Initiating opportunistic breast cancer screening program for asymptomatic self-referring women in Iraq

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Abstract:

Background: Breast cancer is the most frequently diagnosed cancer in women worldwide and organized national mammographic screening has been adopted as gold standard for breast cancer early detection in most developed countries in the world.

Objectives: to evaluate and emphasize the performance of the initiative opportunistic breast cancer screening program in Iraq and to determine the incident malignancy rate of breast cancer among asymptomatic self-referring women aged 40 years or older via digital mammography by mean of the breast imaging reporting and data system (BI-RADS©).

Patients and methods: this retrospective study included a total of 809 asymptomatic self-referring women over age 40 years, mostly consisted of employees of the different Iraqi ministries who attended the national center of early detection of cancer in Medical City Complex at Baghdad for screening purpose during the period from September 2012- October 2013 by using digital mammography. Ultrasound examination performed as complementary study in particular cases and all cases are graded according BIRADS lexicon. BIRADS category 4 and 5 were followed by cytopathological analysis.

Results: 809 asymptomatic self-referring women were included in this initiative screening program for early detection of breast cancer at the main breast care referral center in Baghdad. The mean age at presentation was 49 years (range 40–76 years). The current study found that overall incident malignancy rate among total sample of the study was 1.11% whilst individual malignancy rate per BI-RADS category was 11.1% for BI-RADS 4 lesions and 80% for BI-RADS 5 lesions.

Conclusion: introduction of individual opportunistic screening program of breast cancer has led to a significant increase in early detection rate of breast cancer and enhance the health awareness for breast cancer screening among asymptomatic women.

Keywords: Breast cancer, opportunistic screening, mammography, BIRADS.

Introduction:

Breast cancer is a global public health problem and major health concern in developing countries and its incidence is rising rapidly and early detection of breast cancer represents an important challenge for all the professionals involved.[1,2] Breast cancer is by far, the most common cancer in Iraq; it is consider most frequent among all cancer cases in Iraq.[3-5] Breast cancer is usually diagnosed in late stages in countries with limited resources;[6] for that reasons, screening asymptomatic women by means of mammography can play a significant role in decreasing breast cancer mortality in developing countries and improve survival rates.[7] The WHO guidelines on early detection of cancer distinguish clearly two programmatic approaches: screening which focuses on detecting cancer in asymptomatic at-risk populations and "clinical downstaging" or "early diagnosis" which focuses on detecting cancer early

in symptomatic patients.[8] Screening for breast cancer by mammography has been practiced in western countries for about half a century, with the first randomized controlled screening trial beginning in 1963 and the population screening programs began in several European countries at the end of the 1980s.[9, 10] In, Iraq, though the national program for early detection of breast cancer was initiated by ministry of health in collaboration with WHO since 2000 [11]; however, the organized systemic population-based screening was not established yet because of the lack of infrastructure that is recommended to achieve early detection of breast cancer among a broad segment of the population. The main objectives of the current study are to evaluate the performance of the current status of the initiative opportunistic screening trial for breast cancer in Iraq through a single center practice with reference to international experience and upgrading it into organized populations-based screening program in future and to determine the incident malignancy rate among self-referring asymptomatic women aged 40 years or older by means of digital mammography

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through applying the ACR/BI-RADS classification.

Patients and Methods:

This retrospective study was performed at the National center for early detection of cancer in medical city complex, Baghdad-Iraq [which is considered the main referral center for breast care in Iraq], from September 2012 through to October 2013 included a total of 809 women who were self-referring to the center, generally consisted from employees of different Iraqi ministries who attended the center for screening purpose. Inclusion criteria consisted of asymptomatic woman aged 40 years or older undergoing bilateral digital mammography and women were excluded if they had symptomatic breast or axillary findings (referred directly to the symptomatic breast clinic for appropriate management) and women with incomplete data in pathological reports or women under 40 years were excluded as well. Patient data were collected on a special form designated for breast screening program giving chief complaints, demographic information, risk factors for breast cancer, and history of previous breast surgery, radiological and pathological findings. The age of patients ranged between 40-76 years .All patients were examined by mammography using a full-digital mammography from GE medical system, US (Senographe®) including both mediolateral oblique and craniocaudal views and ultrasound examination performed as complementary study in special cases for further evaluation hence all cases are categorized according to ACR/BI-RADS atlas lexicon by skilled radiologist into 7 categories: BI-RAD 0: incomplete study needs supplementary assessment like additional views or ultrasound examination or comparison with old films or the mammography images are extremely dense masking its underlying lesions that's why the information is insufficient. BI-RADS 1: normal mammographic study needs routine annual screening. BI-RADS 2: benign lesions require routine screening. BI-RADS 3: probably benign lesions need of short interval follow up mammography. BI-RADS 4: suspicious lesions require fine needle aspiration cytology (FNAC) or biopsy. BI-RADS 5: highly suggestive malignant lesion needs FNAC or biopsy then an appropriate action like lumpectomy or mastectomy will be carried out. BI-RADS 6: a known case of breast malignancy needs short interval mammography and appropriate action according to the results. Fine needle aspiration cytology with a 22 gage needle was currently the initial step or core needle biopsy with a 14-16 gage if needed, done under ultrasound guide. The obtained pathological results were reviewed by expert pathologist in the same center. The mammographic follow up interval of BI-RADS 3 lesions ranging from 3-6 months. Statistical analysis were performed with excel Microsoft office 2007, the incidence cancer rate and malignancy rate of breast cancer according BI-RADS lexicon was calculated.

Results:

Demographics:

Between September 2012 and October 2013, 809 asymptomatic self-referring women were screened by digital mammography for early detection of breast cancer at the main breast care referral center in Baghdad. The mean age at presentation was 49 years (range 40–76 years). The majority of these patients were aged between 40 and 49 years (64.9%). Most of sample of the study had at least a high school education (76.5%).

Risk factors:

Regarding the risk factors, the study was revealed personal history of breast cancer in (1.6%) of screened women, family history of breast cancer in (9.2%), history of oral contraceptive pills or hormonal use in (25.7%), early menarche in (9.9%) and late menopause in (1.1%) of sample of study.

Radiological and pathological findings:

After a digital mammography was performed, the radiological findings classified on the basis of ACR/BI-RADS lexicon. The majority (97.7%)of women were normal or had benign looking lesions, only 3 patients of them had non-informative mammography because of extreme density and need further evaluation by ultrasound examination; whereas, 1.1% (n=9) of patients demonstrate suspicious findings on mammogram followed by ultrasound-guide cytopathological examination and 1.2% (n=10) of patients had lesions with malignant criteria on mammogram. The imaging findings of the 908 women examined by mammography were as follows: (3%) microcalcifications alone, (20.4%) mass alone, (0.5%) microcalcifications with mass, (2%) focal asymmetry, (1.5%) macrocalcifications and (72.6%) were normal. Pathological results found that overall incidence rate of breast cancer in total sample of the study were 1.11%. Final results were evaluated for 12 women in age group 40-49 years with positive screening outcomes - BI-RADS 4-5 (6 women found to have breast cancer, 6 false positives) and 7 women aged 50 years or older with positive screening outcomes (3 women found to have breast cancer, 4 false positive). Of 19 total sampled lesions, malignancy rate per BI-RADS category was 11.1% for BI-RADS 4 lesions and 80% for BI-RADS 5 lesions. Cytopathological outcome of BIRADS 4 and 5 lesion summarized in figure (1).

Table (1) BI-RADS classification and cancer status according to age groups

Age at screening (years)	Opportunistic screening				Cancer status	
	BI-RADS 0-3	BI-RADS 4	BI-RADS 5	Total (%)	Negative	Positive
40-49	515	6	4	525 (64.9)	520	5
50-59	210	2	2	214 (26.5)	212	2
60-69	56	1	3	59 (7.3)	58	1
70-80	10	-	1	11(1.3)	10	1
Total	790 (97.7%)	9 (1.1%)	10 (1.2%)	809 (100)	800	9

Table (2) Cancer status in BI-RADS-4 and BI-RADS-5 lesions

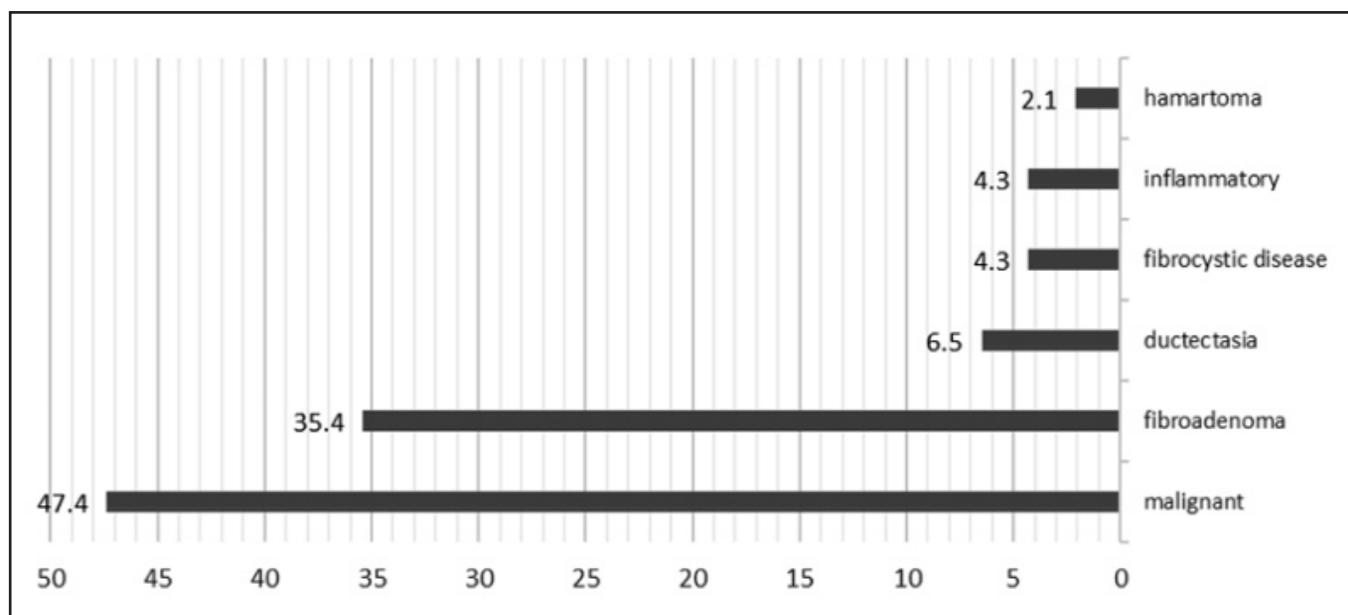|		Positive cancer No. (%)	Negative cancer No. (%)	Total No. (%)
Positive mammogram	BI-RADS 4	1 (11.1)	8 (88.9)	9 (47.4)
	BI-RADS 5	8 (80)	2 (20)	10 (52.6)
	Total	9 (47.4)	10 (52.6)	19 (100)

Figure (1) cytopathological outcome of BIRADS 4 and 5 breast lesion (total No.=19)
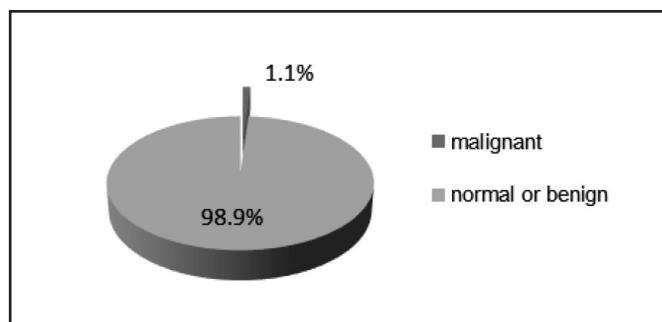

Figure (2) incident cancer rate in total sample of study (total No. = 809)

Discussion:

The currently available scientific evidences confirm that mammographic screening have been able to decrease the mortality related to breast cancer.[3] Since the identification of breast cancer at a time in its natural history when it can be treated and potentially cured with least physical effort.[11] Trials have concluded that mammography screening in women aged from 50 to 59 can reduce breast cancer mortality by 25-30%.[12] Generally, there are two types of screening programs, organized population-based screening prepared by the government and all women of appropriate age are involved and opportunistic screening based on individual centers on a

self-referral basis.[13] In Iraq, the national program for early detection and downstaging of breast cancer was initiated by ministry of health in collaboration with WHO in 2000. The program has been authorized by Iraqi parliament, prime minister's office and ministries of women's affairs, higher education and education with a focus on women aged 40-69 years.[11] however, the national screening program did not apply in recommended manner for organized screening program that managed at a population level and that offers screening, affordable to all individuals of a given age group because of the main political changes that happened in Iraq in 2003; otherwise, without this national cancer control program, most available resources continue to be directed toward cancer therapy in tertiary care facilities. But recently in 2012, the initiative opportunistic breast cancer screening trial done at main referral center for early detection of cancer in medical city-Baghdad consisted in delivering screening to individuals who pro-actively request it or were advised by their doctor to have screening on an individual basis. The breast lesions detected by mammography are classified according to breast imaging reporting and data system (BI-RADS), which is a quality assurance tool introduced by American college of radiology (ACR) in 1993 which includes a lexicon for standardizing mammography reporting, an assessment structure for findings and recommended specific courses of actions on the basis of level of suspicion.[10] Multidisciplinary teamwork allows the all professionals involved to assess and follow up the patient adequately and offer the patients the best therapeutic options.[3] In 2012, the main referral center for early detection of cancer in Baghdad initiated an opportunistic breast cancer screening for individual women who has no symptoms of breast pathology referred for mammographic screening outside of a formal program which may facilitate early diagnosis of non-palpable breast cancers. This screening trial involved women at age of 40 years and older by using dual-view digital mammogram of both breasts. Currently, our center considered pioneered comprehensive self-referred breast screening in Iraq and provides training and expertise in breast radiology and offers essential knowledge and practice regarding ACR/BI-RADS classification of breast lesions; which are necessary requirements for establishing population-based screening. During the period of the study, the majority (64.8%) of attended women were aged 40-49 years and (35.2 %) were aged 50 years or older in contrast with results obtained from Lui CY et al[14] study that found 52% of screened women were aged 50 years or above, which may be explained by our self-referred screening program generally attracts employees of different Iraqi ministries and majority (76.5%) were educated and already received knowledge and practice about breast cancer and low breast cancer awareness among older age-group; therefore, the results obtained from this

study cannot be generalized as population-based screening. Regarding the risk factors, this study was discovered personal history of breast cancer in (1.6%) of patients which is higher than the mean annual metachronous contralateral breast cancer incidence rate was reported by Weir et al and ranged from 2.8 to 7.4 per 1000 women/ year.[15] History of oral contraceptive pills or hormonal use was noticed in (25.7%) of the studied women; however, the contraceptive pill has been shown to slightly increase a woman's breast cancer risk. This risk slowly disappears after stopping the pill.[16] the current study discovered early menarche in (9.9%) of women and late menopause in (1.1%) of women. A collaborative group on hormonal factors in breast cancer reported menarche at age 11 years or younger in (19%) of screened women and menopause in (10%) of women at age 55 years or older and found that breast cancer risk increased by a factor of (1·050; p<0·0001) for every year younger at menarche, and independently by a smaller amount (1·029; p<0·0001), for every year older at menopause.[17] Screening findings by digital mammography graded by ACR/BI-RADS lexicon and BI-RADS 4-5 defined as positive screening outcome and supposed risk of malignancy in BI-RADS 4 category were ranged from 2-95% and more than 95% in BI-RADS 5 category according to the level of suspicion.[10] BI-RADS1-3 regarded as negative screening outcome and risk of malignancy was less than 2% whereas BI-RADS 0 needs additional view or supplementary ultrasound scans, which requested in 0.37% of screening mammograms, which is much better than the recall rate for both additional view and ultrasound study in Lui CY et al study were 2.3%.[14] however, the additional views or complementary ultrasound study cause anxiety to the screened women and financial burden to the screening program.[18] The incidence rate of breast cancer [number of new cases diagnosed in a given population in a given period] estimated as 1.11% [of 809 screening mammograms performed during the study, we detected 9 positive cancers], which is higher than the incident detection rate of cancer in Lui CY et al study done in Hong Kong (3.5 per 1000)[14], and lower than the figure achieved in Kikuchi M et al study in Japan that found the overall screen-detected cancer was 5.6%.[19] the international standard for incident cancer detection rate range between 2-4 per 1000.[20] Detection rate of breast cancers was higher in women with age group 40-49 years than women aged 50 years or older, which is in agreement with Lui CY et al and Kikuchi M et al. [14,19] Whereas the overall malignancy rate was 47.4% of total sampled lesions in both BIRADS category 4 and 5, which is in less than Schueller et al found that breast cancer prevalence was 63.2% [21] and disagreement with Hamy et al identified 32.9% malignancy rate.[22] The individual malignancy rate per BI-RADS 4 was (11.1%) which is inconsistent with Zonderland and Pope study (52.7%) [23] and

malignancy rate per BI-RADS 5 was (80%) which is in agreement with Liberman et al (81%).[24] True positive mammogram in our study was (47.4%) while the false positive mammogram was (52.6%), which is higher than the false positive mammograms achieved by Kikuchi M et al study (25%). [19] The number of false positives was relatively smaller in women in age group 40-49 years than women aged 50 years and older, which goes with Kikuchi M et al study.[19] The number of false negative mammogram could not be ascertained. Pathological results obtained from 9 women with positive breast cancer were ductal carcinoma either invasive or in-situ which is differ from results found in Lui CY et al study were 92% of all cancers whose pathology was available were ductal in origin.[14] Majority of diagnostic intervention were performed percutaneously, ultrasound-guided fine needle aspiration cytology or core needle biopsy and rarely integrated into surgical excisional biopsy. Although the axillary lymphadenopathy noticed in 59.3% of screening mammograms in our study but only 7% of positive screening outcome for malignancy have positive axillary lymphadenopathy regardless of tumor grade. The results were comparable to standards reported internationally [25], which is generally associated with favorable outcome. The current opportunistic breast cancer screening program encountered several limitations. There is no standardized quality assurance or audit program for opportunistic screening dissimilar to population-based screening program has organized auditing system. A second limitation is that false negative results were no ascertained and follow up with cancer registry recommended to overcome this barrier. There is selection bias because of the majority of participant in this individual opportunistic screening at our center from employees of several Iraqi ministries and likely to have high health awareness in compared to those in general population-based screening programs. There is limitation of access to data of other breast clinics or dedicated hospitals in Baghdad remote from this initiative screening program. This current program sometimes fails to complete the patient data and pathology records because of some patients refused underwent the diagnostic intervention in same time or escape from the screening program because of fear from the results or occasionally the patient prefer another opinion or have biopsy in another hospital.

Conclusion:

Currently, there is no population-based breast cancer screening program in Iraq, therefore this current initiative individual opportunistic screening program played an important role in early detection of breast cancer and improves the knowledge and practice of breast screening among asymptomatic women on self-referral basis, which is considered the initial step in establishment of population-based screening through providing the radiologist and radiographer who works in mammography unit the essential training and practice for such program and appropriate usage of ACR/BI-RADS lexicon to standardized the reporting language.

Author contributions:

Abdullateef Aliasghar: Author make substantial contributions to conception and design, and/or acquisition of data, and/or analysis and interpretation of data and drafting the article.
Nada Abdelsahib , Enam Azez: Authors participate in drafting the article or revising it critically for important intellectual content.

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