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.
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).
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Discussion:
The currently available scientific evidences confirm that mammographic screening have been able to decrease the mortality related to breast cancer. 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. Trials have concluded that mammography screening in women aged from 50 to 59 can reduce breast cancer mortality by 25-30%. 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

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

<table>
<thead>
<tr>
<th>Age at screening (years)</th>
<th>Opportunistic screening</th>
<th>Cancer status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BI-RADS 0-3</td>
<td>BI-RADS 4</td>
</tr>
<tr>
<td>-------------------------</td>
<td>------------</td>
<td>----------</td>
</tr>
<tr>
<td>40-49</td>
<td>515</td>
<td>6</td>
</tr>
<tr>
<td>50-59</td>
<td>210</td>
<td>2</td>
</tr>
<tr>
<td>60-69</td>
<td>56</td>
<td>1</td>
</tr>
<tr>
<td>70-80</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>790 (97.7%)</td>
<td>9 (1.1%)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Positive mammogram</th>
<th>Positive cancer No. (%)</th>
<th>Negative cancer No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI-RADS 4</td>
<td>1 (11.1)</td>
<td>8 (88.9)</td>
<td>9 (47.4)</td>
</tr>
<tr>
<td>BI-RADS 5</td>
<td>8 (80)</td>
<td>2 (20)</td>
<td>10 (52.6)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (47.4)</td>
<td>10 (52.6)</td>
<td>19 (100)</td>
</tr>
</tbody>
</table>

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)
self-referral basis. 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. 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. Multidisciplinary
teamwork allows the all professionals involved to assess and
follow up the patient adequately and offer the patients the best
therapeutic options. 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/BIRADS 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 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. 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. 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. Screening findings by digital mammography
graded by ACR/BIRADS 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. 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%. However, the additional views or
complementary ultrasound study cause anxiety to the screened
women and financial burden to the screening program. 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), and lower than the figure
achieved in Kikuchi M et al study in Japan that found the
overall screen-detected cancer was 5.6%. The international
standard for incident cancer detection rate range between 2-4
per 1000. 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. 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% and disagreement with Hamy
et al identified 32.9% malignancy rate. The individual
malignancy rate per BI-RADS 4 was (11.1%) which is
inconsistent with Zonderland and Pope study (52.7%) and

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Vol. 58, No.4, 2016
malignancy rate per BI-RADS 5 was (80%) which is in agreement with Liberman et al (81%). 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%). 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.

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. 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, 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 Abelsahib , Enam Azez: Authors participate in drafting the article or revising it critically for important intellectual content.

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