can still be visible and can grow, especially in the dominant side, although they are undergoing atresia (Hall, 2015).

The ovarian vascular system is divided into external and internal part. The external vascular system consists of arteries that start from big abdominal trunks before they enter the ovary and the homologous venous system. Vessels that enter the gland from the ovarian hilus form the internal vascular system.

These vessels give rise to the microcirculation and form venous drainage.[(6)] The cyclic changes of the ovarian vascularization are manifested most intensively in the internal vascular system. The ovary receives its arterial vascularization from two arteries: the ovarian artery and the utero ovaria branch of the uterine artery. These arteries anastomose, forming an arch parallel to the ovarian hilus, and constitute the vascular genital arcade. The vessels sprouting from the arcade run through the central medullar part of the stroma towards the periphery (Hall, 2015).

In the ovarian cortex, the vessels form vascular arcades in the stroma, surrounding the follicles. In the development of an ovarian follicle during the menstrual cycle, a rich, irregular capillary plexus is progressively formed in the connective tissue layer or theca surrounding a vascular granulosa cell layer of the ovarian follicle.

Several hours before ovulation, vessels penetrate the granulosa cell layer. Following ovulation, there is proliferation of the vessels of the theca layer further vascularize the granulosa cell layer and theca cells merge to form the corpus luteum. Within three or four days after the follicular rupture, the corpus luteum is supplied with a dense, multilayered network of sinusoidal capillaries that are drained by numerous superficial venules (Hall, 2015).

2.2 Postmenopausal state:

The size of the cervix and the body of the uterus decreases gradually as menopause progresses. Uterus measures approximately 4.5 cm length 1.5 cm width 2.5 cm thickness. Body of the uterus shortens and uterus body/cervix ratio increases almost to 1:1. There is a slight difference between women who are obese or using HRT and other postmenopausal women. Uterus body/cervix ratio is falling much slower in the first group than in second. Due to progressive decrease of the ovarian function in postmenopausal women, the endometrium becomes thin and atrophic not subjected to cyclic changes.

In premenopausal phase ovarian follicular depletion starts, diminishing the number of antral follicles for recruitment, resulting in lower production of follicular inhibin, and sooner increase of FSH levels (during the late luteal phase) causing earlier start of follicular development (before menstruation takes place) (Hamidi et al., 2008).

As menopause is approaching, the follicular phase and consequently menstrual cycle get shorter. During the premenopausal years, it is common to have functional cysts and/or multifollicular appearance of the ovaries. During the postmenopausal period, estrogen and inhibin production falls, resulting in an increase of the FSH levels. The ovaries become small and homogenous with altered shape, volume and echogenicity. They are ovoid shaped through the next 5 years with significant decrease of the volume. At this time ovaries measure 2 cm × 1.5 cm × 1.5 cm, with maximum volume of 7 cm^3 (Hamidi et al., 2008)

Due to progressive decrease of ovarian hormones in postmenopausal women, the endometrium becomes thin and atrophic not subjected to cyclic changes leading to the mean endometrial thickness of 2.3 ± 1.8 mm. In postmenopausal state ovaries do not secrete estrogens, but still produce androgen hormones, which together with androgens derived from the adrenal glands are converted to estrogens in peripheral adipose cells.

Production of estrogens at that way may be responsible for endometrial thickening and proliferation changes showed as hyperplasia or neoplasm. In women taking HRT one can tolerate maximum thickness of 8 mm. In patient receiving sequential HRT the endometrium changes according to the phase of the cyclical therapy. In continuous combined regimens, the endometrium is likely to be relatively thin. An endometrial thickness cut-off level of < 5 mm in a symptomatic patient seems to have a high negative predictive value for the presence of endometrial cancer. Once the endometrial thickness is greater than 8 mm in asymptomatic postmenopausal women not taking HRT, an outpatient biopsy is required to exclude endometrial hyperplasia or malignancy (Smith-Bindman et al., 2004).

Kurjak and Kupesic demonstrated that the RI uterine arteries of postmenopausal women increase with years after menopause. The mean ovarian arterial RI in postmenopausal women is approximately 0.94 in the first 5 years of postmenopausal. In older women absent diastolic flow corresponding to RI of 1.0 is usually obtained (Gambacciani et al., 2004).

2.3 Scanning in the postmenopausal:

There are a variety of configuration of transvaginal probes including also the great number of overall size and shape. Examining a woman in the postmenopause the ovaries and the endometrium must be special field of interest. In general the curved linear multielement transducers afford the best density and overall field-of-view for imaging. In elderly women the stenosis of the upper part of the vagina or adhesions of the vaginal walls can occur in addition to the atrophic changes of the epithelia. One must take special care when introducing the probe into the vagina of a woman in the senescence.

Transvaginal sonography can induce unnecessary bleeding and pain. The same caution applies to women who have vaginal adhesions secondary to previous surgery for which the vaginal examination may be painful. Using thinner transducers and lubricant gels could help to avoid the unnecessary injuries. The angled shaped transvaginal transducers (Aloka, Toshiba, General Electric) require narrower movements in the vagina when imaging the lateral structures of the female pelvis thus decreasing the discomfort. It is advisable to have an additional medical person being present during any kind of vaginal procedure (Kasraeian et al., 2011).

2.4 Scanning method:

The first and perhaps most important condition for transvaginal ultrasonography should be a thorough emptying of the urinary bladder. This is the condition, what makes the transvaginal ultrasonography more comfortable for the significant group of incontinent postmenopausal patients comparing to the transabdominal ultrasonography, which requires full bladder. On the other hand, some elderly patients who are unable to empty their bladder completely may need catheterization in order to the better visualization (Ciatto et al., 2002).

Once the probe covered with condom and some ultrasound coupling gel it is inserted into the introitus with slight downward pressure on the perineum while gently separating the labia majora with the fingers of the other hand. A small amount of coupling gel applied to the outside of the condom can act as lubricating interface. If the patient desires she can insert the probe herself.

Inserting the probe into the, midvagina the anteflexed uterus can be normally imaged in its sagittal (long-axis) plane. However, in the postmenopause with lose of the strength of the uterine ligaments and the pelvic support, the uterus is frequently altering its position in the female pelvis. With the advanced ages it is usually situated in the midline in a straighten position and can be imaged only after inserting the probe into the fornix (Sharma and Tiwari, 2016).

Additionally, a descended, even a prolapsed uterus let the examiner to orientate only after the re-establish the about normal situation by pushing the uterus upwards manually and then holding there with the probe. There is less problems with the visualization of the retroverted, retroflexed uterus in this age. Trendelenburg position makes the examination easier, even if the cardiac status of the patient makes it impossible. In the long axis, one can appreciate the different interfaces of the endometrium, beginning with the interface of the cervical canal. Because the echogen cervical mucus is very poor and the endometrium can be very thin and atrophic in the PostmenoPause, visualization of the endometrium can be difficult; usually it appears in the form of a thin, echo-poor line in the midline of the sagittal plane of the uterus.

After adequate image in the long axes are obtained the probe can be moved 90° to image the uterus in a horizontal (semi-coronal, semi-axial) plane. The endometrium again has to be identified in the level of the tubal ostia. Once the endometrium is adequately depicted in its long and short axes, the probe is withdrawn into the midvagina and images of the cervix can be obtained (Sharma and Tiwari, 2016).

The ovaries usually located lateral to the uterus, above and medial to the hypogastric vessels, lying in the area called “Waldeyer’s fossa”. Their size, morphology and locations are altered by the age, previous diseases and surgeries and other factors in the postmenopause. During the reproductive year the follicles serve as sonographic “markers” of the ovaries. After the menopause it is hard to find them because these “markers” are not present, the ovaries themselves atrophy and there is less pelvic fluid to provide an acoustic interface. Their detection becomes more difficult with advancing of the age.

Beside negative bimanual pelvic examination non-visualization of the ovaries can be accepted without serious concern about ovarian pathology. With the introduction of color coded Doppler flow imaging, by finding the color coded flow of the ovarian artery or vein one can better detect the otherwise sonographically “non detectable” ovaries. Using the other hand can be very useful for manipulating the ovaries into the "scanningsight" of the probe by pushing them slightly downward through the lower abdominal wall into the direction of the tip of the probe (Sharma and Tiwari, 2016).

Detecting some free fluid in the cul-de-sac doesn't necessarily means pathological finding, but in the presence of that ovarian pathology must be searched with special care. The same goes for any palpated or visualized solid structure in the cul-de-sac. The vascularization of these gynecological findings must be examined intentionally also by color and pulsed Doppler.

When a large amount of fluid is present, such as in ascites, one of the first questions is whether the pathological condition arises from an ovarian tumor or is related to a nongynecological disorder. Fluid is clearly outline the boundaries of the structures and ovarian pathology may be revealed. If the ovaries appear normal, one may consider other reasons leading to ascites.

Constipation is not rare in postmenopausal patients. Scibalas shouldn't be confused with pelvic masses. Excluding the vascularization of a structure by the color Doppler helps in differentiating normal to abnormal. Solid pelvic masses also must be differentiated from the intestines. In real-time mode the motion of the bowels help to distinguish the peristalting intestines from the fixed structures. In the postmenopause the peristalsis is frequently inert, which requires proper patience from the examiner. In case of a vascularized mass color and pulsed Doppler offers again a quick possibility (Betsas et al., 2008).

From all of the above mentioned it follows, that the sonographer have to get know the finding of bimanual pelvic examination, which should, therefore, precede the transvaginal ultrasound examination. It strengthens the recommendation that the person, who performs the transvaginal ultrasound examination in a postmenopausal patient, should perform a bimanual pelvic examination before, thus orienteering the anatomical situation and obtaining previous information to decide, which is the adequate way for ultrasonography or is there any suspicious structure palpated. In case of uncertainty of the origin of the palpated or visualized structure transrectal examination or enema might be also necessary (Kasraeian et al., 2011).

2.5 The postmenopausal uterus scanning:

The uterus can be imaged in three major scanning planes with TVS. There is generally a homogenous echo pattern in the postmenopause, and the uterine cavity is frequently not imaged. The uterine wall is smooth and clearly outlined against its surroundings. In the myometrium, towards its periphery and often protruding, can be found echoless vessels. In the postmenopause the arteries can calcify in this region. These calcifications appear as small, bright reflections, regularly spread in the uterine wall. They can evoke shadowing, which may impair the assessment of structures lying beyond, e.g. the endometrium.

Unlike in all phases of the menstrual cycles, undulatory motions, i.e. uterine contractions cannot be observed in the postmenopause. As in the case of all genital organs in the female, the development, the maintenance of the fertile size and shape, and the postmenopausal physiologic involution of the uterus are highly dependent on the actual serum level of the estrogen. Measurement of the uterus in the sagittal plane can be carried out either by determination of the portio-fundus distance or in postmenopause the separate measurement of the cervix and corpus uteri can be also used. It was already mentioned in the introduction, that the corpus-cervix ratio of the postmenopausal uterus shows remarkable changes in favor of the cervix, with advanced ages it can even fall below 1 and can reach the 1: 2, like in childhood (Gambacciani et al., 2004).

The sagittal measurement is supplemented by the determination of the largest anterioposterior diameter of the corpus uteri, and of the largest transverse diameter of the corpus. The size of the corpus decreases markedly in the postmenopause, shrinking to average 4.5×1.5×2.5, with the cervix predominantly over the corpus in the sense of the elongation of the cervix. The mean length of the postmenopausal uterus was shown to be 59+/−11 mm by Andolf et al. The upper size limit of the postmenopausal uterus has been suggested to be 3 cm in the anterior-posterior diameter, with a cervical-fundal length of 8 cm. The patient who is only 1–3 years postmenopausal when still has significant endogenous estrogen production by the ovaries, or who has significant endogen estrogen production by fat from adrenal precursors will have larger uterus, than the patient who is over 10 years postmenopausal. Clinical judgment is needed in interpreting normality of uterine size in postmenopausal of uterine size in the postmenopausal patient (Gambacciani et al., 2004).

Uterine involution is a slow process. Myometrial thickness is changed as the years of the postmenopausal progress. In their study Zalud et al did not found significant changes in the myometrial thickness in women without HRT over the years after the menopause, though slow thinning can be observed. Myometrial thickness after the menopause changes less than does endometrial thickness, which may suggest that these changes are more dynamic (Gambacciani et al., 2004).

2.6 The uterus under HRT:

Comparing myometrium thickness between groups of postmenopausal with and without HRT, Zalud et al did not demonstrated statistical difference, though slight difference were found in favor of women, who received HRT more than 5 years. These data are not surprising in the mirror of the findings of the same group, namely that the myometrial involution couldn't be statistically expressed over the years throughout the postmenopause, too. The involutional process of the myometrium is very slow and other factors, than estrogen can also influence, as the sizes of the uteruses of fertile women can show great variability too (Zalud et al., 1993).

2.7 The postmenopausal endometrium:

After the menopause, decrease of ovarian estrogen production leads to atrophy of the endometrium. In consequence the endometrium of postmenopausal women is typically thin when examined by TVS, which corresponds to the stratum basale adjacent to the myometrium. Its sonographic feature is very similar to that of the endometrium in the early follicular phase. The endometrial band is sonographically narrow and the echogenic line of the uterine cavity often cannot be visualized. In the study of Andolf the endometrium couldn't be localized in 7% of postmenopausal women without bleeding disorder. Granberg et al couldn't visualize 10% of the histologically atrophic postmenopausal endometrium. In addition, shadowing arising from myomas or arteriosclerosis make visualization more difficult. Echotexture of the endometrium is usually more echogenic than the surrounding myometrium. In the above mentioned study of Andolf 85% of the assessable endometrium were less echogenic than the myometrium in asymptomatic postmenopausal women (Zalud et al., 1993).

The poorly echogenic myometrial zone, the subendometrial halo round theendometrium is frequently absent in the postmenopause. However, the interrupted subendometrial halo was reported as a common sign of the myometrial invasion of the endometrial carcinoma (Starczewski et al., 2005).

2.8 The Postmenopausal Endometrial Thickness:

Contrary to early methods of measurement of the thickness of the endometrium, today according to general agreement measurement should be carried out as follows: the uterus is viewed vaginosonographically in the longitudinal section and the total thickness of the endometrium is measured in the largest diameter (double layer). In the case of any kind of intrauterine fluid collection, the thickness of the fluid pool in the uterine cavity is subtracted from the total thickness (Paraskevaidis et al., 2002).

The postmenopausal endometrial thickness is 2-4 mm, with a considerable scatter range of 0-10 mm, and consequently there are different limiting values for the normal state in the literature. There is a correlation between the endometrial thickness and the body weight. Women with pure estrogen replacement therapy frequently have endometrial thickness exceeding that of postmenopausal women without it (Paraskevaidis et al., 2002).

2.9 Color Doppler Velocimetry in the Postmenopausal Uterus:

The vascular supply of the uterus is provided by a complex network of arteries originating from the uterine artery, which is a branch of the hypogastric artery. The color Doppler signal from the main uterine vessels can be seen lateral to the cervix at the level of junction between the corpus and cervix. Flow velocity waveforms from the radial arteries can be obtained within the myometrial fibers, while spiral arteries are visualized at the level of endometrial-myometrial junction (Paraskevaidis et al., 2002).

Visualization of both uterine arteries by transvaginal color Doppler can be achieved even in the advanced years of the postmenopause. In contrary, visualization rate of the myometrial and endometrial vessels are highly dependent on the length of the postmenopausal period.

The ageing process affects the uterine perfusion. In general high impedance and high velocity is characteristic for the uterine arteries, though the uterine perfusion is largely dependent on age, phase of menstrual cycle, other conditions (e.g. pregnancy, tumor) and there are complex relationships between the concentration of the ovarian hormones in the serum and uterine artery blood flow parameters (Erdem et al., 2007).

Additionally, there might be also a relationship between the serum gonadotropin level sand uterine perfusion. Examining normal postmenopausal patient and premenopausal patients treated with GnRH analogues Luzi et al found, that the pulsatility index of the uterine artery in spontaneous menopausal women is significantly higher than in artificial menopausal women. This phenomenon may be due to a different hormonal pattern which exists in the two groups, i.e. the gonadotropin levels increased in the former and decreased in the latter. The vascular compliance in artificially induced menopause is higher than that observed in spontaneous menopause, as shown by a higher diastolic flow and a less deep notch. The decrease of the vascular compliance in postmenopause can be caused by progressive sclerosis of the vessel walls (Harrington et al., 1996).

Resistance to blood flow increases in both the main uterine and the radial arteries as the years of postmenopause progress, though the increase of ovarian blood flow impedance is more pronounced. The fact, that uterine artery RI does not change significantly in the first years of menopause strongly supports the thesis that ageing process initially affects the uterus less than the ovary.

The diastolic flow decreases in postmenopause and the systolic peak increases. The RI in the main uterine arteries continuously increases with the number of the postmenopausal ages, but unlike in the case of the ovarian artery, doesn’t reach the maximum in all women even at advanced ages.

Absent diastolic flow in uterine arteries was found in 15% of women with 1–5 years duration of menopause, while clear interruption of diastolic blood flow was observed in the uterine artery of one-third of the women in the next five years of the postmenopausal period. More than half of the women have this finding with 11–15 years lasting postmenopause and finally, 80% of women whom LMB occurred more than 16 years ago demonstrated absent diastolic blood flow signal indicative of high vascular impedance. The changes in flow velocity patterns of the radial arteries in postmenopausal patients parallel the blood flow dynamics of the uterine arteries (Harrington et al., 1996).

Visualization of clear Doppler signals from the spiral artery is possible only in less than one-third of postmenopausal women, in whom LMB occurred 1–5 years previously. The impedance is significantly increased in these vessels, too, when comparing to the premenopausal levels. In normal postmenopausal women already 6 years after the LMB no blood flow signals can be expected from the inner third of myometrium and the area of the myometrio-endometrial junction (Harrington et al., 1996).

2.10 Color Doppler velocimetry:

The visualization rate of the postmenopausal endometrial vessels is very low. The visualization rate of endometrial vessels is in accordance with decreasing endometrial thickness with the postmenopausal years. As it was already mentioned, vascularization of the inner third of the myometrium and the endometrio-myometrial junction is possible only in about or less than one-third of those normal postmenopausal patient, who had the last menstrual bleeding not more than 5 years previously. No flow can be detected in the normal, atrophic endometrium in the postmenopause. Although a thick endometrium may be a sign of pathological processes, no morphological features that are unique to malignant disease have been identified.

Transvaginal color and pulsed Doppler has shown that the presence of intratumoral vascularization with a low impedance to blood flow can be used as an end point in screening programs for some gynecological malignancies.

Bourne et al reported the impedance to blood flow in the uterine arteries and the endometrial thickness in women with postmenopausal bleeding with or without cancer. In the women with postmenopausal bleeding who did not have endometrial cancer and in those without postmenopausal bleeding were similar. Conversely, the highest PI in the group with cancer 1.49 was below the lowest value in the group without cancer (Obstetricians and Gynecologists, 2009).

Data from this study suggest that, in the presence of malignant tissue, the impedance to blood flow within the uterine artery is reduced significantly when compared to control groups. This observation was later confirmed by others.98 If color Doppler is used to interrogate the endometrium in such cases, angiogenesis can be demonstrated as areas of color superimposed on the B-mode gray scale image and the sensitivity of the technique is enhanced.

Hata et al found a feeder artery in patients of endometrial cancer, and in seven out of nine endometrial cancers even venous blood flow in the endometrium could be detected, while no flow was detected around and within the endometrium in noncancer patients (Obstetricians and Gynecologists, 2009).

These findings were confirmed by pelvic angiography. In the work of Kurjak et al visualization rate of the abnormal blood flow within the endometrium was 100% in the cases of endometrial carcinoma. Of the cases with detected endometrial carcinoma 90 had endometrial (tumoral) thickness >10 mm, which is already a suspect sonographic sign alone. However, 10% of these endometrial carcinomas with endometrial thickness 5–10 mm would have been missed without color Doppler. It was also suggested in the same work, that color Doppler should help in distinguishing between cancerous and hyperplastic thickened endometrium. Flow could be detected only in 92% of cases of endometrial hyperplasia. Blood flow pattern was characterized with a low RI near or <0.40, which constituted statistically significant difference compared with that of endometrial hyperplasia, if any flow detected (Obstetricians and Gynecologists, 2009). By using color Doppler and measurement of the endometrium thickness together whilst maintaining the sensitivity, the false-positive rate of the ultrasound-based test is reduced.[(25)] If further data confirm, superimposing the color Doppler onto the endometrium at a questionable thickness (5–10 mm) and searching for vascularization in or around the endometrium might help to determine the further management of the patient and can lead a further reduction of the number of dilatation and curettage in the postmenopause (Obstetricians and Gynecologists, 2009).

2.11 The Endometrium under HRT:

It is now well established that unopposed exogenous estrogen increases a woman's risk for endometrial hyperplasia and thus has an etiologic role in endometrial carcinoma and that this effect is both dose- and duration dependent. Stimulating normal menstrual cycles by the use of progestogens have been found to effectively reduce estrogen-induced breakthrough bleeding and lower the risk of endometrial hyperplasia and carcinoma. Development of a hyperplasia can be prevented and a pre-existing glandular-cystic or adenomatous hyperplasia can be eliminated by regular administration of gestagens (Sharma and Tiwari, 2016).

Some of the most common adverse effects of postmenopausal estrogen treatment are bleeding disturbances, regardless of whether therapy is sequential or continuous estrogen/progestogen. In those women, who receive exogenous hormones continuously, the delicate task of balancing appropriate dosages of estrogen and progestogen may lead to breakthrough bleeding even more often. Since utero-vaginal bleeding is the cardinal symptom of endometrial cancer, a disease which has been found to occur more frequently during unopposed estrogen therapy, it is not a surprise that rising estrogen consumption resulted in a need for appropriate invasive examinations to be carried out more frequently. Jensen et al found that the frequency of D&C and endometrial biopsies in sequentially-treated women as compared with untreated womenwas 3.1 times higher in the 55–59 age group (Ciatto et al., 2002).

Since transvaginal sonography has been progressively used as an alternative recourse of monitoring the endometrium both in the pre- and postmenopause detailed in the previous chapters, it is also suggested that it may be a useful method of monitoring the effects of HRT on the endometrium. Vaginosonography as a screening method enables us to survey the postmenopausal endometrium, but sonographic assessment of endometrium is a completely different manner. It is therefore desirable to correlate hormone replacement regimens with the sonographic appearance of the endometrium.

Establishment of the normal range of endometrial widths for each hormone regimen would help limit unnecessary invasive procedures for suspected endometrial hyperplasia (Ciatto et al., 2002).

Women who are receiving continuous hormone replacement are in favorable position. It is now well established that that kind of therapy is protective for endometrium. There are less cases of endometrial cancer in continuous regime group than in postmenopausal woman without any therapy.

In women receiving sequential hormone replacement, endometrial thickness would be expected to vary throughout the cycle, depending on whether the endometrium was undergoing proliferative or secretory transformation due to estrogenic or progestational stimulation, respectively. For this purpose, the examiner should have knowledge of the type of hormonal replacement therapy and the day of the menstrual cycle, in order to distinguish pathological endometrial findings. It seems to be the best time of examination is in the early postmenstrual period. Contrary, in woman receiving continuous hormone replacement endometrial thickness should be always the same (thin).

On the basis of the current literature and according to the recommendations of Osmers, the following approach can be regarded as guidelines when examining the endometrium of an asymptomatic postmenopausal woman by vaginosonography.

A woman receiving sequential hormone replacement should be examined after completion of the progestational phase of the cycle (days 1–2). All patients with hormonal replacement therapy are advised to undergo sonographic checks of the endometrium in 6 months time.

Endometrial thickness up to 8 mm is regarded as normal finding, however, endometrial thickness between 8 and 15 mm is regarded suspicious. After administration of an oral gestagen, subsequent to the withdrawal bleeding, a second sonography is performed. If the endometrium still measure s more than 8 mm, D & C is recommended. With endometrial thickness of less than 8 mm, control sonography in 3 months time is recommended. Women receiving unopposed estrogen or continuous estrogen and progestogen and having endometrial thickness between 8 and 15 mm need to undergo D&C.

Any patient with endometrial thickness of at least 15 mm should undergo histological diagnosis on grounds of the unusual thickness, regardless of symptoms or hormone status. The endometrium of all postmenopausal women should be assessed vaginosonographically before the onset of HRT, whereas the guidelines for assessing the postmenopausal endometrium detailed in the previous chapter should be taken into consideration.

Above recommendations are only for woman on sequential therapy. Woman on continuous therapy should be regarded and followed as postmenopausal woman without therapy.

2.12 Suspect Postmenopausal Endometrium pathology:

Endometrial carcinoma is the most common invasive gynecological malignancy in the United States and Europe today. The incidence of the disease increases considerably during the fifth decade of life and the average age at diagnosis is 59 years. In the more cosmopolitan, higher income population the rate has overcome the 40 cases per 100.000 related to increased longevity, increased cholesterol in diet, and exogenous estrogen supplementation or substances with an estrogen-like effect. The five-year survival rate is related to myometrial invasion, ranging from 93.7%, when no invasion is present to 36.2% if the invasion is deep. When the first clinical sign, vaginal bleeding occurs, the myometrial infiltration depth is already 10 mm on average. Of endometrial carcinomas 80–90% present with atypical bleeding demonstrating the ineffectiveness of exfoliate cervical cytology and the need for early recognition of this most frequent genital malignancy. Until now curettage and histologic evaluation is the accepted method to assess the background of the atypical bleeding. However, less than 10% of women with postmenopausal bleeding have endometrial cancer. Therefore, a new non-invasive screening method must fulfill at least double requirements: it should be able to recognize the abnormal endometrial process at an earlier stage, than bleeding occurs and it should reduce the number of the "unnecessary" curettage, when postmenopausal bleeding occurs (van Doorn et al., 2004).

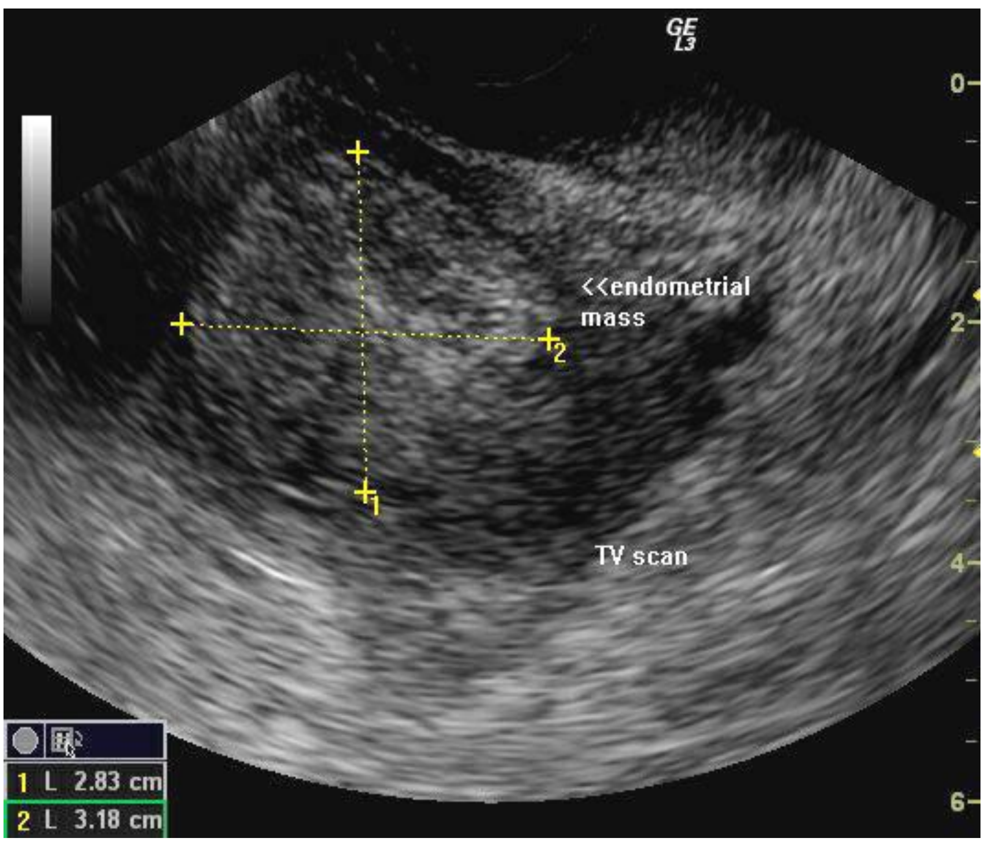
Several publications have reported that endosonographically measured endometrial thickness correlates closely with the presence or absence of endometrial cancer in asymptomatic postmenopausal women. An endometrium, those measures greater than 8 mm from one myometrial endometrial interface to another in postmenopausal woman without HRT is highly likely to be associated with significant endometrium pathology.

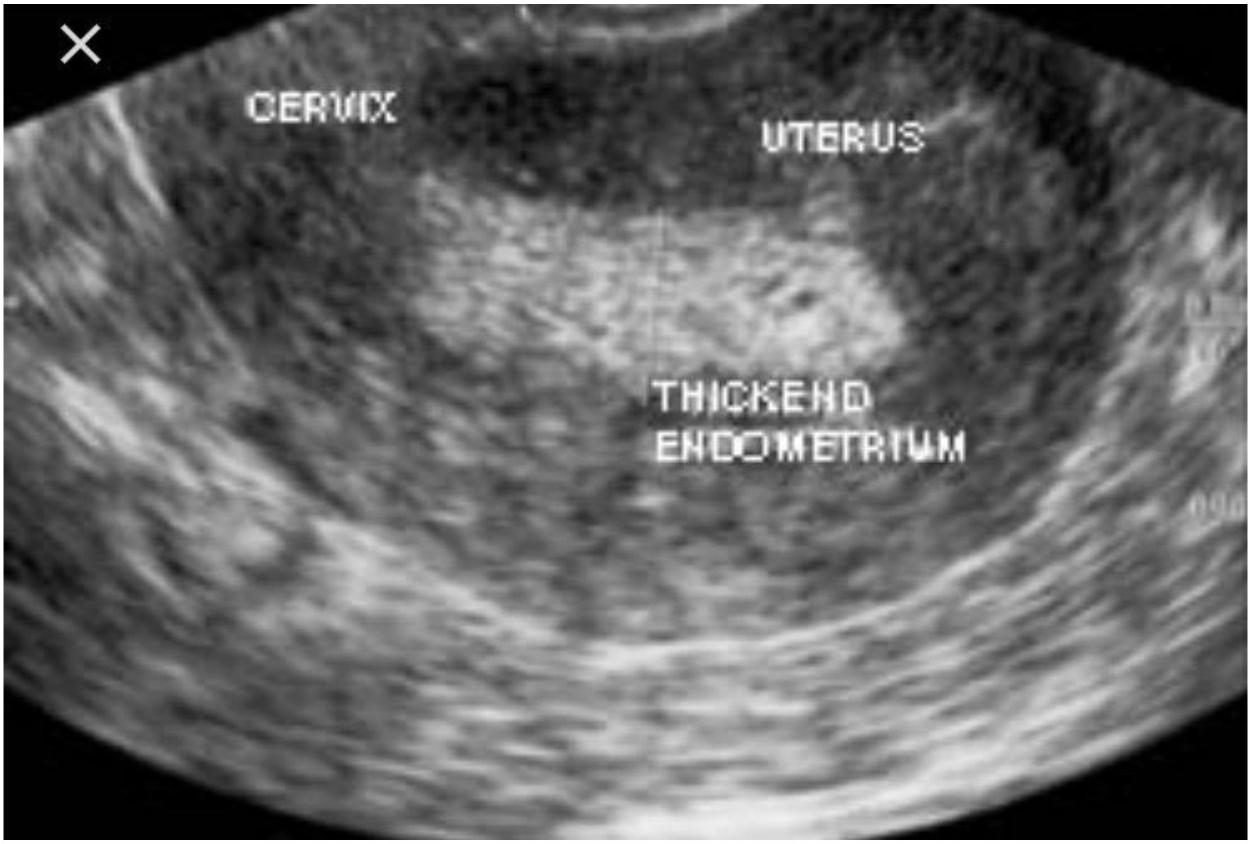
Approximately 10% of asymptomatic postmenopausal women have endometrium exceeding this cut-off level and 3.5% of them can be expected to have endometrial carcinoma. There is, however, a significant false-positive rate. Using a cut off level of 8 mm we have a very high sensitivity, but a low specificity. The only way to increase the specificity would be to adjust the cut-off value to a higher level, but in this case the sensitivity of the screening would decrease and more positive cases might be overlooked (Ciatto et al., 2002).

Another possible approach to reduce the number of false-positive findings could be the use of color Doppler. The realistic approach is that endometrial thickness up to 5 mm can be regarded as completely normal finding in the postmenopause. Endometrial thickness 6–9 mm requires control examination in 3–6 months' time, if the patient really asymptomatic. Endometrial thickness of 10 mm and above requires urgent histological examination (Ciatto et al., 2002).

The most essential characteristic of a cancer screening method is not only detecting the malignancy, but also improve the prognosis by early detection.

Osmers et al compared the myometrial invasion depth, the most prominent prognosis factor of asymptomatic endometrial cancers detected by TVS (cutoff value 8 mm) and symptomatic cancers (atypical bleeding). They concluded that early endometrial cancers detected by TVS will have better prognosis than symptomatic ones, since the average myometrial invasion was 4 mm and 10 mm, respectively. Up to now, there are no sonomorphologic criteria to differentiate between benign and malignant endometrial neoplasm. Therefore we cannot detect endometrial cancer by TVS alone, but TVS is an excellent tool to define a risk group in postmenopausal women (Osmers et al., 1995).





2.13 Myomas and Malignant Potential after the Menopause:

Uterine fibroids of 0.5 cm can be detected by TVS and their relationship to the endometrial cavity precisely defined (e.g. submucous, intramural, subserous). They appear with TVS as rounded, well defined, space occupying structures.

Growth of myomas is known to be estrogen dependent. The management of the myoma around the menopause is highly conservative, since after the menopause they supposed to regress in the lack of the hormonal support. Myomas with good vascularization can be seen less frequently after the menopause. They show more hypoechogenic structure, compared to the normal uterine tissue, while homogenous, hyperechogenic myoma have often undergone regressive changes and have a large amount of connective tissue. Other regressive changes such as necrosis and caseous and cystic degeneration can be recognized by the presence of hypoechogenic regions or regions without echogenicity in the myoma. Such a necrotic myoma can be confounded with an ovarian cyst or a colliquated endometrial carcinoma depending on its localization. Hyalinization and calcifications of the myoma responsible for bright reflections can be seen frequently in the postmenopause. Transvaginal color Doppler can be used to assess leiomyoma vascularity, as well as the physiological and pathophysiological characteristics of uterine artery blood flow (Erdem et al., 2007).

The vascularization of leiomyomas is supported by pre-existing myometrial vessels originating from terminal branches of uterine arteries. Since the leiomyoma grows centripetally as proliferation of smooth muscle cells and fibrous connective tissue, the color Doppler demonstrates most of the leiomyometrial blood vessels at its periphery. While their visualization rate high in the premenopausal period (58–70%), it decreases after the menopause with the decreased blood supply of the uterus (Erdem et al., 2007).

The growing inclination of the myoma is in correlation with the increased blood flow in the uterine network, the latter is thought to be a result of large concentration of estrogen receptors and estrogens. Whether the regression of the myoma after the menopause is resulted directly by the fallen estrogen levels or it is only a secondary consequence of the decreased perfusion, still not known. Though Doppler studies on the perfusion of the uterine fibroids in the postmenopausal are not available yet, it can be anticipated from the Doppler studies on myomas under treatment with GnRH analogu that with the decreasing estrogen levels the previously decreased impedance of the uterine artery and the supplying myometrial vessels are increasing to the level of a normal postmenopausal uterus leading to the involution of the myoma. It must be emphasized, that in case of necrotic, degenerative changes in the myoma the presence of blood vessels in the central portion is usual and the impedance of them can be so low, that might be misinterpreted as malignant neovascularization (Stachowiak et al., 2016).

One can use TVS as a means of monitoring the size and the ability for growth of the leiomyomas around and after the menopause. If there is evidence of rapid growth of a pre-described myoma in a postmenopausal women, and in ultrasound an increase of echoless areas as a sign of necrosis, laparotomy should be performed because of a suspected malignant transformation.

Though the sarcomas are account for only 1–3% of the malignant tumors of the uterus (including the endometrium), their early diagnosis can greatly depend on an occasional but accurate ultrasound examination, since there are scarcely any symptoms of an early process. It is expected to be more common, since the conservative treatment of uterine myomas is becoming more reliable alternative to the surgery (Stachowiak et al., 2016).

Nevertheless, there are, similar to macroscopic aspects, sonographic indications for the existence of sarcoma. Primary sarcomas in ultrasound examinations appear as poorly outlined masses, partly hyperechogenic, partly irregularly limited and hypoechogenic, or without echogenicity. Morphological differentiation from myoma can be facilitated by the absence of any systematic structure (onion-skin or whirlpool pattern). Differential diagnosis of inhomogenous, myometrial masses can be myomas undergoing carneous degeneration, with a pool of liquid or bleeding into the myoma.

Application of the color and pulsed Doppler may confirm or preclude the in vivo diagnosis of uterine sarcoma. The presence of irregular, thin and randomly dispersed vessels in the peripheral and/or central area of tumor, with very low impedance shunts characterizes intratumoral neovascularization and is in favor of the malignant transformation. In benign uterine lesions, even if intratumoral vascularization can be detected, the resistance to blood flow was found significantly higher. Furthermore, in the case of the uterine sarcoma, both uterine arteries show low impedance in comparison with that of normal, even the postmenopausal or myomatous uterus (Stachowiak et al., 2016).

Unfortunately as the result of the wide range of the biological variations and the vascular characteristics of tumors an overlap exists between the blood flow patterns of benign and malignant uterine tumors. At the moment the realistic approach is to consider the above mentioned guidelines only in general, but one has to take the decreased intratumoral impedance and increased vascularity into serious consideration, especially it is accompanied with rapid growth of the tumor during the serial examination (Turnbull et al., 2017).

2.14 Leiomyomas under HRT:

Leiomyomas are the most common pelvic tumors in women of the reproductive age; 20–25% of women have uterine myomas. Higher concentrations of estrogens, and estrogen receptors within leiomyoma than in adjacent myometrium were taken as evidence of the hormone dependence of their growth (van Doorn et al., 2004).

Though they tend to regress after menopause with the decreasing serum level of the promoter estrogen, it is questionable, whether the introduction of the HRT promotes the growing process again. The data are confronting, in some papers myoma growing, in some there is no difference in size and in some there is even decreasing in size. However, even if there are increasing in myoma size, this does not appear to cause clinical symptoms. In practice, uterine and fibroid size can be closely monitored by ultrasound and HRT can be easily discontinued if the fibroid enlarge (van Doorn et al., 2004).

2.15 Postmenopausal bleeding and transvaginal sonography:

In atypical bleeding in the postmenopause, besides clinical and cytological examination, careful sonographic assessment should be made of the ovaries and the cervix uteri. Transvaginal ultrasound has become an important tool for diagnosing endometrial pathology in women with postmenopausal bleeding, too. In patients with postmenopausal bleeding, the endometrium is considerably thicker, than in asymptomatic women (Harrington et al., 1996).

Several studies have been investigated the effectiveness of the endometrial thickness measurement in detecting malignancy in patients with postmenopausal bleeding, using different cut-off levels. Summarizing the results of the published works in none of the case was endometrial carcinoma found below 5 cm. According to the examinations of Osmers et al with a chosen cut-off level of 8 mm, endometrial carcinoma could not be detected either in case of atypical bleeding. This cut-off level applies not only to carcinoma, but also its preliminary stages, such as adenomatous hyperplasia with atypia (Osmers et al., 1995).

One might conclude at the first sight, that measuring an endometrium less than 5 mm is safe enough to exclude the possibility of endometrial carcinoma in case of postmenopausal bleeding. As far as we have very little knowledge about the origin and behavior of cancers, it is up to future studies to clarify how far, in patients with endometrial thickness below 5 mm and atypical bleeding, dilatation and curettage might be avoidable under certain circumstances with the help of sonographic follow-up. While morphological criteria for the assessment of the endometrium have so far not gained acceptance, again transvaginal color Doppler can be proved to be a help of the clinician in the future (Kasraeian et al., 2011).

Nevertheless, if this method is to be used for identifying those women who will not have a dilatation and curettage performed, based on the findings on the endometrium, training is needed to minimize the error. Karlsson et al found considerable differences, when compared the measurements of experienced and inexperienced examiners (Kasraeian et al., 2011).

2.16 Postmenopausal intrauterine fluid collection:

Occasionally, a small amount of intraluminal fluid may be detected in the postmenopausal uterus; the detection rate of it can reach the 16% in asymptomatic postmenopausal women. We can only speculate as to the pathophysiology of fluid accumulation in the uterine cavity. Senile cervical stenosis can prevent drainage of possibly minimal endometrial secretion leading to small intrauterine pools. This, however, speculative as some degree of cervical stenosis is ubiquitous in postmenopausal women, whereas intrauterine fluid is rare finding. Patients with ascites are more likely to have intrauterine fluid. The possibility of the tubal cancer is rather theoretical, than practical, although one case one reported by Carlson. Cancer of the cervix may obstruct the cervical canal and can cause intrauterine fluid accumulation. However, the main suspected reason must remain the endometrial malignancy. Though the presence of intrauterine fluid has been considered ominous and related to malignancy by some authors, the significance of this finding is still not clear, especially in routine examinations. Management and clinical evaluation have also not determined (Turnbull et al., 2017).

In their recent series of twenty postmenopausal women with intrauterine fluid collection, Pardo et al revealed 3 cases of endometrial carcinoma, though it must be emphasized, that all of these positive cases the endometrial thickness was more than 4 mm. Carlson et al reported also twenty cases of endometrial fluid collection in the postmenopausal, of which five proved to be results of some kind of genital malignancy (two ovarian, one tubal, one endometrial, and one cervical). However, examining the fluid pools in the uterine cavity Osmers et al did not find association with pathological changes in narrow endometrium. The extensive use of sonography will lead to an eventual increase in the number of postmenopausal patients diagnosed with intrauterine fluid. In every case, careful scanning is recommended to rule out ovarian and tubal pathology. Obviously, the endometrium must be submitted serious examination by transvaginal ultrasound (Pardo et al., 1994).

Polyploid growths and irregularity of the endometrial surface are particularly well seen when surrounded by intraluminal fluid. Certainly, cytological evaluation of the cervix, with special regard to the cervical canal is essential. Additionally, both Pardo and Carlson recommend immediate endometrial sampling even in the cases of thin endometrium, until accumulated data permit dismissal of endometrial sampling in that cases. According to Osmers et al indication for D&C is given only when there are pathological endometrial findings. In the lack of any other suspicious finding and beside thin endometrium Fleischer also allows rescanning, but if it is present or even volume increase on repeat scans, this finding should be considered suspicious for an endometrial disorder. Undoubtedly, color Doppler offers an additional help in getting closer to the proper management, as it is able to assess the vascularization around this questionable ultrasound finding of postmenopausal intrauterine fluid collection (Pardo et al., 1994).

Previous related studies:

Study of Smith entitled: How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding.

Objective: Transvaginal sonography (TVS) is routinely performed as part of a pelvic sonogram in postmenopausal women, and images of the endometrium are frequently obtained. In women without vaginal bleeding, the threshold separating normal from abnormally thickened endometrium is not known. The aim of this study was to determine an endometrial thickness threshold that should prompt biopsy in a postmenopausal woman without vaginal bleeding. *Methods:* This was a theoretical cohort of postmenopausal women aged 50 years and older who were not receiving hormone therapies. We determined the risk of cancer for a postmenopausal woman with vaginal bleeding when the endometrial thickness measures > 5 mm, and then determined the endometrial thickness in a woman without vaginal bleeding that would be associated with the same risk of cancer. We used published and unpublished data to determine the sensitivity and specificity of TVS, the incidence of endometrial cancer, the percentage of women symptomatic with vaginal bleeding, and the percentage of cancer that occurs in women without vaginal bleeding. Ranges for each estimate were included in a sensitivity analysis to determine the impact of each estimate on the overall results. RESULTS: In a postmenopausal woman with vaginal bleeding, the risk of cancer is approximately 7.3% if her endometrium is thick (> 5 mm) and < 0.07% if her endometrium is thin (< or = 5 mm). An 11-mm threshold yields a similar separation between those who are at high risk and those who are at low risk for endometrial cancer. In postmenopausal women without vaginal bleeding, the risk of cancer is approximately 6.7% if the endometrium is thick (> 11 mm) and 0.002% if the endometrium is thin (< or = 11 mm). The estimated risk of cancer was sensitive to the percentage of cancer cases that were estimated to occur in women without vaginal bleeding. For the base case we estimated that 15% of cancers occur in women without vaginal bleeding. When we changed the estimate to project that only 5% of cancers occur in women without vaginal bleeding, the projected risk of cancer with a thick measurement was only 2.2%, whereas when we estimated that 20% of endometrial cancers occur in women without bleeding, the projected risk of cancer with a thick measurement was 8.9%. As a woman's age increases, her risk of cancer increases at each endometrial thickness measurement. For example, using the 11 mm threshold, the risk of cancer associated with a thick endometrium increases from 4.1% at age 50 years to 9.3% at age 79 years. Varying the other estimates used in the decision analysis within plausible ranges had no substantial effect on the results.

Conclusions: In a postmenopausal woman without vaginal bleeding, if the endometrium measures > 11 mm a biopsy should be considered as the risk of cancer is 6.7%, whereas if the endometrium measures < or = 11 mm a biopsy is not needed as the risk of cancer is extremely low (Smith-Bindman et al., 2004).

Study by Zalud entitled Measurement precision and normal range of endometrial thickness in a postmenopausal population by transvaginal ultrasound:

Objectives: The aim of this study was to examine the endometrial thickness (ET) in an asymptomatic postmenopausal population, and to assess the long-term variability.

Methods: A total of 1182 asymptomatic generally healthy postmenopausal women were enrolled into this cross-sectional evaluation of the ET. Measurements were performed by transvaginal ultrasound. A subset of the women (n = 178) was examined twice 3 months to 2 years apart to assess the long-term variability.

Results: Cross-sectionally, ET varied with length of menopause. During the first 5 years after menopause (YSM) the mean ET was 2.3 mm but it decreased by 0.03 mm/year ($P < 0.01$). From 5 to 13 YSM the ET remained stable at a mean of 1.8 mm with no significant changes ($P = 0.13$). Thereafter there was a minimal increase of 0.01 mm/year ($P < 0.05$). In order to minimize the influence of natural changes on ET, only women who had reached the menopause more than 5 years earlier were entered into the subsequent long-term study. The mean ET was 2.0 mm ± 1.0 mm with no significant differences within or between the observers' measurements. The precision errors were less than 1 mm.

Conclusions: The normal range of the thickness of the postmenopausal endometrium in asymptomatic women varies with YSM. There is a high long-term agreement within and between observers in measuring the endometrial thickness (Zalud et al., 1993).

CHAPTER 3
MATERIALS AND METHODS

3.1 Materials:

3.1.1 Subjects:

This is a prospective, descriptive case study, conducted to assess the endometrium thickness in postmenopausal Sudanese women. The study was carried out in the period from October 2016 to April 2017 in different hospitals and clinics in Khartoum State.

The study was conducted on (50) postmenopausal Sudanese women, their age 45 years and above, and they had amenorrhea for 6 month and presented to the Ultrasound Department as volunteer or patients complaining from others than gynecological symptoms during the study period. Subjects with any risk factor for endometrial pathology e.g.: history of postmenopausal bleeding, PCOS, patients with medical diseases such as diabetes, hypertension and obese women were excluded.

Ethical clearance and approval for conducting this research was received from our supervisor, and from the general managers of the hospitals. Informed consent was obtained verbally from the women.

3.1.2 Machine used:

the transvaginal ultrasound scanning using a transvaginal transducer of variable frequency (7.5, 6.5 or 5 MHz) on either a Siemens Sonoline Versa Pro (manufactured by Matsushita Communications Industrial, Japan, for Siemens Medical Solutions Systems, Issaquah, Washington, USA), or Aloka 1700 (Aloka, Tokyo, Japan) ultrasound machine.

3.2 Methods:

3.2.1 Technique used:

The study subjects were scanned twice in international scanning guideline protocols by transvaginal scan. First by the researcher, second by sonologist to confirm the finding, endometrial thickness was measured at the thickest part of the endometrium in the longitudinal plane (approximately 1 cm from the endometrial–myometrial interface at the fundus) and included both endometrial layers; from the base of the hyper-echoic (bright echo) layer of the posterior endometrium to the base of the hyper-echoic layer on the anterior endometrium as described by (Granberg et al., 1991).

3.2.2 Data collection:

Data was collected by ultrasound report and by direct interview of the volunteers using data collection sheet.

3.2.3 Data analysis:

Data analyzed by computer using Statistical Package for Social Sciences (SPSS); descriptive statistics, correlation and analysis of variance were performed.

Ethical considerations:

- The proposal thesis was submitted to Ethics review committee of Sudan University of Sciences and Technology, College of Graduate Studies, Ultrasound Department for approval of the study.
- The permission to conduct the study was obtained from Administrations of the study area.
- Verbal consent was taken from all participants in this study.

CHAPTER 4

RESULTS

Table 4.1: Distribution of the study population according to age

Age (in years)	Frequency	Percentage
45 – 50	14	28.0
51 – 60	20	40.0
> 60	16	32.0
Total	50	100.0

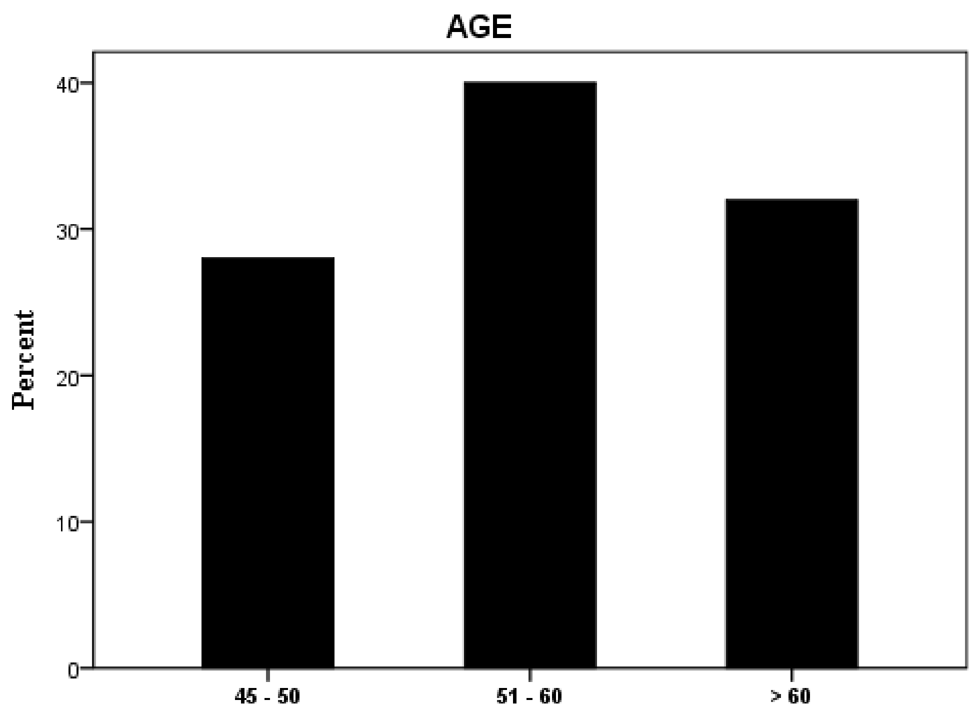


Figure 4.1 Age distribution

Table 4.2: Distribution of the study population according to marital status

Age (in years)	Frequency	Percentage
Married	37	74.0
Single	13	26.0
Total	50	100.0

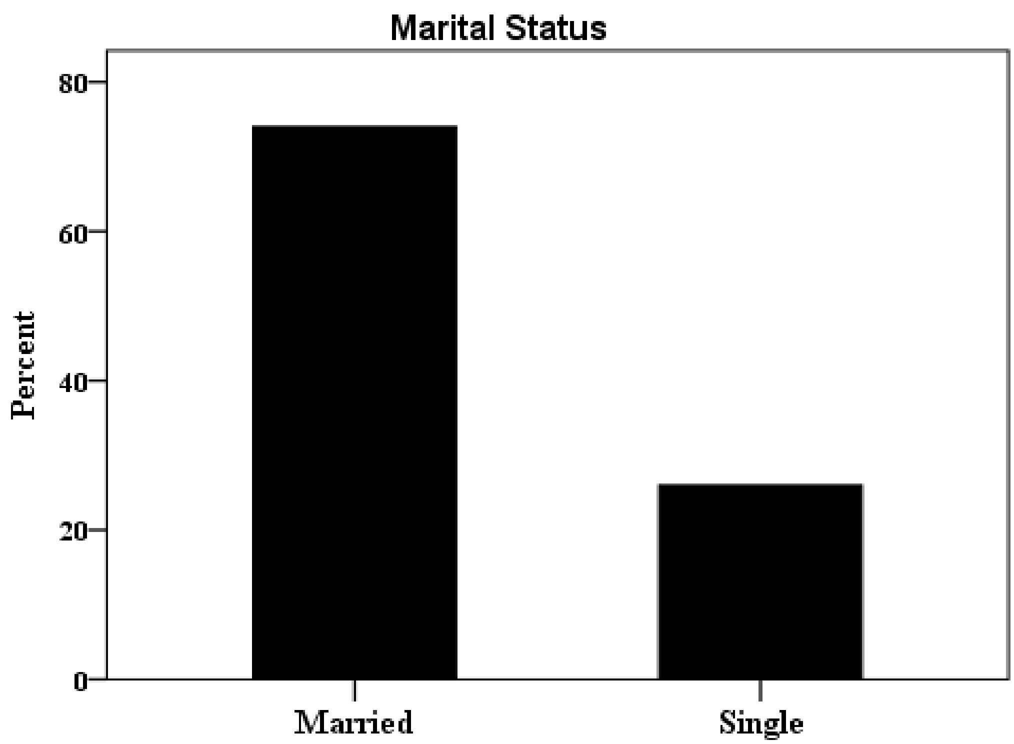


Figure 4.2 Marital status

Table 4.3: Distribution of the study population according to clinical presentation

Clinical presentation	Frequency	Percentage
Pelvic Pain	43	86.0
Vaginal Bleeding	7	14.0
Total	50	100.0

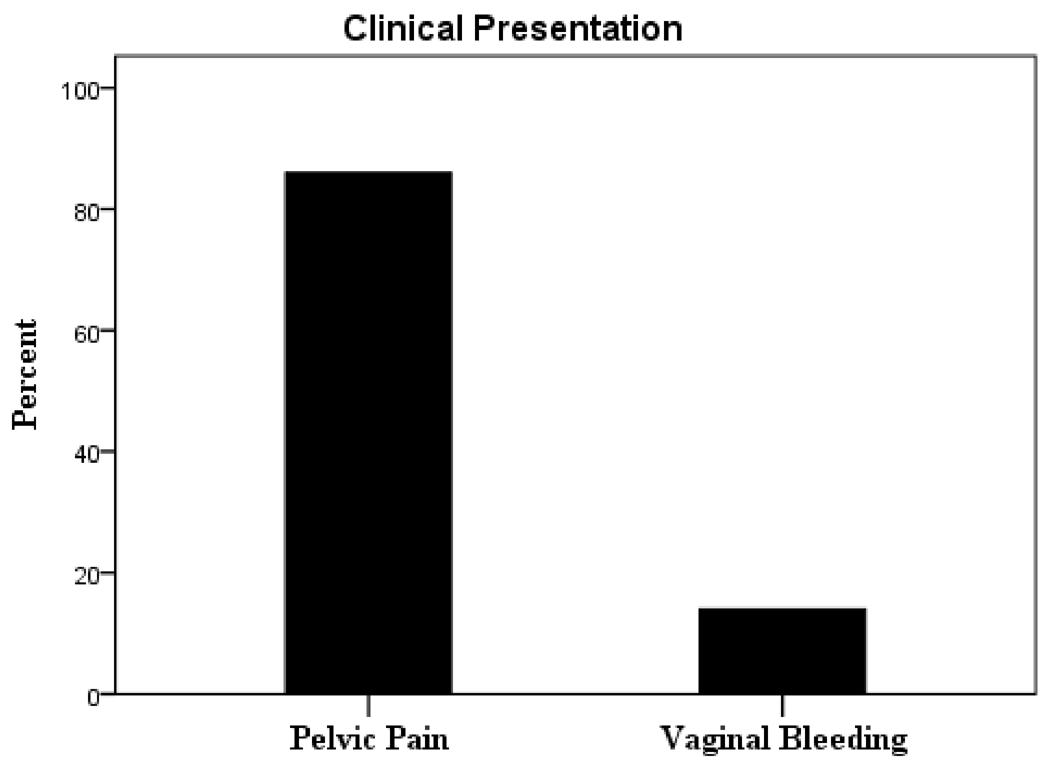


Figure 4.3 Clinical presentation

Table 4.4: Distribution of the study population according to ultrasound findings

Ultrasound findings	Frequency	Percentage
Normal	43	86.0
Abnormal	7	14.0
Total	50	100.0

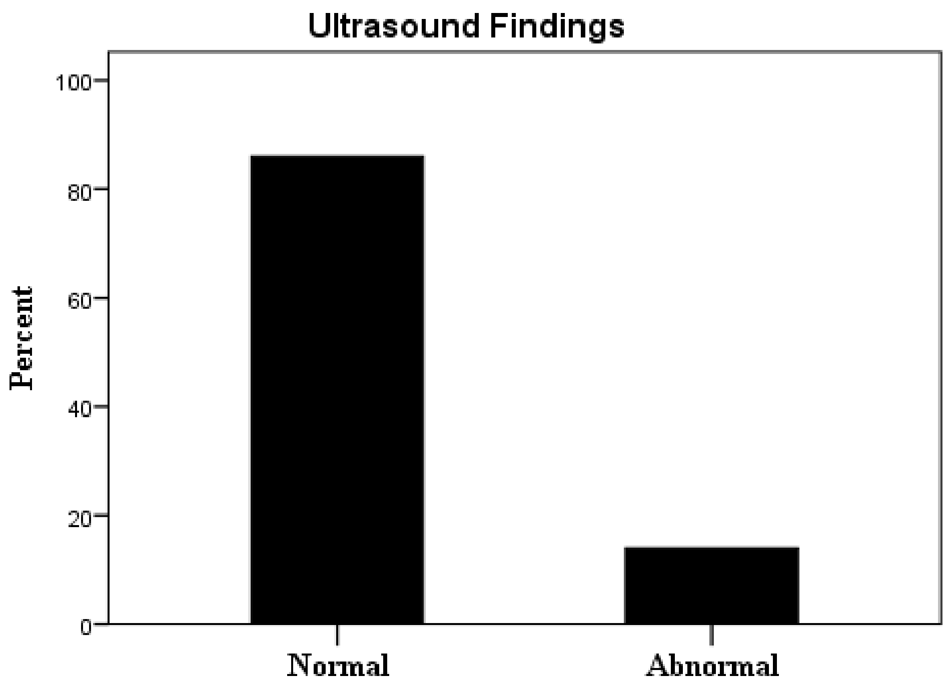


Figure 4.4 Ultrasound finding

Table 4.5: Descriptive statistics of uterine measurements

Uterine measures	N	Minimum	Maximum	Mean	Std. Deviation
Uterine Length	50	3	13	6.88	1.803
Uterine Width	50	2	10	3.66	1.423
Endometrium Thickness	50	1	18	4.56	3.406

Table 4.6: Descriptive statistics of uterine measures (millimeter) according to age

Uterine measure	Age group	N	Mean	Std. Deviation
Uterine Length	45 - 50	14	8.07	.616
	51 - 60	20	7.35	1.981
	> 60	16	5.25	.931
	Total	**50**	**6.88**	**1.803**
Uterine Width	45 - 50	14	4.21	.893
	51 - 60	20	3.95	1.905
	> 60	16	2.81	.403
	Total	**50**	**3.66**	**1.423**
Endometrium Thickness	45 - 50	14	7.57	3.480
	51 - 60	20	4.60	2.927
	> 60	16	1.88	.619
	Total	**50**	**4.56**	**3.406**

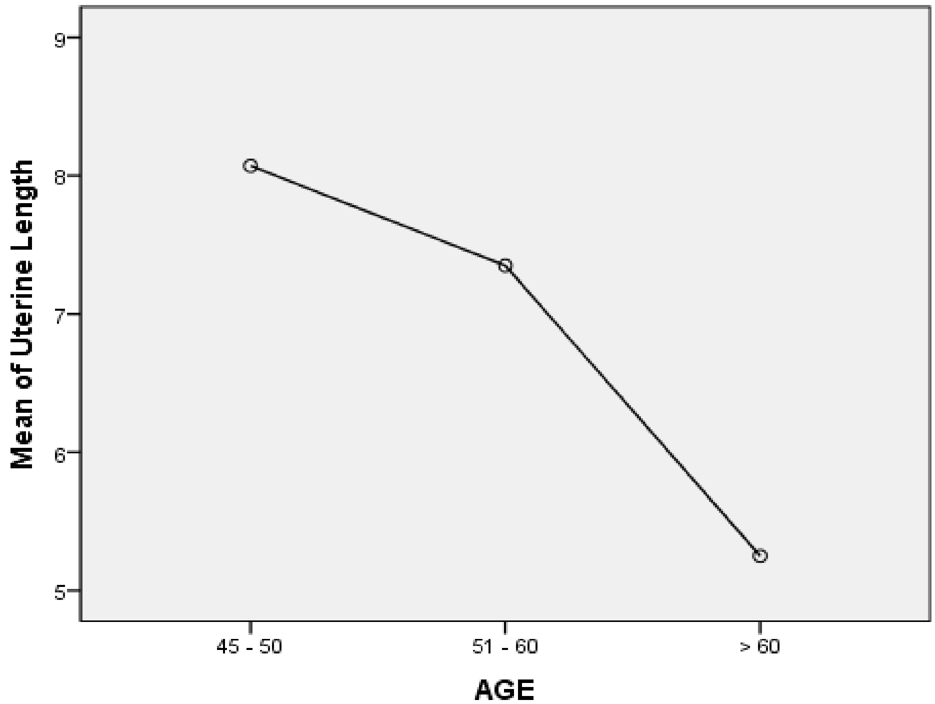


Figure 4.5 Plot of mean of uterine length in age groups

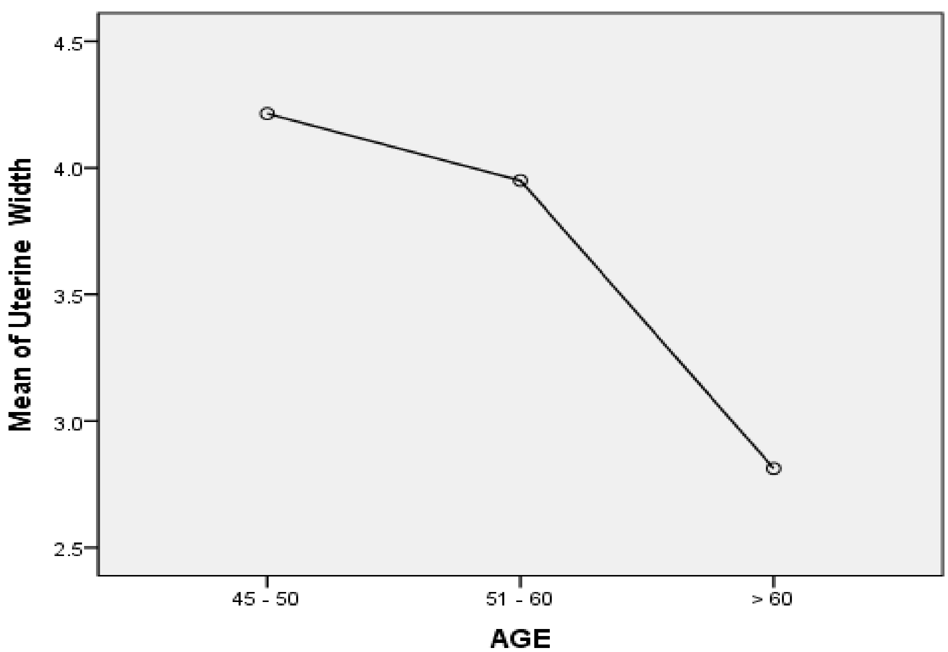


Figure 4.6 Plot of mean of uterine width in age groups

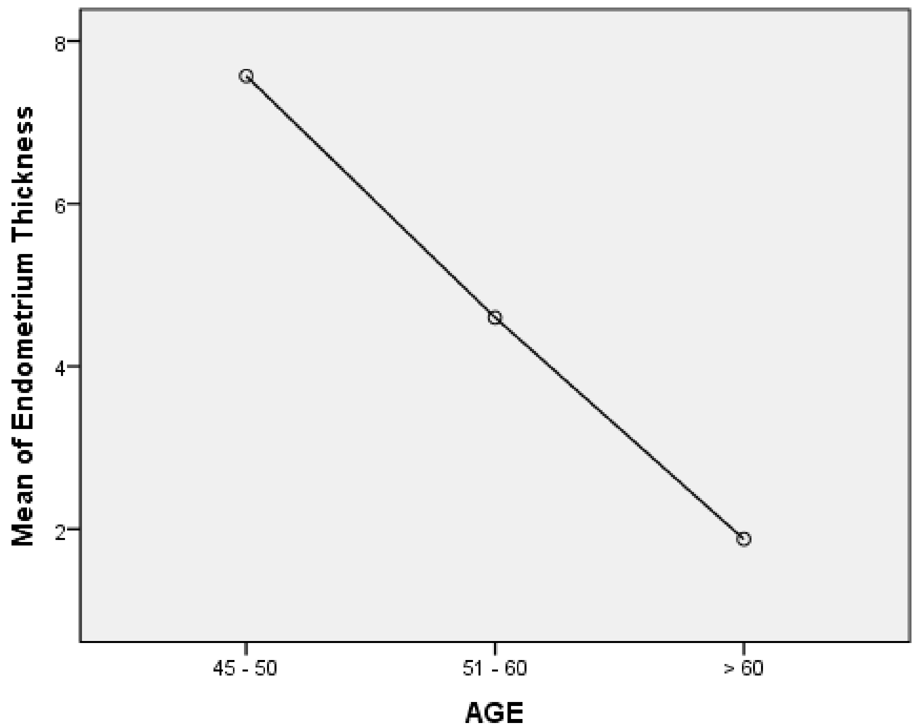


Figure 4.7 Plot of mean of endometrial thickens in age groups

Table 4.7: Analysis of variance among uterine measures

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
Uterine Length	Between Groups	66.801	2	33.401	16.975	.000
	Within Groups	92.479	47	1.968		
	Total	**159.280**	**49**			
Uterine Width	Between Groups	17.475	2	8.738	5.024	.011
	Within Groups	81.745	47	1.739		
	Total	**99.220**	**49**			
Endometrium Thickness	Between Groups	242.341	2	121.171	17.471	.000
	Within Groups	325.979	47	6.936		
	Total	**568.320**	**49**			

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion:

In this study which aimed to assess the endometrial thickness in postmenopausal women, a total of 50 women were investigated. Most of them 20 (40.0%) in age group 51-60 years, followed by 16 (32.0%) in age group >60 years and 14 (28.0%) in age group 45-50 years (Table 4.1).

Pelvic pain was the most clinical presentation among 43 (86.0%) women in this study, while 7 (14.0%) women presented with vaginal bleeding (Table 4.3). In this study, to ultrasound findings showed that the majority of women 43 (86.6%) had normal ultrasound findings, while 7 (14.0%) had abnormal ultrasound findings (Table 4.4).

Uterine measurements among the study population showed that the minimum uterine length was 3(mm), maximum 13 mm with mean 6.88 ± 1.80 mm. The minimum uterine width was 2 mm, maximum 10 mm with mean 3.66 ± 1.42 mm. The minimum endometrium thickness was 1 mm, maximum 18 mm with mean 4.56 ± 3.40 mm (Table 4.5).

In this study, the uterine measurements in different age of postmenopause were obtained; it showed that the mean of uterine length was 8.07 ± 0.616 mm in age group 45-50 years, the mean of uterine length was 7.35 ± 1.981mm in age group 51-60 years, while the mean of uterine length was 5.25 ± 0.93mm in age group > 60 years. The mean of uterine width was 4.21 ± 0.893 mm in age group 45-50 years, the mean of uterine width was 7.35 ± 1.981mm in age group 51-60 years, while the mean of uterine width was 5.25 ± 0.93mm in age group > 60 years.

The mean of endometrium thickness was 7.57 ± 3.480 mm in age group 45-50 years, the mean of endometrium thickness was 4.60 ± 2.927 mm in age group 51-60 years, while the mean of endometrium thickness was 1.88 ± 0.619 mm in age group > 60 years. The endometrial thickness of more than 5mm was observed in age group (45-50) and starts to decrease with increasing age as shown in the plot of mean (figure 4-7). This result was in line with the previous studies (Zalud et al., 1993).

Similarly to previous studies, our results suggest that there is no evidence supporting routine screening for asymptomatic endometrial thickening, and instead suggest the possibility of a risk of over-diagnosis in postmenopausal women with an endometrium ≥ 5 mm identified as abnormal without considering other risk factors (Goldstein, 2010, Obstetricians and Gynecologists, 2009).

5.2. Conclusion:

- Transvaginal/transabdominal ultrasound is superior to the abdominal in the detection of endometrial thickness; it is highly sensitive, not invasive and easy to perform by expert personals.
- The average thickness of endometrium in asymptomatic post- menopausal women was decreased with advance of age.
- There was statistically significant relation between age group and endometrium thickness.

5.3 Recommendations:

- Routine ultrasound should be performed for post-menopause women, so as to evaluate endometrial thickness and uterine abnormalities, early diagnosis and management.
- Availability of ultrasound units at health centers especially in peripheral areas.
- Awareness should be increased among menopause women about ultrasound and its role in detected uterine abnormities.
- Introduction of transvaginal ultrasounds with sufficient training for the staff.

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Appendices

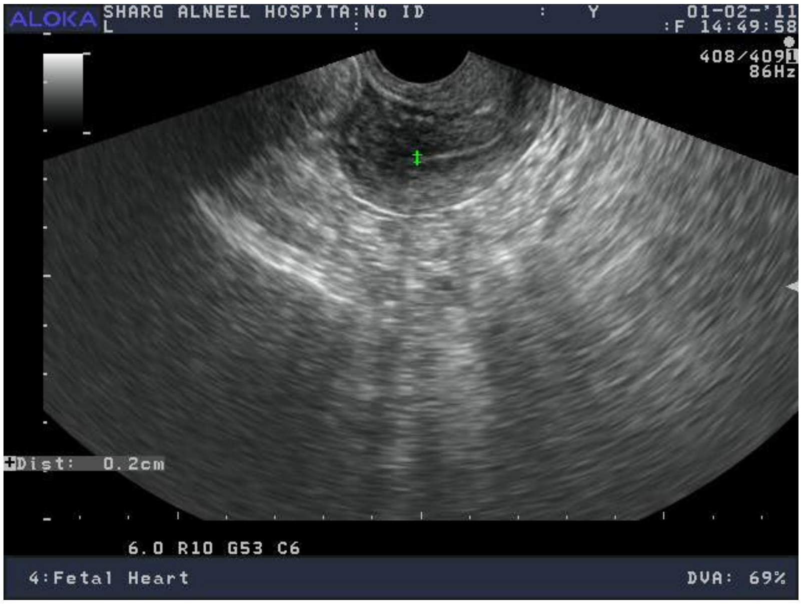

Image No. (1): Illustrate gray scale of, transvaginal scan, sagittal view of 54 years old postmenopausal woman, normal scan. Endometrial thickness 2mm.

Image No. (2): Illustrate gray scale of, transvaginal scan, sagittal view of 51 years old on HRT. Endometrial thickness 2 mm.

Image No. (3): Illustrate gray scale of, transvaginal scan, sagittal view of 58 year old. endometrial thickness 3mm.

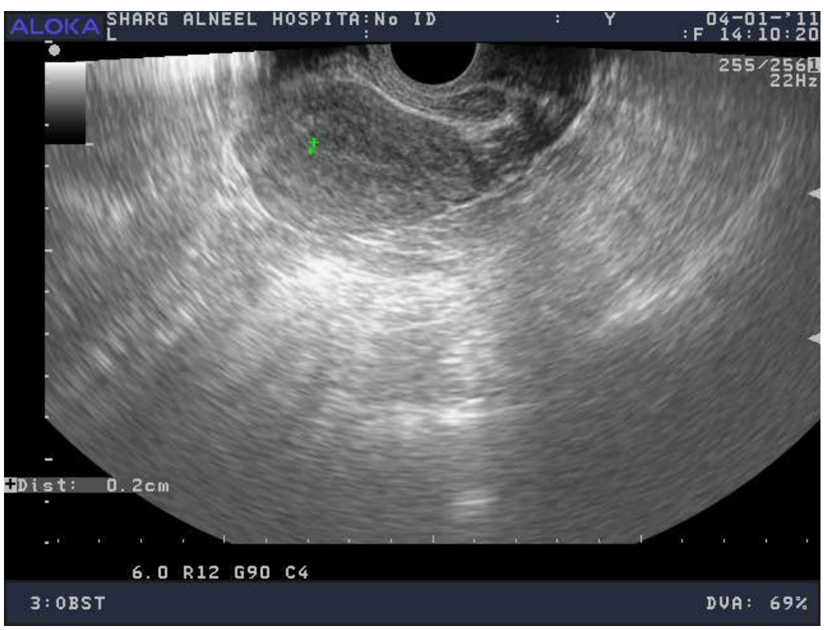

Image No. (4): Illustrate gray scale of, transvaginal scan, sagittal view of 55 year old. Normal scan, endometrial thickness 2mm.

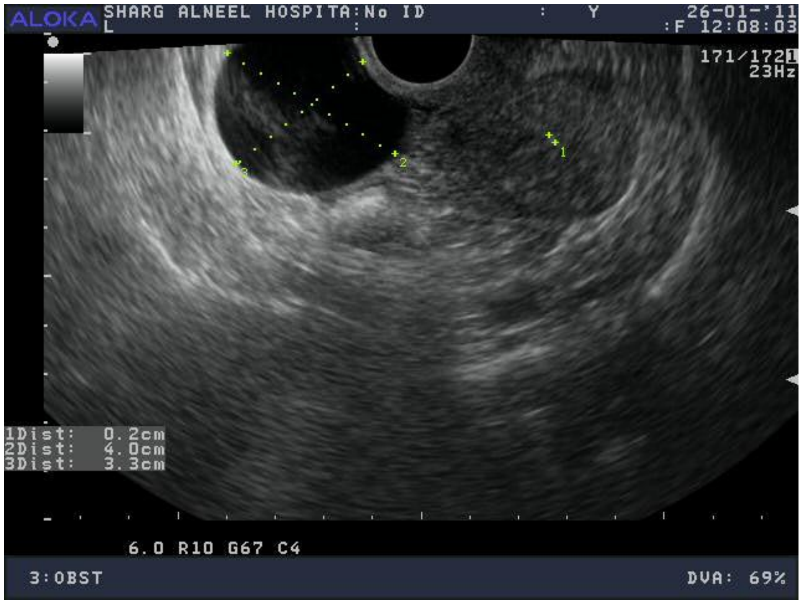

Image (5): Illustrate gray scale of, transvaginal scan, sagittal view of 58 year old woman with adenxial cyst, endometrial thickness 2mm.

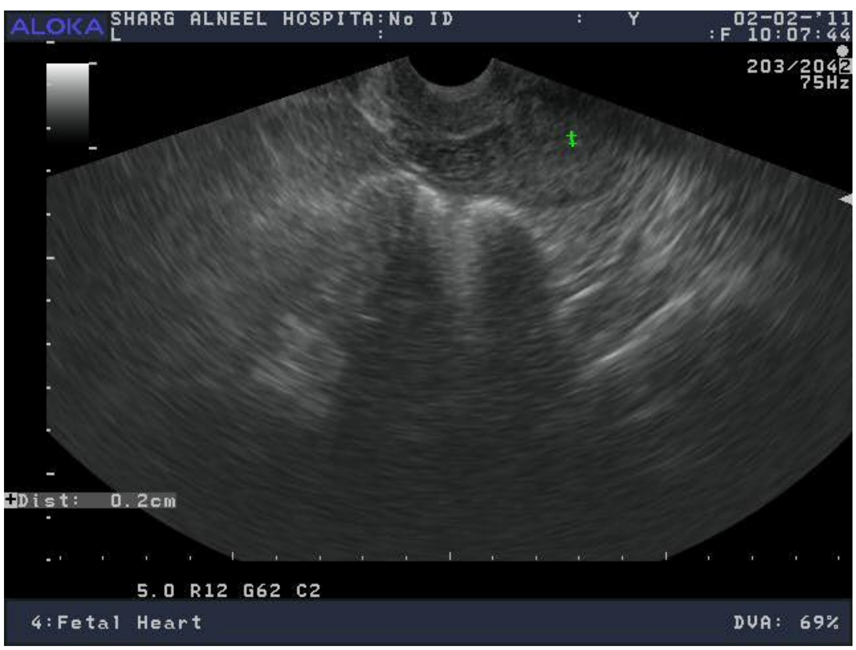

Image (6): Illustrate gray scale of, transvaginal scan, sagittal view of 60 year old. Normal scan, endometrial thickness 2 mm.

Image (7): Illustrate gray scale of, transvaginal scan, sagittal view of 51 year old with fundal fibroid, endometrial thickness 2 mm.

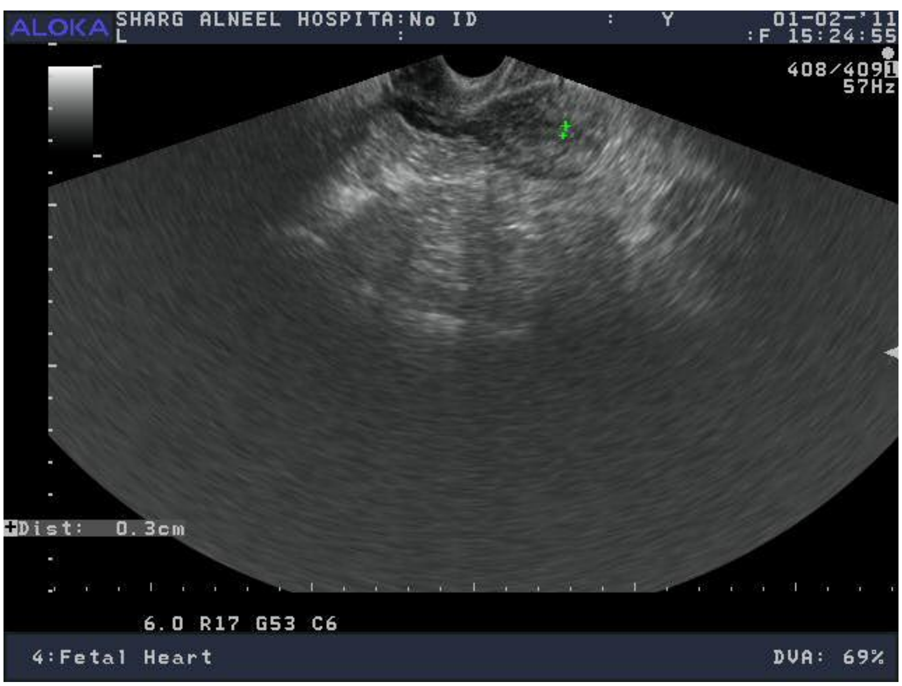

Image (8): Illustrate gray scale of, transvaginal scan, sagittal view of 53 year old woman, normal scan, and endometrial thickness of 3mm.

Faculty of Graduate Studies and Scientific Research

Data Collection Sheet

Assessment of Endometrial Thickness in Asymptomatic Postmenopausal Sudanese Women by Transvaginal Scan

- **Date** …………….. **Serial No.** ……………….

Personal Data:

- **Name**……………………………………. Telephone…………………………

A- Age (in years):

1- 50 – 55 ☐
2- 56 – 60 ☐
3- 61 – 65 ☐
4- >65 ☐

B- Geographical Area:

1- North ☐
2- East ☐
3- West ☐
4- South ☐
5- Central ☐

C- Residence ……………………………………………………………

D- Parity:

1- Nulliparous ☐
2- Multiparous ☐
3- Grandmultiparous ☐

E- Occupation:

1- Employee ☐
2- Worker ☐
3- Not Employee ☐

F- History of Receiving Hormonal Replacement Therapy :

1- Yes ☐
2- No ☐

G- Smoking :

1- Yes ☐
2- No ☐

<u>Ultrasound Finding:</u>

H- Endometrial Thickness ☐ mm

I- Associated Pelvic Pathology:

1- Uterine Fibroid ☐
2- Endometrial polyp ☐
3- Adnexial Mass ☐
4- Pelvic Inflammatory Disease (PID) ☐
5- No Pelvic Pathology ☐