

Chapter One

1.1 Introduction:

The Ultrasound is one of the first modalities used in the radiologic work-up of endometrial disease, the use of multiple imaging modalities is common. Radiologists must take into account the patient's age, stage in the menstrual cycle, and pregnancy status and whether she has undergone hormonal replacement therapy or tamoxifen therapy, in addition to clinical history and physical examination findings, to make an accurate diagnosis.

The uterus lies between the bladder and rectum, it is a muscular pear-shaped structure measuring 7.5cm in length, 5cm in width and 2.5cm in thickness.

The uterus has several stages of development

- 1-fetus (in foetus): the cervix is larger than body.
- 2-puberty the uterus attains the classic pear shape and the body larger than cervix.
- 3-adult: the body is twice the length of the cervix.
- 4-postmenopausal: the uterus becomes atrophied and fibrous.

The uterus consists of three tissue layers (inner to ---- outer) endometrium, myometrium and serous.

1.1.2 Tamoxifen (nolvadex):

* Tamoxifen has been used for over 40 years old to treat breast cancer that are hormone receptor positive . Hormone receptor positive breast cancers need the hormone estrogen (and/or progesterone) to grow.

*Tamoxifen use to slow or stop the growth of tumour cells.

*Tamoxifen can be use to treat breast cancer in both permenopausal and postmenopausal women and men.

1.1.3 Treatment with tamoxifen lowers the risk of:

- 1- Breast cancer recurrence.
- 2- Breast cancer in the opposite breast.
- 3- Death from breast cancer.

Tamoxifen is apill taken every day for at least five years the benefits from it tamoxifen last long after you stop taking it.

Ultrasound can detect the early change in endometrium thickness better than biopsy.

1.2 Problems of the study:

The tamoxifen use to treat the breast cancer, the thickness of endometrium of breast cancer patients needs to be evaluate by ultrasound to detect the change during treatment by tamoxifen.

As well as the tamoxifen usually associated by side effect ,there for the evaluation of these, therefore the evaluation of these side effects by using ultrasound will alleviate many problems that might be associated with this practices and hence improving the quality of the health life of the patients.

1.3 Objective

Evaluation and check the uterine cavity of patients of cancer.

- 1- To know the early change in uterus.
- 2- To improve the health of patients.
- 3-To determine the beginning of change in endometrium thickness during treatment.

1.4 Overview of the study:

This study will falls into five chapters, with chapter one is an introduction, which include the problem of the study, objectives and overview, Chapter two will include literature review while Chapter three include methodology which discusses the material used and the method of data collection including the method of data analysis, Chapter four

include data presentation and finally, Chapter five will include discussion, conclusion and recommendation.

Chapter Two

Section one

2.1 Anatomy:

2.1.1 The female reproductive organs:

The uterus is a dynamic female reproductive organ that is responsible for several reproductive functions, including menses, implantation, gestation, labor, and delivery. It is responsive to the hormonal milieu within the body, which allows adaptation to the different stages of a woman's reproductive life. The uterus adjusts to reflect changes in ovarian steroid production during the menstrual cycle and displays rapid growth and specialized contractile activity during pregnancy and childbirth. It can also remain in a relatively quiescent state during the prepubertal and postmenopausal years. (Norman C Smith et al 2006)

2.1.2 Embryology:

The embryonic origin and development of the uterus is relatively complex. Until approximately 8 weeks' gestation, primordia for both male and female internal genitalia—the mesonephric (Wolffian) and paramesonephric (Mullerian) ducts, respectively—coexist in the embryo. The sexual differentiation process involves multiple steps in which hormonal signals, growth factors, and specific genetic influences are required. (Ritchard S snell 1995).

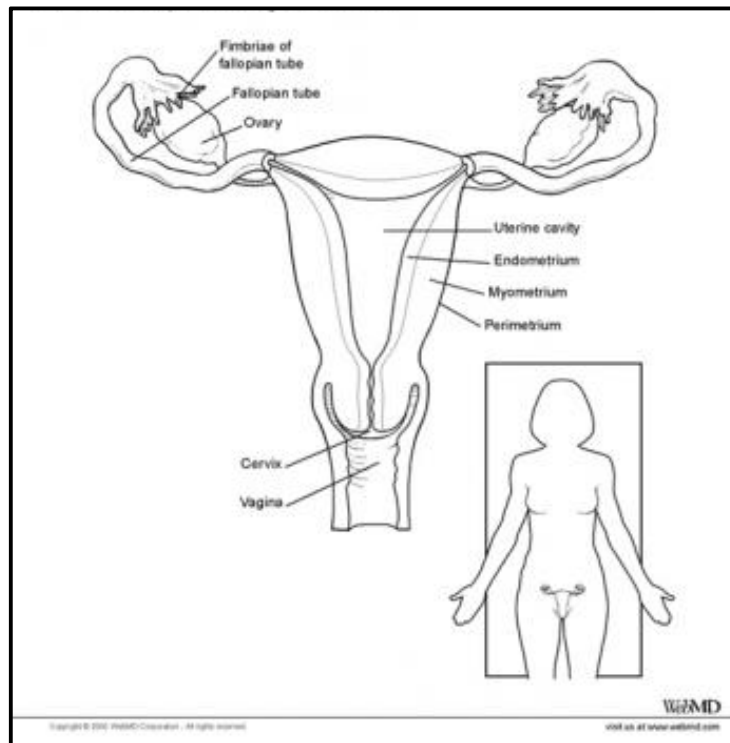
In the female embryo, due to the absence of a Y chromosome and lack of exposure to testosterone from functional testicular tissue, the normal developmental sequence of events results in fusion and canalization of the paramesonephric (Mullerian) ducts in the midline pelvis to form the female pelvic organs. Meanwhile, regression of the mesonephric (Wolffian) ducts occurs. Abnormalities in this process may occur during embryogenesis, which can result in the range of known paramesonephric anomalies. (Nalboff KM ET AL 2001).

The anatomy of the uterus consists of the following 3 tissue layers .

The inner layer, called the endometrium, is the most active layer and responds to cyclic ovarian hormone changes; the endometrium is highly specialized and is essential to menstrual and reproductive function

The middle layer, or myometrium, makes up most of the uterine volume and is the muscular layer, composed primarily of smooth muscle cells

The outer layer of the uterus, the serosa or perimetrium, is a thin layer of tissue made of epithelial cells that envelop the uterus .(Richard Ssnell 1995).



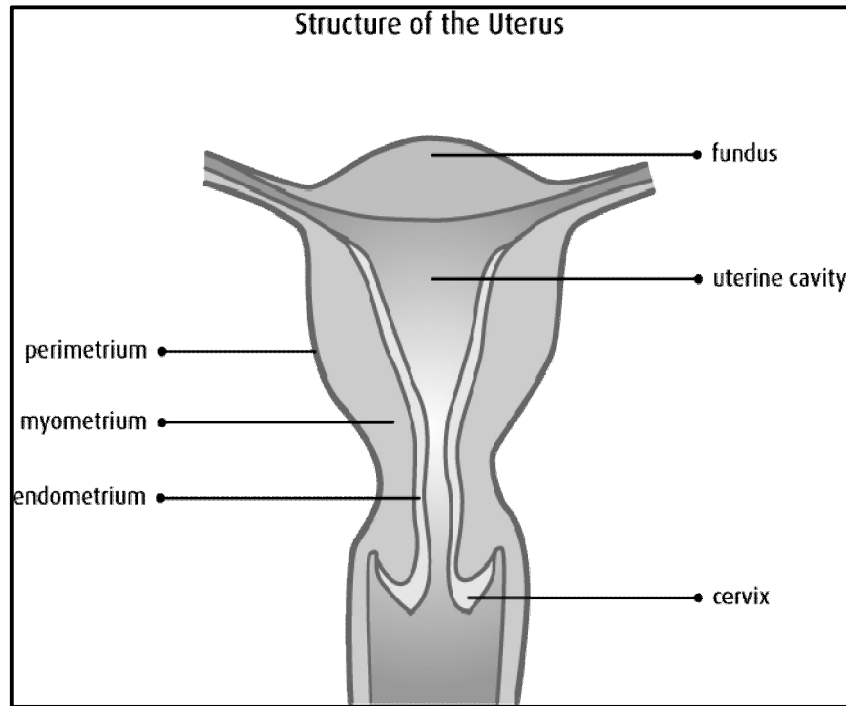
Graph (2.1) Female reproductive system

2.1.3 Structure

The uterus is a hollow, muscular organ that is shaped like an inverted pear. It has 3 parts:

- fundus (top)
- body (the main parts of the uterus, including the uterine cavity)
- cervix (lower, narrow part).(Carol A.Kerbs et al 1993).

The uterus is located above the vagina, above and behind the bladder and in front of the rectum. It is about 7 cm long and 5 cm wide (at the widest point).



Graph (2.2) Structure of the uterus

2.1.4 Function:

The uterus receives a fertilized egg (ovum) and protects the fetus (baby) while it grows and develops. The uterus contracts to push the baby out of the body during birth.

Every month – except when a woman is pregnant or has reached menopause – the lining of the uterus is shed through the cervix, into the vagina and out of the body. This is called menstruation.

The normal endometrium changes in appearance as well as in thickness throughout the menstrual cycle:

In the menstrual and early proliferative phase it is a thin, brightly echogenic stripe comprising of the basal layer .(Carol A .Kerbs et al 1993).

In the late proliferative phase it develops a trilaminar appearance: outer echogenic basal layer, middle hypoechoic functional layer, and an inner echogenic stripe at the central interface.

In the secretory phase it is at its thickest and becomes uniformly echogenic, as the functional layer becomes oedematous and isoechoic to the basal layer.

The postmenopausal endometrium should be smooth and homogeneous in normal range of endometrial thickness.

2.1.5 Premenopausal:

In premenopausal patients, there is significant variation at different stages of the menstrual cycle.

- during menstruation 1,4: 2-4 mm
- early proliferative phase (day 6-14): 5-7 mm

- late proliferative-pre ovulatory phase: up to 11 mm
- secretory phase: 7-16 mm

Following dilatation and curettage or spontaneous abortion: <5 mm, if it is thicker consider retained products of conception.(Syed Amir Gilani)

2.1.6 Postmenopausal:

Will depend on the whether or not there is a history of vaginal bleeding, and on the use of hormonal therapy / tamoxifen.

2.1.7 Vaginal bleeding (and not on tamoxifen):

Suggested upper limit of normal is <5 mm 5 risk of carcinoma is 7% if endometrium is >5 mm and 0.07% if endometrium is <5 mm 8 on hormonal replacement therapy: upper limit is 5 mm no history of vaginal bleeding:

Acceptable range of endometrial thickness is less well established in this group, cut-off values of 8-11 mm have been suggested risk of carcinoma is 7% if the endometrium is >11 mm, and 0.002% if endometrium is <11 mm 8 if on tamoxifen 3: <6 mm (although 50% of those receiving tamoxifen have been reported to have a thickness of >8 mm 7).

Abnormally thickened endometrium on imaging may occur for a number of reasons which may be categorised by whether or not they are related to pregnancy. Aetiologies may also be classified by whether the patient is premenopausal or postmenopausal.(Carol A. Kerbs et al 1993)

Pregnancy related: early pregnancy, prior to sac being visualized (<5 weeks of gestation); ectopic pregnancy; retained products of conception: heterogeneously thickened endometrium, with increased vascularity; intra-uterine blood clot: heterogeneous endometrium with no vascularity.

Molar pregnancy: thickened with multiple small cystic spaces; recent gestational state (delivery); endometritis; Non-pregnancy related. Endometrial carcinoma: variable appearance; endometrial hyperplasia: usually uniformly hyperechoic and tends to be diffuse; endometrial polyp: usually hyperechoic, often focal, look for vascular stalk. (Carol A. Kerbs et al 1993)

Tamoxifen related endometrial changes: variable appearance; hormone replacement therapy (HRT) related in postmenopausal female; endometritis; ovarian tumours associated with endometrial thickening

Endometrioid carcinoma of the ovary; granulosa cell ovarian cancer

Practical points: endometrial thickness in the secretory phase (days 14-28) may normally be up to 12-16 mm (see: endometrial thickness); no emergent ultrasounds are optimally evaluated at day 5-10 of the menstrual cycle to reduce the wide variation in endometrial thickness; the thickest portion of the endometrium should be measured; if there is fluid in the uterine cavity, it should be excluded from the measurement, which

would be the sum of the two sagittal plane thicknesses 10% of endometrial carcinoma occurs in premenopausal women. (Carol A. Kerbs et al 1993)

2.1.8 Role of Ultrasound:

- To examine the uterus, ovaries, cervix, vagina and adnexae.
- Classification of a mass identified on other modalities eg solid, cystic, mixed.
- Post surgical complications eg abscess, oedema.
- Guidance of injections, aspiration or biopsy.
- Assistance with IVF.
- To identify the relationship of normal anatomy and pathology to each other. (Norman C. Smith et al 2006)

2.1.9 Indications:

- P/V bleeding/discharge
- Menorrhagia
- Metrorrhagia (irregular uterine bleeding)
- Polymenorrhea
- Menometrorrhagia (excessive irregular bleeding)
- Amenorrhea
- Oligomenorrhea
- Pelvic pain

- Dysmenorrhea (Painful Menses)
- F/H uterine or ovarian Cancer
- Palpable lump
- Infertility- primary or secondary (evaluation, monitoring and/or treatment)
- Anomalies/evaluation.
- Follow-up of previous abnormality
- Precocious Puberty, delayed menses or vaginal bleeding in a prepubertal child postmenopausal bleeding.
- Signs/symptoms of pelvic infection. IUCD Localization (intrauterine contraceptive Device)
- Guidance for interventional or surgical procedures urinary incontinence or pelvic organ prolapse. (Peter W. Callen 2008)

2.1.10 Limitations:

Transvaginal scanning is contra-indicated if the patient is not yet sexually active or cannot provide informed consent.

Large patient habitus will reduce detail, particularly via the transabdominal approach.

Excessive bowel gas can obscure the ovaries.

Patients who are unsuitable for transvaginal scanning but cannot adequately fill their bladder for an acoustic transabdominal window.

2.1.11 Common pathologies:

Endometrial

- Endometrial Polyps
- Endometrial Carcinoma
- Endometrial hyperplasia
- Endometritis
- Cystic hyperplasia secondary to Tamoxifen
- Adhesions- Ashermans Syndrome
- Submucosal fibroids
- Arterio-venous malformation (AVM)
- Hydro/haematometra blood/fluid/infection or retained products of conception (RPOC). (Peter W. Callen 2008)

Chapter TWO

Section Two

2.2 Previous study:

2.2.1 Tamoxifen:

Tamoxifen a nonsteroidal antiestrogen, is the endocrine therapy of choice for all stages of breast cancer. Because tamoxifen is well tolerated and has minimal side effects, it is currently being evaluated in large scale trials as a chemopreventive agent for women at risk for developing breast cancer. The potential adverse effects of tamoxifen, specifically the development of proliferative lesions of the endometrium, coupled with the prospect of its wider use, places new emphasis on recognizing tamoxifen-associated histologic and cytologic changes in the female genital tract. (Ascher SM et al 2000)

Nolvadex (tamoxifen citrate) is a nonsteroidal antiestrogen used to treat breast cancer that has spread to other parts of the body (metastatic breast cancer), to treat breast cancer in certain patients after surgery and radiation therapy, and to reduce the chances of breast cancer in high-risk patients. Common side effects of Nolvadex include hot flashes, flushing, changes in menstrual periods, nausea, leg cramps, abdominal cramps, bone pain, muscle pain, cough, swelling, fatigue, hair thinning, headache, depression, and loss of sexual ability/interest in men.

The recommended daily dose of Nolvadex for patients with breast cancer is 20-40 mg per day, in tablet form. Patients taking anastrozole or letrozole should not take Nolvadex as serious interactions could occur.(Barkat RP et al 1999).

2.2.2 Treatment with tamoxifen lowers the risk of:

- Breast cancer recurrence.
- Breast cancer in the opposite breast.
- Death from breast cancer.

Tamoxifen is a pill taken every day for at least five years the benefits from it tamoxifen last long after you stop taking it. (Gibso LE et al 1995)

Increased bone and tumor pain and, also, local disease flare have occurred, which are sometimes associated with a good tumor response. Patients with increased bone pain may require additional analgesics. Patients with soft tissue disease may have sudden increases in the size of preexisting lesions, sometimes associated with marked erythema within and surrounding the lesions and/or the development of new lesions. When they occur, the bone pain or disease flare are seen shortly after starting NOLVADEX (tamoxifen citrate) and generally subside rapidly.

In patients treated with NOLVADEX (tamoxifen citrate) for metastatic breast cancer, the most frequent adverse reaction to NOLVADEX (tamoxifen citrate) is hot flashes.(Gibso LE et al 1995)

Other adverse reactions which are seen infrequently are hypercalcemia, peripheraledema, distaste for food, pruritus vulvae, depression, dizziness, light-headedness, headache, hair thinning and/or partial hair loss, and vaginal dryness. (Gibso LE et al 1995)

Tamoxifen has been utilized for almost three decades as an adjuvant treatment for breast cancer, and also is effective in the chemoprophylaxis of this disease. However, this drug presents endometrial proliferation as a side effect, with a low, but real, risk for the development of endometrial cancer. This risk is of almost two cases of cancer for every 1000 women under tamoxifen therapy during a year, similar to the postmenopausal women submitted to single-dose hormone replacement therapy. Studies have demonstrated that the majority of cases of endometrial cancers in women under tamoxifen therapy were found at their early stages, and the treatment has been successfully instituted; however, in women who have developed endometrial cancer whose diagnosis was made at later stages, the prognosis has been poorer.(Fung MFK et al 2003)

Tamoxifen has pro-oestrogenic effects on the endometrium and is associated with a number of pathologies. It is associated with an increased prevalence of endometrial hyperplasia: can occur in 1-20% of women treated ref endometrial polyps: can occur in 8-36% of women in treated ref endometrial carcinomacystic endometrial atrophy (AmirRezae and Radswiki et al 2001).

2.2.3 Radiographic features:

Ultrasound

Tamoxifen may cause the endometrium to appear thickened, irregular, and cystic. Changes tend to be subendometrial in location and cause subendometrial cysts that can be demonstrated at ultrasound.

Most patients tend to have a multiplicity of findings. According to one study, 50% of sonograms in those on Tamoxifen revealed an endometrial thickness of 8 mm or more .

It has also been reported that the degree of endometrial thickening corresponds to the duration of Tamoxifen therapy.(Fung MFK et al 2003)

Chapter Three

Methodology

3.1 Population of the study:

The present study was developed in period between 2014 -2015 ,including patients under tamoxifen therapy for breast cancer ,and presenting with endometrial thickening $>5\text{mm}$.

3.2 Study sample:

The study group consisted of fifty (50) patients, was taken as case study.

3.3 Material:

- Thesonographic examination performed with a high resolution real time scanner (Siemevsacuson cv70) with a 3.5 MHz convex transducer.
- Gel
- Tissues

3.4 Method:

By measurement the thickness of endometrium of breast cancer patients whose treated by tamoxifen.

3.5 Method and technique:

The preparation of patient:

The bladder must be full in the transabdominal transducer. And the bladder must be empty in the transvaginal transducer.

Position of the patient:

The patient is usually scanned while lying comfortable on her back (supine).

Scanning technique:

The scanning should be done in both longitudinal and transverse scans, turn the patient obliquely (30-40 degrees) if necessary .each ovary requires careful scanning in different planes.

3.6 Equipment Selection and Technique:

Transabdominal approach initially. Use the highest frequency probe to gain adequate penetration. This will be between a 2-7MHz range curved linear array or sector probe with Colour Doppler capabilities.

Transvaginal probe 4-7MHz.

If possible, scan the patient in the first 10 days of the cycle. Preferably Day 5-10 for improved diagnostic accuracy in the assessment of the endometrium and ovaries.

A full bladder is required . Instruct the patient to drink 1 Litre of water to be finished 1 hour before and they cannot empty their bladder before the scan.

The patient empties their bladder before the transvaginal scan is started.

3.7 Scanning technique:

Trans-abdominal approach:

- This is a generalised overview to identify the cervix, uterus and ovaries.
- Check for the orientation the uterus (anteverted V's retroverted)
- Assess the uterine size and shape.
- Assess the myometrium
- Assess the endometrial status and measure the thickness: <10mm pre menopausal; <4mm post menopause or ,<6mm if post menopausal on HRT.
- Assess the cervix
- Look for free fluid in the pouch of douglas
- Check the ovaries and adnexae
- Assess bladder
- Scan sagittally in the midline immediately above the pubis. Heel the probe to get the bladder over the fundus of the uterus. In this plane you should be able to assess the uterus, vagina and cervix.

- Zoom the image to assess and measure the endometrial thickness.
- Rotate into transverse and angle slightly cranially to be perpendicular to the uterus. Whilst in transverse and slightly right of midline, angle left laterally to identify the left ovary using the full bladder as an acoustic window. Examine the ovary in two planes. Now repeat this for the right ovary.

Chapter Four

Results

Table (4.1):Age of patient

Cumulative Percent	Valid Percent	Percent	Frequency	
2.0	2.0	2.0	1	35.0 Valid
4.0	2.0	2.0	1	0
14.0	10.0	10.0	5	38.0
18.0	4.0	4.0	2	0
20.0	2.0	2.0	1	39.0
24.0	4.0	4.0	2	0
30.0	6.0	6.0	3	40.0
40.0	10.0	10.0	5	0
46.0	6.0	6.0	3	41.0
50.0	4.0	4.0	2	0
54.0	4.0	4.0	2	42.0
64.0	10.0	10.0	5	0
68.0	4.0	4.0	2	44.0
72.0	4.0	4.0	2	0
78.0	6.0	6.0	3	45.0
82.0	4.0	4.0	2	0
88.0	6.0	6.0	3	46.0
92.0	4.0	4.0	2	0
94.0	2.0	2.0	1	47.0
96.0	2.0	2.0	1	0
100.0	4.0	4.0	2	48.0
	100.0	100.0	50	0
				49.0
				0
				52.0
				0
				53.0
				0
				55.0
				0
				59.0
				0
				60.0
				0
				62.0
				0
				68.0
				0
				69.0
				0
				70.0
				0
				Total
				1

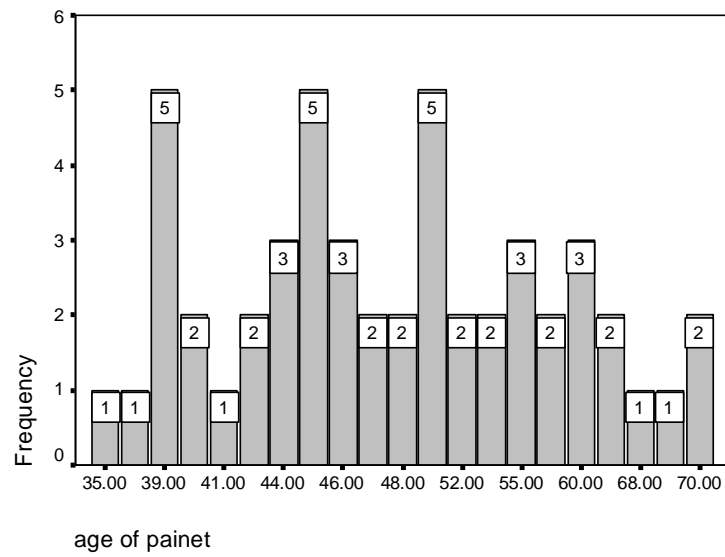


Figure (4.1):Age of patient

Table (4.2): pathology of disease

Cumulative Percent	Valid Percent	Percent	Frequency	Valid
60.0	60.0	60.0	30	adenocarcinoma
82.0	22.0	22.0	11	squamous cell
100.0	18.0	18.0	9	epithial
	100.0	100.0	50	Total

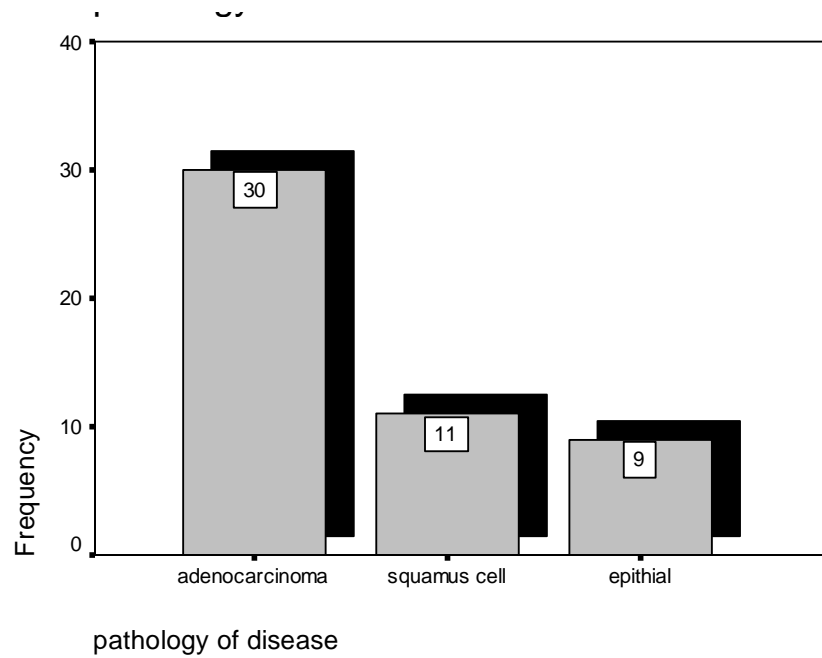


Figure (4.2):Pathology of disease

Table (4.3): metastatic of disease

Cumulative Percent	Valid Percent	Percent	Frequency	Valid
16.0	16.0	16.0	8	inbrain
32.0	16.0	16.0	8	Bone
40.0	8.0	8.0	4	Spine
100.0	60.0	60.0	30	None
	100.0	100.0	50	Total

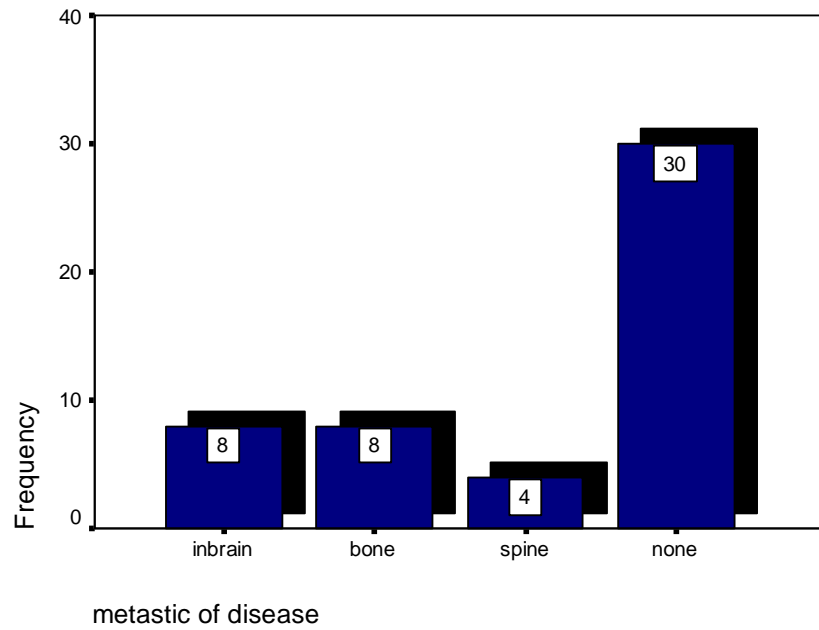


Figure (4.3): metasticof disease

Table (4.4): Duration of taking tamozifen

Cumulative Percent	Valid Percent	Percent	Frequency	Valid
8.0	8.0	8.0	4	8.00
10.0	2.0	2.0	1	10.00
20.0	10.0	10.0	5	12.00
26.0	6.0	6.0	3	15.00
28.0	2.0	2.0	1	18.00
34.0	6.0	6.0	3	19.00
44.0	10.0	10.0	5	20.00
50.0	6.0	6.0	3	21.00
70.0	20.0	20.0	10	24.00
78.0	8.0	8.0	4	29.00
80.0	2.0	2.0	1	31.00
90.0	10.0	10.0	5	36.00
94.0	4.0	4.0	2	44.00
100.0	6.0	6.0	3	48.00
	100.0	100.0	50	Total

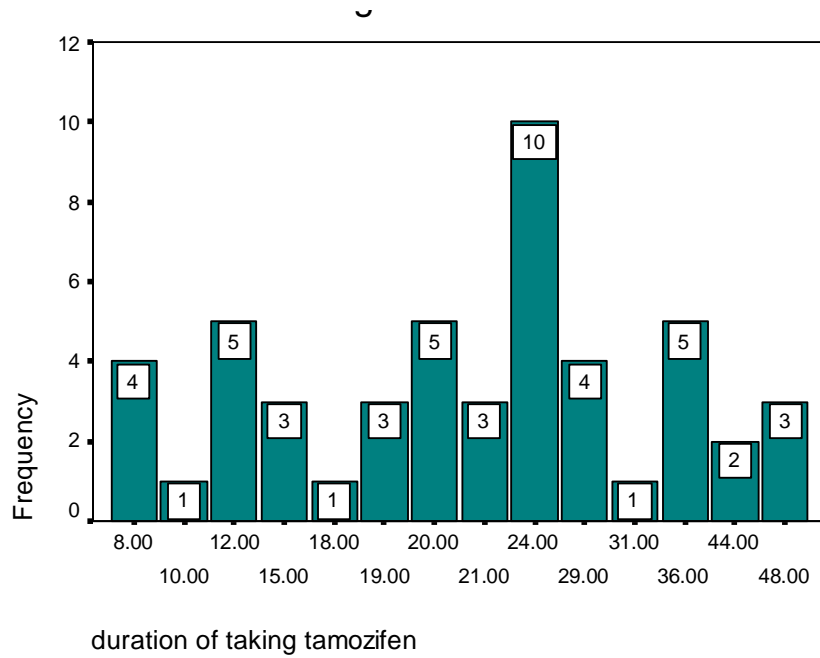


Figure (4.4): Duration of taking tamoxifen

Table (4.5): Thickness of endometrium in previous investigation

Cumulative Percent	Valid Percent	Percent	Frequency	Valid
20.0	20.0	4.0	2	7.00
40.0	20.0	4.0	2	8.00
70.0	30.0	6.0	3	9.00
100.0	30.0	6.0	3	10.00
	100.0	20.0	10	Total
		80.0	40	Missing
		100.0	50	Total

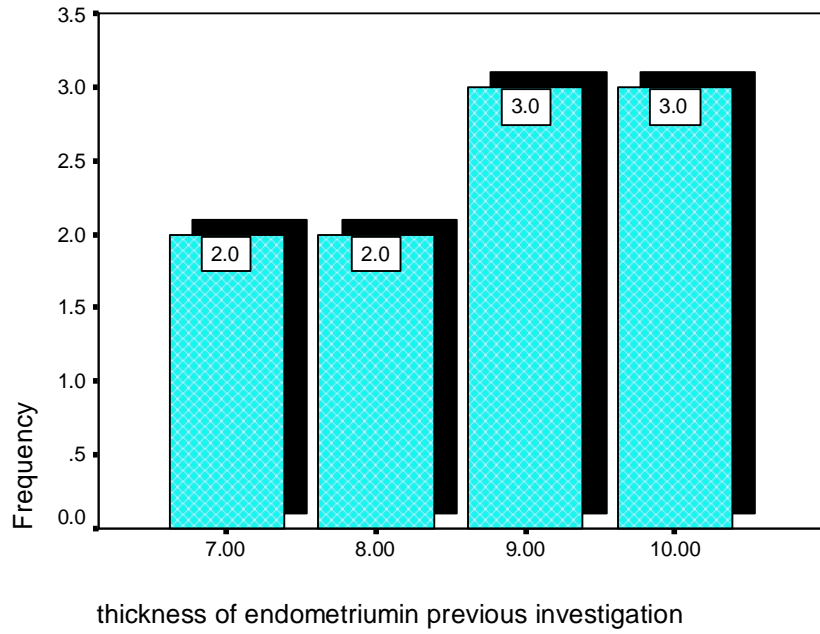


Figure (4.5): Thickness of endometrium in previous investigation

Table (4.6): Thickness of endometrial after treatment

Cumulative Percent	Valid Percent	Percent	Frequency	Valid
2.0	2.0	2.0	1	9.00
10.0	8.0	8.0	4	10.00
18.0	8.0	8.0	4	11.00
30.0	12.0	12.0	6	12.00
46.0	16.0	16.0	8	13.00
52.0	6.0	6.0	3	14.00
60.0	8.0	8.0	4	15.00
68.0	8.0	8.0	4	16.00
72.0	4.0	4.0	2	17.00
74.0	2.0	2.0	1	18.00
86.0	12.0	12.0	6	19.00
88.0	2.0	2.0	1	20.00
92.0	4.0	4.0	2	21.00
96.0	4.0	4.0	2	25.00
100.0	4.0	4.0	2	29.00
	100.0	100.0	50	Total

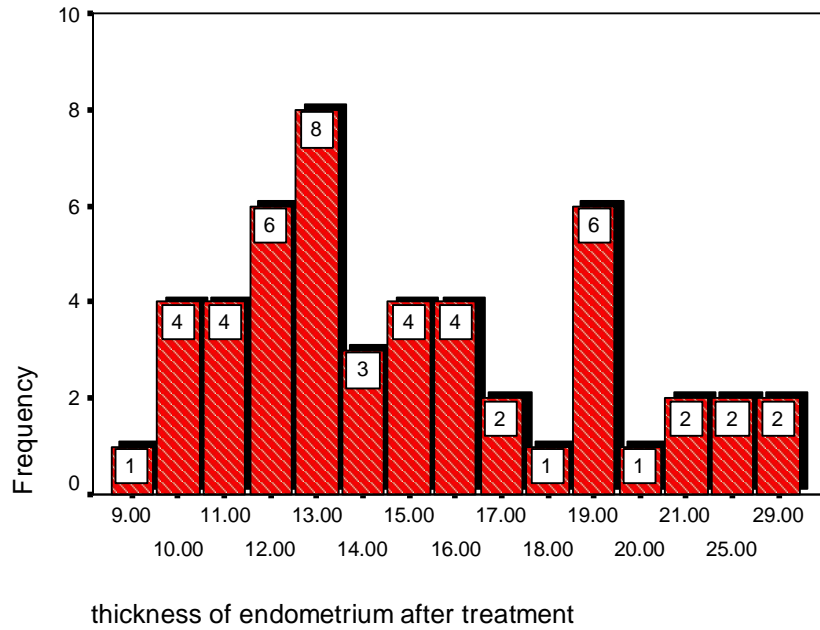


Figure (4.6):Thickness of endometrial after treatment

Table (4.7): One-Sample Test

95% Confidence Interval of the Difference		Test Value = 0				
		Mean Difference	Sig. (2-tailed)	Df	T	
Upper	Lower					
16.7580	14.0820	15.4200	.000	49	23.159	thickness of endometrium after treatment duration of taking tamoxifen
26.7701	20.5899	23.6800	.000	49	15.400	

Table (4.8):Correlations

duration of taking tamozifen	thickness of endometrium after treatment		
.878(**)	1	Pearson Correlation	thickness of endometrium after treatment
.000	.	Sig. (2-tailed)	
50	50	N	
1	.878(**)	Pearson Correlation	duration of taking tamoxifen
.	.000	Sig. (2-tailed)	
50	50	N	

** Correlation is significant at the 0.01 level (2-tailed).

ANOVA

Table (4.9):Thickness of endometrium after treatment

Sig.	F	Mean Square	df	Sum of Squares	
.000	22.258	74.307	13	965.997	Between Groups
		3.338	36	120.183	Within Groups
			49	1086.180	Total

Table (4.10): Paired Samples Test

Sig. (2- tailed)	df	t	Paired Differences					
			95% Confidence Interval of the Difference		Std. Error Mean	Std. Deviation	Mean	
			Upper	Lower				
.008	9	-3.419	-1.6576	-8.1424	1.43333	4.53260	-4.9000	thickness of endometrium in previous investigation - thickness of endometrium after treatment

Chapter Five

5.1 Discussion

The researcher selected the patient age range was 35 to 70 year old which showed the relation between age of patients and frequency demonstrated in table 4-1 and **Figure 4-1**.

In table 4.2 and **Figure 4.2** were presented the data for frequency of pathology of disease, the study found that the percentage of adenocarcinoma was 60% ,squamous cell was 22% , and epithial cell was 18%.

In table 4.3 and **Figure 4.3** were presented the data for frequency of metastatic disease ,the study found that the percentage of brain was 16%,bone was 16%, spine 8%, and none was 60%.

In table 4.4 and **Figure4.4** were presented the data for frequency of duration (in months) of taking tamoxifen, the study found that the percentage of 8moth-8%,10month -2,12 month -10%, 15 month -6%,18 month -2%,19 month -6%, 20 month -10%, 21 month -6%, 24 month -20%, 29 month -8%, 31 month -2%, 36 month 10%, 44 month -4%, 48 month -6%.

In table 4.5 and **Figure 4.5** were presented the data for frequency of thickness (in mm) of endometrium in previous investigation , the study

found that the percentage of 7mm -4%, 8mm -4%, 9mm -6%, 10mm -6%, and the missing cases 40% .

In table 4.6 and **Figure 4.6** were presented the data for frequency of thickness (in mm) of endometrium after tamoxifen treatment , the study found that the percentage of 9mm -2%, 10mm -8%, 11mm -8%, 12mm -12%, 13mm -16%, 14mm -6%, 15mm -8%, 16mm -8%, 17mm -4%, 18mm -2%, 19mm -12%, 20mm -2%, 21mm -4%, 25mm -4%, and 25mm -4%.

Table 4.7 (One sample test)

- H_0 mean null hypothesis or no relation between duration of taking tamoxifen and endometrial thickness.
- H_1 mean there is relation between duration of taking tamoxifen and endometrial thickness.

The result give T. test sig = 0.000, that mean there is high hypothesis, so we reject H_0 and accept H_1 because there is relationship between duration time of taking tamoxifen and endometrial thickness.

5.2 Conclusion

Patients who are being treated with tamoxifen require a rigorous endometrial management, because of the increased risk for development of endometrial cancer. Ultrasound should be recommended as an initial endometrial screening of breast cancer patients treated with tamoxifen, considering that the disease prognosis is highly dependent on an early diagnosis.

In case endometrial alteration suggesting neoplasm is found, hysteroscopy is required for direct visualization of the endometrial cavity as well as a guided-biopsy aimed at a definite diagnosis. Therefore, study should be performed in all of these cases, independently from the imaging findings special when the measurement above 10 mm. .

It is important to emphasize the need for an association between clinical symptoms and imaging findings as criteria for establishing the strategy for management of this group of patients.

5.3 Recommendations

- The monitoring of endometrium of the patient under the tamoxifen treatment is recommended at the early time by using Ultrasound.
- To analyses the main echotextural changes in the endometrium by means of ultrasound in group of patients under tamoxifen treatment for determining the abnormality that could occur in the uterine mucosa.
- Physicians should be aware of the higher risk of endometrial cancer in tamoxifen users

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Appendix (1)

Sheet of data collection

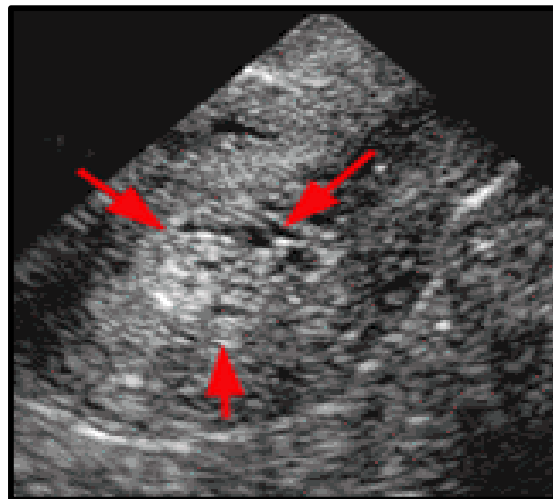
File Number of patient	
Age of patient	
Pathology of Disease	
Duration of taking tamoxifen	
Thickness of endometrium	
Previous investigation	
Thickness of endometrium after treatment	

Appendix(2) cases



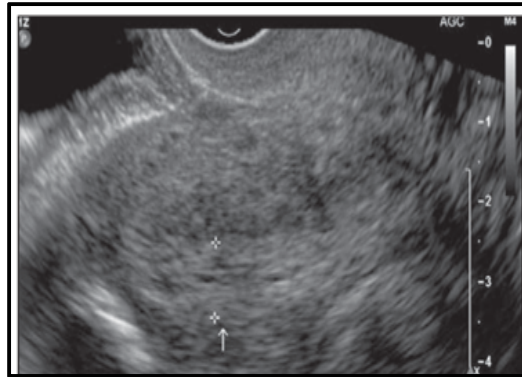
Case 1

Patient age 47 yrs , endometrial thickness 20mm



Case 2

Patient age 70 yrs, endometrial thickness 20mm



Case 3

Patient age 55 yrs , endometrial thickness 10mm



Case 4

Patient age 63 yrs , endometrial thickness 15mm