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Age Distribution of Breast Mass and Validity of Used Measures in Its Diagnosis at Breast Disease Clinic in Thi-Qar 2018.

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Abstract

Objective: of this study to study the effect of age and specific age groups in the distribution of breast mass in Thi-Qar, to determine the effect of most determinant factors included in obstetric history on that distribution, and to assess the validity of radiological investigations and FNA about histopathological diagnosis of breast masses for patients counseling breast disease clinic in Thi-Qar 2018.
Design: A cross sectional analytical design was used.
Patients: All women presented with breast mass at defined age, were included.
Results: The rate of malignancy increased with age; at ages >45 years about half of cases were malignant (47%), and constitute(57.4%) of the total malignancies, while the other ages categories of ≤ 45 years, the proportion of malignancy among cases of the same categories about (16%), and constitute (25%), (17%) for ages interval (30-45), (<30) respectively On other hand FNA are 82% specific and 96% sensitive compared to definitive histopathologic results in the diagnosis of breast masses.
Conclusion
The findings of the current work suggested that age was a strongly correlated factor and about 57.5% of the malignancies were above 45.
FNA are 82% specific and 96% sensitive in relation to definitive histopathologic results.
Keywords: Breast mass, validity of breast diagnostic measures.
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Introduction

Although most masses are benign, but on other hand breast cancer is the most common cancer in females worldwide and the commonest cause of cancer related death among females in developed and developing countries including Iraq. [1,2]

According to the American Cancer Society's the breast cancer is the most common cancer of women in USA, except for skin cancers, the average risk of a woman having breast cancer sometime in her life is about 12%. [3]

Breast cancer rates in Iraq were generally stable between 2000 to 2009, but newer data from the Iraqi Cancer Registry show rising rates since 2009 with women over 50 years; making the age as a major contribution to that increase. [4]

most women in whom invasive breast cancer is diagnosed do not have

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identifiable risk factors. [5] Risk factors with high relative risk (of >4.0) for breast cancer include [6,7,8,] female sex, increasing age (65 years), certain genetic mutations such as BRCA1 and/or BRCA2, two or more first-degree relatives with breast cancer diagnosed premenopausally and personal history of breast cancer.[8]

Other risk factors with lower relative risks (1.1 to 2.0) include age at first delivery (>30), early menarche (<12 years), late menopause (>55years), nulliparity, no history of breastfeeding, recent and long-term use of hormone replacement therapy with estrogen and progestin, obesity (postmenopausal), personal history of endometrial, ovary, or colon cancer, and alcohol consumption. [6,7,9]

The triple test is the combination of results from complete breast examination, imaging, and tissue sampling. Ultrasonography can efficiently distinguish solid masses from cysts.[10] Though ultrasonography is not regarded as a screening test, it is more sensitive than mammography in detecting lesions in women with dense breast tissue.[11] mammography is the primary breast imaging modality for the investigation of symptomatic women 35 years and over, for the follow-up of women with a previous diagnosis of breast cancer and the screening of asymptomatic women. When the three assessments are performed adequately and produce concordant results, the triple test diagnostic accuracy approaches near 100%. Discordant results or results that cannot be evaluated may indicate the need for excisional biopsy.[12,13]

1.2 The objectives were to study the effect of age and specific age groups in the distribution of breast mass in Thi-Qar, to determine the effect of most determinant factors included within an obstetric history on that distribution, and to assess the validity of radiological investigations and FNA in relation to histopathologicl diagnosis of breast masses at breast disease clinic in Thi-Qar 2018.

2. Materials and Methods

2.1Type of the study

This is a cross-sectional analytical hospital based study, conducted at Al-Hussein teaching hospital in Thi-Qar governorate. The duration of the study was extended from the first week of February 2018 to the second week of September 2018.

2.2 Population of the study

The study population includes all adult females having a breast mass attending or referred to the breast clinic and those were admitted for surgical wards in Al-Hussein teaching hospital. The cases were diagnosed depending on the examination by a general surgeon or a family physician experienced in breast diseases and then confirmed with radiological, cytological and or histopathological investigation.

2.3 Criteria for Inclusion and Exclusion

The study including all adult women presenting with breast mass or was discovered accidentally for breast clinic, surgical wards in Al-Hussein teaching hospital within the time of the study with age $\geq$ 18. Male gender, female patients presenting with other symptoms rather than mass, less than 18 and defaulters were excluded from the study.

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2.4 Ethical consideration

Necessary permissions were obtained from the Thi-Qar Health Directorate, breast clinic, pathological and histological units in Al Hussein teaching hospital. Consent was also taken from all participants.

2.5 Tools of study:

- **2.5.1 The questionnaire** Data collection was done by using a pre-designed pre- studied Performa.
- **2.5.3 Diagnostic procedure** was mainly done based on triple assessment including clinical examination of mass then radiological investigations (ultrasound and or mammography) confirm the diagnosis with cytological and or histopathological diagnosis, (wherein 19% of patients there isn't histopathological confirmation and only diagnosed with FNA as its mostly inflammatory or cystic lesion and disappear with aspiration where the patients followed).

3. Results

3.1 Different ages categories

3.1.1 . Age at the diagnosis:

Table (3.1) shows the relationship of different age categories and the type of tumor, about 1/2 of the studied population were at age interval of 30-45, the other half concluded <30 and >45. The relation appears significant statistical association with p-value of (0.001) and confirmed with statistical correlation. The rate of malignancy increased with age; at ages >45 years about half of the cases were malignant (47%), and constitute(57.4%) of the total malignancies, while the other ages categories of ≤ 45 years, the proportion of malignancy among cases of the same categories about (16%), and constitute (25%), (17%) for ages interval (30-45), (<30) respectively (Table 3.1).

3.1.2. Age at marriage:

For those married at <20 y age group the proportion of malignant masses was (55%) of the total malignancy, (25%) for at 20-30 years, and (6%) for those married after 30, table (3-2) but the highest proportion of malignancy (33.3%) among breast masses for those married at age > 35 but the relation showed non-significant statistical value for that association. (Table 3.1).

3.1.3. Age at first birth

Even non-significant association with the type of tumor but the proportion of malignancy among the total cases raising slowly (26.3%, 27.3%, and 39%) for those having a first child at ages interval (<20, 20-30 and >30) respectively **(**Table 3.1).

3.1.4. Age of menarche: Most common ages for menarche from the studied population were at interval (12-14) about 74.5% , the proportion of malignancy to the total masses for the same interval was at < 11 years and the relation are non-statically related. (Table 3.1)

3.1.5. The age of menopause

It shows non-significant relation, but the highest proportion of malignant to the total masses lies within those menarches at <12 years age interval (29.7%). (Table 3.1).

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(Table 3.1) : Relationship between different age category and type of tumor

Age category	Type of tumor		Total	X2
	benign	malignant		P value
Age of studied population				
18-29	41	8	49	19.825 0.001
	83.7%	16.3%	100.0%	
30-45	63	12	75	
	84.0%	16.0%	100.0%	
>45	30	27	57	
	52.6%	47.4%	100.0%	
Total	134	47	181	
	74.0%	26.0%	100.0%	
Age of menarche*				
<12	26 (70.3%)	11 (29.7)	37 (100.0%)	4.376 0.497
12-14	101 (74.8%)	34 (25.2%)	135 (100.0%)	
>14	7 (77.8%)	2 (22.2%)	9 (100.0%)	
Total	134 (74.0%)	47 (26.0%)	181 (100.0%)	
Age at-marriage				
15-20	65	26	91	0.704 0.703
	71.4%	28.6%	100.0%	
20-30	40	12	52	
	76.9%	23.1%	100.0%	
>30	6	3	9	
	66.7%	33.3%	100.0%	
	111	41	152	

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Total	73.0%	27.0%	100.0%	
Age bearing of 1st child				
15-20	42	15	57	0.061 0.970
	73.7%	26.3%	100.0%	
20-30	56	21	77	
	72.7%	27.3%	100.0%	
>30	7	3	10	
	70.0%	30.0%	100.0%	
Total	105	39	144	
	72.9%	27.1%	100.0%	
Age at menopause				
<45 year**	8	3	11	2.489 0.085
	72.7%	27.3%	100.0%	
>45	13	16	29	
	44.8%	55.2%	100.0%	
Total	21	19	40	
	52.5%	47.5%	100.0%	

* age at first menstrual period in years
** may be natural after age 40, or artificial due to hysterectomy.

3.2 Obstetric history

3.2.1 Number of pregnancies:

The proportion of malignancy to the total mass increased with increasing the gravida, it's the higher for gravida more than 5 (32.8%) and about 43% of the total malignancies, but the relation statically non-significant (Table 3.2).

3.2.2 Frequency of abortion:

For women having no abortion, the proportion of malignancy to the total mass was 26%. Those having one fetal loss the proportion about 22%, and 33% for those losing 2-4, and increasing up to 66% for women with frequent abortion >4, among the total masses of the same category (Table 3.2).

3.2.3 Birth control:

Regarding the users, the combined contraceptive pills institute about 67% of benign, and 55.5% of the total malignant users alone, also 27% using CCP with other modalities.

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The proportion of malignancy to the total masses was recorded as the highest value for those where tubal ligation was done and the same proportion (50%) for using CCP with TL (Table 3.2).

3.2.4 Numbers of born children:

It's clear that the proportion of malignancies within the total masses is directly related to increasing parity especially after 6 children with significant statistical relation, (Table 3.2**)**.

(Table 3.2): Relationship between obstetric history and type of tumor.

Type of tumor				Total	X2 P value
Obstetric conditions		Benign	Malignant		
Gravida	<2	28 (80%)	7 (20%)	35 (100.0%)	2.46 0.289
	2-5	43(75.4%)	14(24.6%)	57(100.0%)	
	>5	41(67.2%)	20 (32.8%)	61(100.0%)	
Total		112(79.7%)	41(20.3%)	153(100.0%)*	
Number of abortion**	0	93(73.8%)	33(26.2%)	126(100.0%)	6.872(F.E.T) 0.077
	1	14(77.8%)	4 (22.2%)	18 (100.0%)	
	2-4	4(66.7)	2 (33.3)	6 (100.0%)	
	>4	1 (33.3)	2 (66.7)	3(100.0%)	
Total		112(79.7%)	41(20.3%)	153(100.0%)	
Birth control ways	CCP	33 (76.7%)	10 (23.3%)	43 (100.0%)	5.264(F.E.T) 0.743
	Injection	3 (75.0%)	1(25.0%)	4(100.0%)	
	TL	2 (50.0%)	2 (50.0%)	4(100.0%)	
	No	66(74.2%)	23(25.8%)	89(100.0%)	
	CCP+TL	2 (50.0%)	2 (50.0%)	4(100.0%)	
	CCP+ IUD	4 (57.1%)	3(42.9%)	7(100.0%)	
	Injection + IUCD	1 (100.0%)	0 (0.0%)	1(100.0%)	
	IUCD	1(100.0%)	0(0.0%)	1(100.0%)	
Total		112(79.7%)	41(20.3%)	153(100.0%)	
Parity	1-3	42(80.7%)	10(19.3%)	52(100%)	20.684 (F.E.T) 0.057
	4-6	43(72.8%)	16(27.2%)	59(100%)	
	7-9	11(52.3%)	10(47.7%)	21(100%)	
	>10	6(66.7%)	3(33.3%)	9(100%)	
Total		102(72.3%)	39(27.7%)	141(100%)***	

***** we abstract the unmarried from the total**.**

****** till the time of study.

*** we abstract the unmarried and nulliparous.

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3.3 Distribution among nulliparous women:

Regarding the nulliparous women this study including 9 nulliparous women with breast mass, 55.5 % of them under 35years of age, and 44.5% of total them were under the age of 25years, in another word the proportion of malignancy among nulliparous above the 35 years was 50% (Table 3.3).

(Table 3.3): Distribution of malignancy among nulliparous women and age

Age interval	Benign	Malignant	Total	FE, p value
<25	4(100%)	0 (0%)	4(100%)	**8.400 0.497**
26-35	1(100%)	0 (0%)	1(100%)	
>35	2(50%)	2(50%)	4(100%)	
Total	7(77.8%)	2(22.2%)	9(100%)	

3.4. Duration of breastfeeding :

The proportion of malignancies decreasing with increasing the duration of breastfeeding and the proportion after 6 years of feeding seams the same (Table 3.4).

Table (3.4): Relationship of breastfeeding and type of tumor

Duration*	Benign	malignant	Total	X^2, p value
≤ 2	18 (64%)	8 (36%)	26 (100.0%)	6.364 0.013
- 5	25 (75.8%)	8 (25.2%)	33(100.0%)	
- 10	38 (83.3%)	19 (16.7%)	57 (100.0%)	
>10	8 (83.3%)	2 (16.7%)	10 (100.0%)	
Total	87 (70.2%)	37 (29.8%)	124(100.0%)	

* duration of the total breastfeeding for all born in years.

3.5. Site of breast masses:

The upper outer quadrant malignant mass constitutes 34% of the total malignancies, while the central and LOQ masses 23.4 ,% of the total malignancies for each ones, UIQ about 11% and LIQ malignancies about 6% and metacentric 2%. Even the malignant mass was having UOQ predilection but the LOQ mass usually malignant 40.7% of the total mass in that site(Table 3.5).

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(Table 3.5): Site of mass and type of tumor

Site	Benign	Malignant	Total	X^2, P value
LIQ	23	3	26	29.876 0.002
	88.5%	11.5%	100.0%	
LOQ	16	11	27	
	59.3%	40.7%	100.0%	
UIQ	18	5	23	
	78.2%	11.8%	100.0%	
UOQ	40	16	54	
	74%	26%	100.0%	
Central	25	11	36	
	69.4%	30.6%	100.0%	
Multicentric	12	1	13	
	92.3%	7.7%	100.0%	
Total	134	47	181	
	74.0%	26.0%	100.0%	

3.6 Validity of the test USED

The validity was assessed according to the study results, regardless that it is highly operator dependent.

3.6.1 US:

The no. of true positive with Us = 24+ 18 (highly suspicious+ suspicious) so = 42 patients

The total positive with standard = 47-2 = 46 (excluded that need further test)

The no. of true negative by (US) = 81 + 1 (benign result+ normal one) so = 82 The total negative (benign) with histopatholgy = 99-13 =86

The results account according to the flowing (Table 3.6).

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Table (3.6): Relation of US results and type of tumor

US results	Histopathology		Total
	Benign	Malignant	
Need further investigation	13	2	15
Normal	1	2	3
Suspicious	4	24	28
Highly suspicious of malignancy	0	18	18
Benign	81	1	82
Total	99	47	146

3.6.2 Mammography:

If we subtract patients whom mammography not done to them,

The no. of true positive with mammography =23+ 17 (highly suspicious+ suspicious)
So = 40
The total positive with gold standard = 47 – 5 (5 patients didn't have mamograph)
So = 42

The no. of true negative(benign) = 16 + 38 (benign+ negative in mamo.)
So = 54

The total negative with standard = 99 – 36 (not do mamograph)
So = 63

those taken from relation in the (Table 3.7**).**

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(Table 3.7): Relation of Mammography results and type of tumor

Mammography	Type of tumor		Total
	Benign	Malignant	
Negative	16	1	17
Benign finding	38	1	39
Suspicious	6	23	29
Highly suspicious	0	17	17
Not done	36	5	41
Small dense breast	3	0	3
Total	99	47	146

3.6.3 FNA :

If we abstract the no. of patients whom FNA not done to them,
The no. of true positive by FNA = 23
The total positive with gold standard = 47-19-2 (19 not do and inadequate FNA)
So = 26
The no. of true negative with FNA = 78
The total negative with standard = 99-18-2 (not do FNA)
So = 79
These results are derived from (Table 3.8).

(Table 3.8): FNA and histopathology results

FNA results	**Histopathology**		**Total**
	Benign	Malignant	
Not done	18	19	37
Suspicious	0	3	3
Malignant	1	23	24
Benign	78	0	78
Inadequate	2	2	4
Total	99	47	146

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3.6.4 Summary:

According to the relations from paragraphs (3.6.1, 2,3), so we can summarize the following tables of validity in (Tables 3-9 and 10).

Table (3.9) Relation of different modalities of investigation

Histopath				
mammogram	items	B	M	T
	B	40	9	49
	M	2	54	56
	T	42	63	105
US results	items	B	M	T
	B	42	4	46
	M	3	82	85
	T	45	86	131
FNA cytology	Items	B	M	T
	B	23	1	24
	M	3	78	81
	T	26	79	105

(Table 3.10): Validity of the tests.

Test	Sensitivity	specificity	+ve. P. value	-ve. P. value
US	42/45 ×100% = 93%	82/86 ×100% = 95%	42/46 × 100% = 91%	82/85 × 100% =95%
Mamo.	40/42 × 100% 95%	54/63 × 100% 85.7%	40/49×100% = 82%	54/56 × 100% = 96%
FNA	23/26 × 100% 88%	78/81× 100% 96%	23/24×100% = 96%	78/81 × 100% = 96%

Discussion

4.1 Different age groups

The most common age group affected by the breast cancer was >45 years, constitute (57.4%) of cases, and the proportion of malignant mass among the total mass was (47.4%) within this ages interval, previous studies in Iraq support that, one of them in the south of Iraq.[14] The age of marriage shows no valuable significance for the association but the results showed that early marriage or early sexual contact increases the risk for breast cancer, for

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those married below 20 years of age, these results reinforced with a case control study, in the Eastern Region of Saudi Arabia showed that early marriage is a potential risk factor for breast cancer and the researchers explain that the most likely due to the inconsistency or raising in the secretion of the female sex hormones (such as estrogen hormone) among female teenagers.[15]

The proportion of malignant lesion to the total malignancy was 40%, for post-menopausal women, its higher for women whom cessation of menses at age >45 about five times than at earliest age (38%, of those post-menopausal reach that before the 45years, either naturally after age 40, or artificially due to hysterectomy whatever the cause). In general, the proportion of malignant to the total mass higher for postmenopausal than premenopausal ones, were the possibility of malignancy about 50% for our study, The higher proportion of malignancy for late menopause similar to a case control study of Al Riyadh. [16] That could be explained by the fact that breast cancer risk is related to the degree of mitotic activity in the breast which is determined by estrogen and progesterone exposure throughout the luteal phase of the menstrual cycle.[17]

The above explanation also elucidated that the early menarche increases these mitotic activity of the periods in the breast and later increases the risk of breast cancer, where woman with early menarche (age less than 12y) increased risk of breast cancer when compared with a woman with late menarche, that explanations abstracted the previous results in Saudi.[18]

4.2 Obstetric history

The current study found that the more the number of pregnancies, the higher the risk of breast cancer, this Inconsistent with previous known because age confounder as most women with few numbers of gravida is at younger age group compared to those with larger number.[19]

The proportion of malignancy among the total cases of masses within the age of women at her firstborn directly proportionate to the increasing age, thus mimic the previous study in Iceland.[20]

For women having no abortion, the proportion of malignancy to the total mass was 25%, Those having one fetal loss the proportion about 22%, and 33% for those losing 2-4, and increasing up to 66% for women with frequent abortion >4, among the total masses of the same category, the previously designed prospective evidence are inadequate as an evidence for positive association between abortion and breast cancer,[21] but a very old study animal study as observed by Russo,[22] during the first trimester of a pregnancy, where they found that the hormonal changes force newly produced breast cells to differentiate, so a full-term pregnancy allows complete differentiation of that epithelial cells, which reduces the risk of future breast cancer. In contrast, an interruption by abortion (either spontaneous or induced) will arrest this differentiation process and then increase the risk of breast cancer.[22]

Regarding the birth control risk, users of combined contraceptive pills constitute about 67%, of the total users contraceptive modalities, and 55.5% of the total malignant users, but within the same group, there isn't a clear association between ever use of CCP and breast cancer where the proportion of malignant mass to the total using CCP was 23% compared to 25% among non-users, this result is supported by the previous

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epidemiological review which shows that not strong association,[23] but that may be due to age and duration effect as the extent of under 35 age among users about 72%, so it is clear that the age confusing that effect.

Our study showed the risk of breast malignancy was high among those whom tubal ligation was done, like that supported with the previous study, but without significant statistical relation.[24]

The nulliparity act as an important factor that increases the risk of breast cancer, especially after removing the age effect as a factor confounding that association, this result is supported by a previous study in Kurdish women of northern Iraq.[25]

The proportion of malignancies decreasing with increasing the duration of breastfeeding, and no valuable difference in the proportion after 6 years of feeding, those results are similar to a case control study that showed such reduction for premenopausal women and that justify insignificant effect after 6 years as after this duration most of the females were at postmenopausal.[26]

4.3 Mass location

The upper outer quadrant malignant mass constitute 34% of the total malignancies, while the central and LOQ masses 23.4% of the total malignancies for each ones, UIQ about 11% and LIQ malignancies about 6% and multicentric 2%, but the LOQ mass usually malignant 40.7% of the total mass in that site, these consequences similar but less than that for another study, Where upper outer (62%), Upper inner (18%) Lower inner (5%) Lower outer (9%) Retroareolar 5 (3%).[27]

4.4 Validities of used modalities

i. Screening mammography of an asymptomatic woman provides two views of each breast using x-ray and will detect 78% of breast cancers in women with an 83% sensitivity for women over 50. About 17% breast cancers will be missed on routine breast imaging.[28]

Diagnostic mammography is up to 95% sensitive and specific in 85%, While in comparison with other tests, it's 87 percent sensitive in detecting cancer. Its specificity is 88. Percent,[29] the reason in higher sensitivity may be due to age effect; where's the majority of cases where >35years.

ultrasonography has a sensitivity nearer than previous studies. Where sensitivity was 89 percent and a specificity of 78 percent in detecting abnormalities.[29]

The sensitivity of FNA in this study 82%, and specificity was 96%, similar to another previous study where the sensitivity was 88.24% and specificity 100%.[30]

5.Conclusion

1. Age-matched multiple logistic regression methods point to that the age is most important detrminant factor for females in Thi-Qar about 57.5% of the malignancies were above 45.
2. The results showed that early marriage, or early sexual contact increases the risk for breast cancer.
3. The proportion of malign masses to the total malignancy were higher for women whom cessation of menses at age >45 about five times than at earliest age (occurrence before the 45ages, either naturally after age 40, or artificially due to hysterectomy whatever the cause).

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4.Even the malignant mass was having UOQ predilection but the LOQ mass usually malignant.
5. FNA is 82% specific and 96% sensitive in relation to definitive histopathologic results.

Recommendations

1. Further studies with different designs permit longer duration, are required and preferred to be follow-up type to determine the effect of confound risk factors like age, stress and radiation rather than defined ones, also studies required about the response to therapy and follow the complication.
2. Regular programmed screening required to detect cancer in the earlier stage, and facilitate the availability of screening tools at the health care centers and in peripheries hospitals of Thi-Qar.

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التوزيع العمري لكتلة الثدي وصلاحية المقاييس المستخدمة في تشخيصه بعيادة أمراض الثدي في ذي قار 2018.

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المستخلص:

الأهداف: من هذه الدراسة لدراسة تأثير العمر والفئات العمرية المحددة في توزيع كتلة الثدي في ذي قار, لتحديد تأثير معظم العوامل المحددة المدرجة في تاريخ الولادة على هذا التوزيع، وتقييم صحة الفحوصات الإشعاعية وFNA في فيما يتعلق بالتشخيص النسيجي لكتل الثدي لعيادة المرضى الذين يقدمون المشورة لأمراض الثدي في ذي قار 2018.

التصميم: تم استخدام تصميم تحليلي مقطعي.

المرضى: أدرجت كل النساء اللاتي تعرضن بكتلة الثدي في عمر محدد.

النتائج: يزداد معدل سرطان الثدي مع تقدم العمر في ذي قار، في الأعمار >45 سنة حوالي نصف الحالات كانت خبيثة (47%), وتشكل (57.4%) من اجمالي الأورام الخبيثة، في حين ان الفئات العمرية الأخرى أقل من 45 سنة، كانت نسبة الأورام الخبيثة بين الحالات من نفس الفئات حوالي (16%), وتشكل (25%)، (17%) للفترات العمرية (30-45), (أقل من 30) على التوالي، من ناحية أخرى فان قدرة FNA بتشخيص سرطان الثدي هي 96%لكن حساسيتها في تحديد الخلو من المرض كانت 82% مقارنة بنتائج التشريح المرضي النهائية في تشخيص كتل الثدي.

الاستنتاج: تشير نتائج العمل الحالي الى أن العمر كان عاملا مترابطا بشدة وأن حوالي 57.5% من الأورام الخبيثة كانت فوق 45.

فحص FNAله حساسية عالية بتشخيص سرطان الثدي في ذي مقارنة بنتائج التشريح المرضي النهائية في تشخيص كتل الثدي.

الكلمات المفتاحية: عقده الثدي، دقة تشخيص فحوصات الثدي.