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Comparison of the diagnostic precision for ultrasound and mammogram in dense breasts tissue of young females

Mahmoud H. Alkhasawneh[1]✉, **Asma'a Al-Mnayyis**[2], **Maria Alawi**[3], **Ekatereena Obaisat**[4], **Eman M Alzyoud**[5]

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Author Affiliation:
[1]Division of Radiology, Faculty of Medicine, Mutah University, Alkarak, Jordan; Email: mahmoudalkasawneh@yahoo.com
[2]Department of Clinical Sciences, Faculty of Medicine, Yarmouk University, Jordan; Email: asmaa.mnayyis@yu.edu.jo
[3]Alkarak Tertiary Teaching Hospital, Ministry of Health, Jordan; Email: mariaalawi1979@gmail.com
[4]Alkarak Tertiary Teaching Hospital, Ministry of Health, Jordan; Email: dr_katreenobaisat@yahoo.com
[5]Sixth year student, Faculty of Medicine, Mutah University, Alkarak, Jordan; Email: emansameer14@gmail.com

✉**Corresponding author**
Division of Radiology, Faculty of Medicine, Mutah University, Alkarak, Jordan;
Email: mahmoudalkasawneh@yahoo.com

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ABSTRACT

Background: Globally, breast cancer accounts for a third of womens' cancer cases. It is experinced in 1-3% of females with clinical breast findings, negative mammogram and ultrasound. *Aim*: This retrospective study aimed to compare the diagnostic precision of mammogram and ultrasound in detecting breast malignancy. *Patients and methods*: 332 females from the southern region of Jordan 34-75 years old were enrolled in the study. They were subjected to clinical examination, mammogram, ultrasound and histopathological study for their breast masses at Alkarak teaching hospital. The differential diagnostic precision of both imaging modalities were analyzed in terms of breast density and patient's age. Based on the breast imaging reporting and data system, mammograms were analyzed into five diagnostic categories (1-5), four grades of breast tissue density (I-IV), while, ultrasound diagnosis was based on five diagnostic categories of the same system. *Results*: The histopathological examination showed 155 (19.4%) malignant and 177 (4.5%) benign lesions. All malignancies were diagnosed by ultrasound and mammogram, respectively. The obtained results showed statistically significant difference of sensitivies and specificities between the overall ultrasound and mammogram ($P<0.05$). Regarding breast tissue density, mammogram sensitivity was 83.3% and 0% in grade I and grade IV, respectively. It was 66.7% and 40% in the same grades for ultrasound. *Conclusion*: The diagnostic precision of ultrasound in differentiating between benign and malignant lesions was significantly higher than mammogram in young Patients with clinical breast findings and dense breast tissue.

Keywords: breast, benign, malignant, diagnostic precision, mammogram, ultrasound

1. INTRODUCTION

Breast cancer is the most common cancer among women and is responsible for around one third of all cancers in women worldwide. The overall probability of developing an invasive breast cancer in a woman during her life is approximately 12% (Bowles and Ann, 2016, American Cancer Society, 2020).

Breast cancer is the commonest type of cancers in Jordan accounting for around 40% of all women cancers (Kaplan, 2001). Additionally, it is the third leading cause of cancers related deaths after colorectal and lung malignancies (GBD 2015 Eastern Mediterranean Region Cancer Collaborators, 2018; Ministry of Health, 2020). The world health organization has addressed breast screening and early diagnosis as important strategies that would reduce the associated mortality and morbidity rates of breast cancer (World Health Organization, 2020). Screening and early diagnosis is largely dependent on clinical assessment, imaging, including ultrasound and mammogram, and histopathology at a later stage (Vetto et al., 1995).

Mammogram can be used for screening and for diagnosis. Screening mammogram can detect up to 75% of breast carcinomas as early as one year before they are palpable and is usually indicated every 1-2 years after the age of 40 years and every year after the age of 50 years, or before that if there is a family history of breast carcinoma (Schonberg et al., 2006; Badgwell et al., 2008; Samarkandy et al., 2020; Irandoost et al. 2020). Such protocol can reduce the risk of late stage breast carcinoma in females aged 80 years and more. On the other hand, diagnostic mammogram is performed in females with clinical breast complaints such as the presence of nipple discharge or breast changes. Overall, mammogram has a false negative rate of 8-10% (Devolli-Disha et al., 2009).

Ultrasound is an important tool in assessing females with clinical breast findings. Additionally, in asymptomatic females younger than 50 years old with dense breast on mammogram, ultrasound showed a higher sensitivity in identifying breast carcinoma than mammogram (Hille et al., 2004; Boyd et al., 2005). It has been estimated that mammogram occult carcinomas may be identified by ultrasound in 10-40% based on breast tissue density and female age (Vercauteren et al., 2008). However, around 1-3% of females with clinical breast findings, negative mammogram and negative ultrasound, could experience breast malignancy due to many factors such as technical reasons and factors related to the malignant lesion itself (Kopans, 2002).

Aim

Our study aimed to compare the differential diagnostic precision between mammogram and ultrasound in detecting breast malignancies taking into considerations breast tissue density and subject's age.

2. SUBJECTS AND MATERIALS

Study design

This retrospective study included a total of 332 female patients, aged 34-75 years old with clinical breast complaints. The study was performed at Alkarak teaching hospital, Ministry of health in Jordan during the period between 2016-2019, after obtaining approval from the Ethical and Research Board Review Committees. All patients underwent mammogram and ultrasound while breast masses were examined histopathologically.

Study procedure and data analysis

Traditional mammogram positions were performed with medio-lateral -oblique and cranio-caudal projections for each breast. Mammogram was analyzed based on the breast imaging reporting and data system (BIRADS) where: Five diagnostic categories: 1-negative, 2-benign, 3-probably benign, 4-suspected abnormal, and 5-highly suspected malignant. Four grades of breast tissue density: I-nearly totally fatty, II-scattered fibro glandular, III-heterogeneous, and IV-dense breast (American college of Radiology, 1998). High resolution breast ultrasound was performed using the linear array probe. Diagnosis was based on the five diagnostic categories of breast imaging reporting and data system. Fifteen Statistical analysis were carried out using χ^2 and Student's t test to assess the significance of difference, a p value less than 0.05 was considered statistically significant.

3. RESULTS

The patients and lesions characteristics are shown in Table 1. Histopathological exam showed a total of 155 malignant and 177 benign lesions in patients. The histopathological types of carcinoma in 155 patients were: ductal (61.3%), lobular (11.6%), ductal and lobular (25.8%) and medullary (1.3%). The median age of all patients was approximately 53.9 years. In 332 patients, mammogram identified 55 patients (mean age 71.98 years) with grade I breast density (30 malignant and 25 benign), 121 patients (mean age 58.28 years) with grade II breast density (60 malignant and 61 benign), 120 patients (mean age 47.38 years) with grade III breast density (55 malignant and 65 benign) and 36 patients (mean age 36.98 years) with grade IV breast density (10 malignant and 26 benign).

Table 2 shows the overall sensitivity of ultrasound detection of malignant lesions in all breast densities was significantly higher than mammogram (71.6% vs 57.4% with p value < 0.05). The sensitivity of mammogram and ultrasound was respectively as follows; for grade IV was 0% (0 of 10) and 40% (4 of 10), for grade III was 30.9% (17 of 55) and 58.2% (32 of 55), for grade II was 78.3% (47 of 60) and 91.7% (55 of 60) and for grade I was 83.3% (25 of 30) and 66.7% (20 of 30). Table 2 also shows that the overall

specificity of ultrasound in detecting benign lesions in dense breast tissue was significantly higher than mammogram (88.1% vs. 68.9% with p value < 0.05). The specificity for mammogram and ultrasound was respectively as follows; for grade IV was 19.2% (5 of 26) and 69.2% (18 of 26), for grade III was 64.6% (42 of 65) and 86.2% (56 of 65), for grade II was 98.4% (60 of 61) and 93.4% (57 of 61) and for grade I was 100% (25 of 25) for both.

Therefore, with increasing fibro glandular density, the sensitivity and specificity of mammogram was decreasing compared to the sensitivity of ultrasound which was increasing.

Table 1 Patients and lesions characteristics

	overall	Age(yrs.)no.			Age (yrs.) Mean	Breast Density Grade (N, mean age)			
Range		34-50	51-70	71-75		I	II	III	IV
Overall	332	112	155	65	53.88	55 (72y)	121(58.3y)	120 (47.4y)	36 (37y)
Benign	177	63	80	34	53.38	25	61	65	26
malignant ductal lobular duct-lob medullary	155 95 18 40 2	49	75	31	54.44 52.91 56.08 55.34 63.05	30	60	55	10

Table 2 Differential diagnostic precision of mammogram and ultrasound based on breast tissue density

	No.	malignant		No.	Benign	
		sensitivity			Specificity	
Breast Density		mammogram	ultrasound		mammogram	ultrasound
I	30	25/30=83.3%	20/30=66.7%	25	25/25=100%	25/25=100%
II	60	47/60=78.3%	55/60=91.7%	61	60/61=98.4%	57/61=93.4%
III	55	17/55=30.9%	32/55=58.2%	65	42/65=64.6%	56/65=86.2%
IV	10	0	4/10=40%	26	5/26=19.2%	18/26=69.2%
Overall	155	89/155=57.4%	111/155=71.6%	177	122/177=68.9%	156/177=88.1%
P value	<0.05			<0.05		

Table 3 shows that 19.4% (30/155) of all malignancies were recognized on ultrasound but not recognized on mammogram, while 5.2% (8/155) of all malignancies were recognized on mammogram but not on ultrasound. The table also shows that 15.3% (27/177) of all females with benign lesions had false negative lesions using mammogram but were recognized as true benign lesions on using the ultrasound.

In addition, Mammogram had 42.6% (66/155) and 25.4% (45/177) false negative rate in diagnosing malignant and benign lesions respectively compared to 28.4% (44/155) and 11.9% (21/177) using ultrasound.

Table 3 The overall differential diagnostic precision of mammogram and ultrasound.

		Ultrasound					
		malignant			Benign		
		+ve	-ve	overall	+ve	-ve	overall
mammogram	+ve	81/155=52.3%	8/155=5.2%	89/155=57.4%	129/177=72.9%	3/177=1.7%	132/177=74.6%
	-ve	30/155=19.4%	36/155=23.2%	66/155=42.6%	27/177=15.3%	18/177=10.2%	45/177=25.4%
	No.	111/155=71.6%	44/155=28.4%	155	156/177=88.1%	21/177=11.9%	177
	P	<0.05			<0.05		

Ultrasound and histopathological studies were shown for invasive ductal carcinoma case in figures 1 and 2, while, figures 3 and 4 were for a case of benign fibroadenoma. Figure 5 showed bar charts of the statistical reports in the present study, for

histopathologic characterstics of the obtained lesions, the sensitivity for malignant lesions detection using mammogram and ultrasound, and the specificity for benign lesions detection using mammogram and ultrasound

Figure 1 Ultrasound study of both breasts A: Normal left breast, B: invasive ductal carcinoma in the right breast, C: invasive ductal carcinoma in the right breast using Elastoscan.

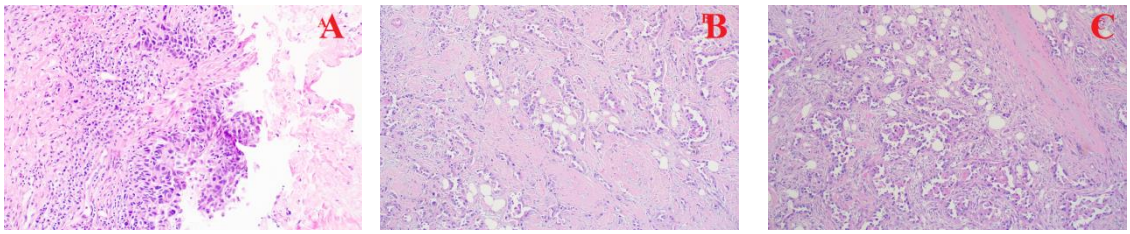

Figure 2 A, B and C represent the histopathological study of the right breast biopsy showing a highly suspicious invasive ductal carcinoma.

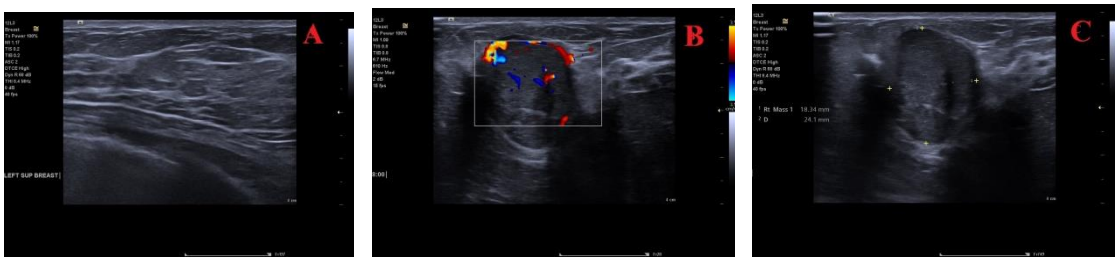

Figure 3 Ultrasound study of both breasts A: Normal left breast, B and C: represent right breast benign fibroadenoma with blood flow and without blood flow, respectively.

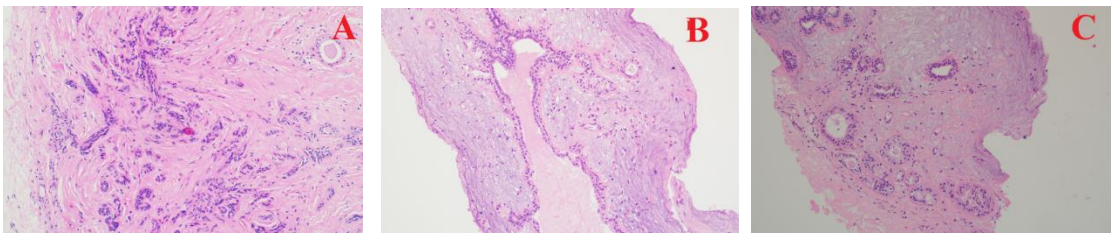

Figure 4 A, B and C represent the histopathological study of the right breast biopsy showing benign fibroadenoma.

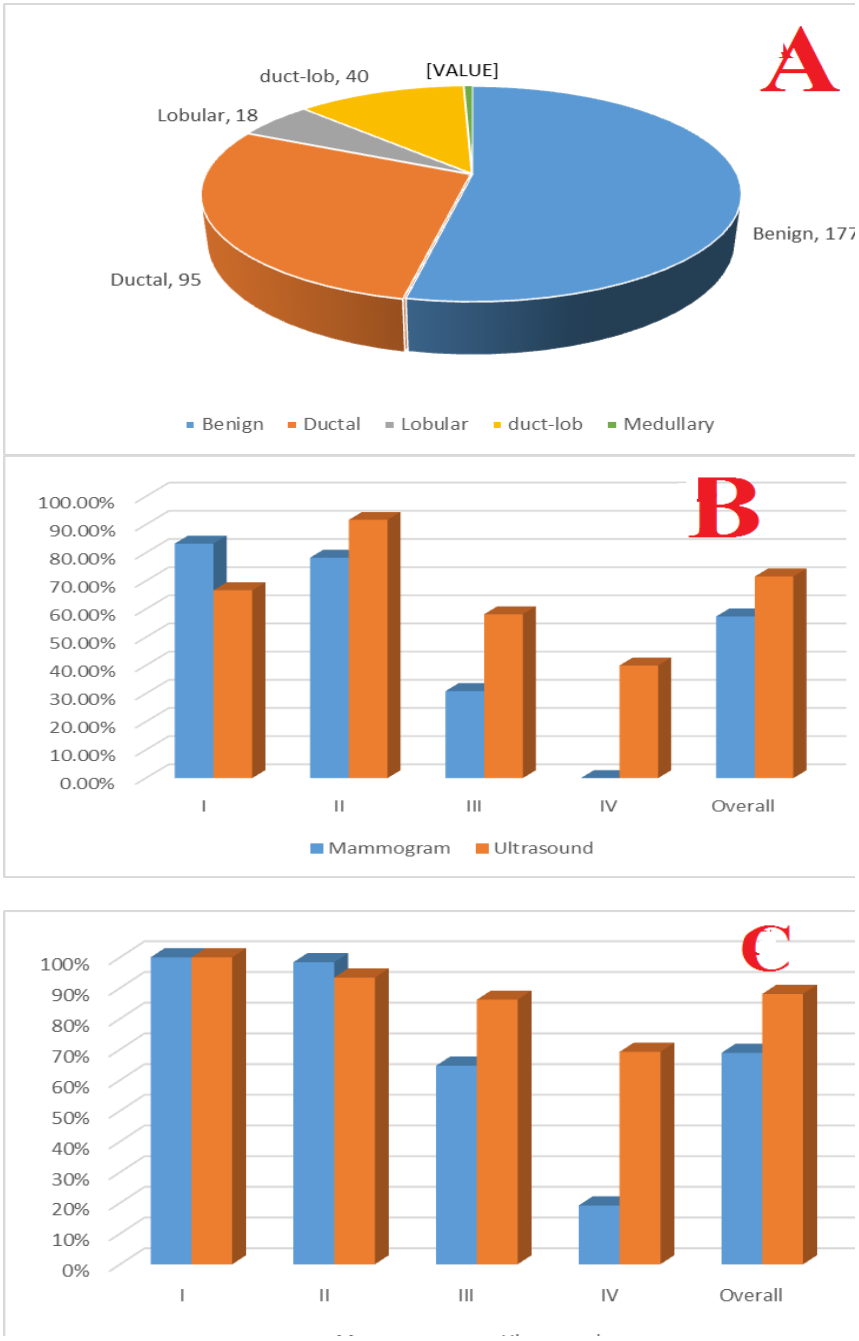

Figure 5 Bar chart of the statistical reports of the obtained results A: Cases histopathologic characterstics, B: Sensitivity for malignant lesions detection using mammogram and ultrasound, C: Specificity for benign lesions detection using mammogram and ultrasound.

4. DISCUSSION

Breast cancer is an important global health problem. All females have a risk of developing breast carcinoma but the majority of cases are reported in females aged more than 50 years old. Early screening and detection is very important to the mortality that can result from spread of malignant lesions (Devolli-Disha et al., 2009). Ultrasound and mammogram are the standard modalities for recognition and assessment of breast problems in females with breast clinical features or palpable structures recorded on clinical examination (Schonberg et al., 2006). The initial selection between mammogram and ultrasound for a female with clinical features depends on age. Females aged less than 35 years old should be examined using ultrasound and females aged more than 35 years old should be examined using mammogram as first initial modality (Dixon and Mansel, 1994). Sensitivity changed remarkably with age and breast density.

The current study showed that the overall differential diagnostic precision of ultrasound was significantly higher than mammogram. Ultrasound was capable of detecting 19.4% of all malignant lesions which were missed using mammogram, compared to 5.2% detected using mammogram and missed when using ultrasound. In addition, a significant percentage (15.3%) of females with benign lesions had false negative diagnosis and missed using mammogram but was recognized as true benign lesions on using the ultrasound.

Mammogram had a higher false negative rate in diagnosing malignant and benign lesions (42.6% and 25.4% respectively) when compared to ultrasound (28.4% and 11.9%). More particularly, the current study found that the sensitivity of ultrasound for detecting malignant lesions in all breast densities was 71.6% which was significantly higher when compared to 57.4% for mammogram. Such higher sensitivity is in agreement with previously published findings (Houssami et al., 2005). The sensitivity of ultrasound in breast density grade IV was 40% while it was 0% for mammogram, while for grade I it was 66.7% and 83.3% respectively.

The overall ultrasound specificity in detecting benign lesions was significantly higher than mammogram (88.1% vs. 68.9%) which is also in agreement with previous studies (Moy et al., 2002). Ultrasound was more specific in breast density grade III (86.2%) and grade IV (69.2%) compared to 64.6% and 19.2% using mammogram. Therefore, with increasing fibro glandular density, the sensitivity and specificity of ultrasound was increasing compared to that of mammogram which was decreasing which is supported by findings of previous studies which suggested that ultrasound is more sensitive than mammogram in recognizing lesions in females with dense breast. Dense fibro glandular tissue is the most important limitation of mammogram in breast carcinoma recognition (Boyd et al., 2005; Carney et al., 2003; Wang et al., 2007). Therefore, bilateral breast ultrasound can be an excellent assessment modality of females with dense breast seen at mammogram.

5. CONCLUSION

Our results indicates that the overall diagnostic precision of ultrasound is higher than mammogram and Ultrasound is more effective than mammogram in younger females and ones with dense breasts, while the differential diagnostic precision of mammogram increased with fattier breasts.

Author contribution

Mahmoud H. Alkhasawneh- Concepts of ideas, literature search, experimental studies, data acquisition, manuscript preparation and editing

Asma'a Al-Mnayyis-	Manuscript preparation, editing and revision, Experimental studies, data acquisition
Maria Alawi-	Design, data analysis, statistical analysis, manuscript revision
Ekatereena Obaisat-	Experimental studies data acquisition, manuscript preparation and editing

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Informed consent

Written and oral informed consent was obtained from each participant in the study

Ethics approval

The study has been approved by the Scientific and Ethics Committees of the Faculty of Medicine, Mutah University, Jordan (The reference number of the ethical approval is: 9022021).

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. American Cancer Society. Detailed Guide: Breast Cancer: What Are the Key Statistics for Breast Cancer? American Cancer Society Cancer Resource. http://www.cancer.org/docroot/home/ index.asp. [Accessed November 15, 2020]
2. American college of Radiology. Illustrated breast imaging reporting and data system (BI-RADS) 3rd ed. Reston VA: American college of Radiology, 1998.
3. Badgwell DB, Giordano HS, Duan ZZ, Fang S, Bedrosian I, Kuerer MH, Singletary ES, Hunt KK, Hortobagyi NG, Babiera G. Mammogram before diagnosis among women age 80 years and older with breast cancer. J Clin Oncol., 2008; 26(15):2482-2488.
4. Bowles D, Ann Quinton A. The Use of Ultrasound in Breast Cancer Screening of Asymptomatic Women with Dense Breast Tissue: A Narrative Review. JMIRS 2016; 47(3):s21-s28.
5. Boyd FN, Rommens MJ, Vogt K, Lee V, Hopper LJ, Yaffe JM, Paterson DA. Mammographic breast density as an intermediate phenotype for breast cancer. Lancet Oncol 2005; 6:798-806.
6. Carney AP, Miglioretti LD, Yankaskas CB, Kerlikowske K, Rosenberg R, Rutter MC, Geller MB, Abraham AL, Taplin HS, Dignan M, Cutter G, Ballard-Barbash R. Individual and combined effects of age, breast density and hormone replacement therapy use on the accuracy of screening mammogram. Ann intern med 2003; 138(3):168-175.
7. Devolli-Disha E, Manxhuka-Kërliu S, Ymeri H, Kutllovci A. Comparative accuracy of mammogram and ultrasound in women with breast symptoms according to age and breast density. Bosn J Basic Med Sci 2009; 9(2):131-136.
8. Dixon JM, Mansel RE. ABC of breast diseases. Symptoms assessment and guidelines for referral. BMJ 1994; 309(6956):722-726.
9. GBD 2015 Eastern Mediterranean Region Cancer Collaborators: Burden of cancer in the Eastern Mediterranean Region, 2005-2015: Findings from the Global Burden of Disease 2015 Study. Int J Public Health 2018; 63:151-164.
10. Hille H, Vetter M, Hackelöer BJ. Re-evaluating the role of breast ultrasound in current diagnostics of malignant breast lesions. Ultraschall Med 2004; 25(6):411-417.
11. Houssami N, Irwig L, Simpson MJ, McKessar M, Blome S, Noakes J. The influence of knowledge of mammogram findings on the accuracy of breast ultrasound in symptomatic women. Breast J 2005; 11(3):167-172.
12. Irandoost SF, Ahmadi S, Sajjadi H, Rafiey H, Nejad FN, Gharehghani MAM, Soleimanvandiazar N, Hosseini SM, Karimi SE. Factors related with breast selfexamination in women: A cross-sectional study in Tehran Province, Iran. Med Sci, 2020, 24(101), 190-200
13. Kaplan SS. Clinical utility of bilateral whole-breast US in the evaluation of women with dense breast tissue. Radiology, 2001; 221:641-649.
14. Kopans D.B. Negative mammographic and US findings do not help exclude breast cancer. Radiology 2002; 222(3): 857-858
15. Mara AS, Radhika AR, Ellen PM, Edward RM. Decision making and counseling around mammogram screening for women aged 80 or older. J Gen Intern Med 2006; 21(9):979-985.
16. Ministry of Health: 2014 Information and research report, MOH, Jordan. http://www.moh.gov.jo/Echobusv3.0/SystemAssets/2d0cc71d-d935-4d6f-a72c73d60cd0a16c.pdf. [Accessed November 15, 2020].
17. Moy L, Slanetz JP, Moore R, Satija S, Yeh DE, McCarthy AK, Hall D, Staffa M, Rafferty AE, Halpern E, Kopans BD. Specificity of mammogram and ultrasound in the evaluation of a palpable abnormality: retrospective review. Radiology 2002; 225:176-181.
18. Samarkandy S, Alamri A, Alradadi B, Almalki B. Basal cell carcinoma over the breast with unusual presentation: A case report. Med Sci, 2020, 24(105), 3266-3269
19. Vercauteren LD, Kessels AG, van der Weijden T, et al. Clinical impact of the use of additional ultrasonography in diagnostic breast imaging. Eur Radiol 2008;18(10):2076-2084
20. Vetto J, Pommier R, Schmidt W, Wachtel M, DuBois P, Jones M, Thurmond A. Use of the "triple test" for palpable breast lesions yields high diagnostic accuracy and cost savings. Am J Surg 1995; 169:519-522.
21. Wang J, Chang JK, Kuo HW, Lee TH, Shih FTT. Efficacy of mammographic evaluation of breast cancer in women less than 40 years of age: experience from a single medical center in Taiwan. J Formos med assoc 2007; 106(9):736-747.
22. World Health Organization (WHO). WHO Guide to Cancer Early Diagnosis. WHO; 2017. http://www.who.int/iris/handle/10665/254500. [Accessed April 12, 2020].