Review Article

Iraqi Initiative of a Regional Comparative Breast Cancer Research Project in the Middle East

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Abstract

Breast cancer is the commonest malignancy among women in countries within the Eastern Mediterranean Regions (EMR). In Iraq, it comprises approximately one third of the registered female cancers. Other features that justify increasing efforts for breast cancer control in the EMR include the obvious rise in the incidence rates, the higher frequencies of younger ages and advanced stages at the time of presentation and the likely prevalence of more aggressive tumors resulting in high mortality/incidence ratios.

At the level of national registration, most of the cancer registries of those countries lack data regarding tumour staging and mortality rates. In fact, within the hospital records, there is no proper documentation on critically important risk factors and clinical characteristics of the disease including stage distribution at the time of initial diagnosis, hormonal receptor status, proportion of women presenting with distant metastases, treatment modalities and survival rates.

In an attempt to address the aforementioned information needs on the clinical profile of breast cancer patients, and emphasizing the role of research as one of the basic pillars in the adoption of the cancer control strategy, a "National Breast Cancer Research Program-NBCRP" was established in Iraq in 2009. In collaboration with the International Agency for Research on Cancer (IARC) and WHO, the Iraqi researchers developed a comprehensive information system for Iraqi patients diagnosed with breast cancer. Thereafter, that data base model was utilized to compare the demographic characteristics, clinicopathological presentations and management outcomes of breast cancer patients inhabiting selected countries in the EMR (so far Iraq, Jordan, Lebanon and Egypt are included).

BACKGROUND

Globally, breast cancer is the most common cancer among women, comprising 23% of the female cancers [1]. It is also the leading cause of cancer-related deaths. The case fatality rates are highest in low resource countries [1,2]. Although substantial improvement in survival from this disease has been reported in high-income countries such as the USA, the risk continues to increase and survival rates in middle-and low-income countries remain low. According to Globocan [1], in 2008 the total number of newly diagnosed breast cancer cases worldwide was 1.38 million, and the total number of deaths from the disease was 458,367; 59% of the mortality rates were recorded in less developed regions of the world.

Within the Eastern Mediterranean Region (EMR), according to WHO mortality estimates, cancer is the fourth ranked cause of death; succeeding cardiovascular diseases, infectious/parasitic diseases and injuries [3-5]. The largest increase in cancer incidence among the WHO regions in the next 15 years is likely to be in the EMR [6], where breast cancer is reported as the most common type of female malignancy in almost all national cancer registries [1].

Significance of initiating breast cancer control programs in the EMR

In addition to being the most important cancer, there are other features that justify increasing efforts for breast cancer control within the EMR. These include the obvious rise in the incidence rates, the higher frequencies of younger ages and

advanced stages at the time of presentation [7-12] and the likely prevalence of more aggressive tumours resulting in greater fatality rates [1,11,13]. These factors lead to low five-year survival rates (10-50%) from breast cancer in many low- and medium-resource countries (LMC) as compared to more than 85% 5-year survival in high-income countries [1,14].

Information on the putative risk factors for breast cancer and the clinical profile of patients with the disease in terms of clinical stage at presentation, proportion of cancers with regional lymph node metastases, estrogen receptor positivity, treatment patterns and survival outcomes are of utmost importance in the context of breast cancer control in the EMR [7,15]. Two different approaches have to be undertaken to address these two distinct information needs: Properly designed analytical studies such as case-control or cohort studies are needed to address breast cancer risk factors. On the other hand, well conducted descriptive studies can address the pathological, clinical and survival outcome profiles in breast cancer patients.

At the level of national registration, most of the cancer registries of countries belonging to the EMR lack data regarding stages of the disease at presentation [7], age-specific incidence and survival rates. Furthermore, within the hospital records, there is no proper documentation on critically important clinical factors such as tumor size, nodal status, stage distribution at the time of initial diagnosis, hormonal receptor status, proportion of women presenting with distant metastasis, proportion of patients treated with radical mastectomy versus breast conservation surgery, other prevailing treatment modalities (including radiotherapy, chemo and hormonal therapies) and two- and five-year survival rates. A critically important factor in clinical research is an up to date medical record which is often underemphasized. Collecting good quality data from breast cancer patients in LMC depends upon documentation of clinical findings accurately in medical records in cancer treatment centers [2,3,5,14].

In Iraq, breast cancer is the most common type of malignancy among the Iraqi population in general. It accounts for approximately one third of the registered female cancers according to the latest Iraqi Cancer Registry [16] which shows a trend for the disease to affect younger age groups [9,16]. Within the last two decades, there has been an obvious increase in the incidence rates of breast cancer, which became one of the major threats to Iraqi female health. Regrettably, many cases in Iraq tend to be diagnosed at advanced stages [9] with a prevalence of poorly differentiated pathological grades; illustrated in DNA nuclear aneuoploidy and thus yielding a mortality incidence ratio equivalent to 60% [1,13].

In one of the studies that was designed to review the demographic characteristics and clinico pathological presentation of Iraqi patients complaining of breast cancer [9], it was observed that approximately one third were diagnosed at age (40–49) years; 71.9% came from urban areas; and 75% were married. History of lactation was reported in 63.1% and hormonal therapy in 29%. Positive family history was recorded in 16.2%. Although the lump was detected by the patient herself in 90.6% of cases, only 32% sought medical advice within the first month. Accordingly, 47% of those patients presented in advanced Stages (III and IV). The main histological type was Invasive Ductal Carcinoma (IDC),

in which pathological changes signifying Grades II and III were observed in 56.6% and 39.9% respectively. DNA analysis, using quantitative image cytophotometry showed that 80.3% of the carcinomas were aneuploid [13]. Estrogen and Progesterone Receptor positive tumour contents were demonstrated in 65.1% and 45.1% respectively, while Her-2/ neu positive expression was displayed in 46.4% of the examined cases. Overall, triple negative mammary carcinomas were displayed in 16.7% of the cases.

In a more recent survey [17] that evaluated the knowledge, attitude and practice towards breast cancer and breast self-examination (BSE) among a sample of educated Iraqis affiliated with two major universities, it was documented that almost half of the participants had a low knowledge score (< 50%). Although 90.9% had heard of BSE, only 48.3% practiced the technique.

The findings of those two studies clearly justify the demand for increasing efforts to establish comprehensive breast cancer control programs in Iraq and the region.

Introducing a comprehensive information system data base on breast cancer control in iraq and the EMR

In an attempt to address the aforementioned information needs on the clinical profile of breast cancer patients, and emphasizing the role of research as one of the basic pillars in the adoption of the cancer control strategy, a "National Breast Cancer Research Program-NBCRP" was established in Iraq in 2009. In collaboration with the International Agency for Research on Cancer (IARC) and WHO, a comprehensive information system was developed for Iraqi patients diagnosed with breast cancer. Thereafter, that data base model was utilized to compare the demographic characteristics, clinico- pathological presentations and management outcomes of breast cancer patients inhabiting selected countries in the EMR (so far Iraq, Jordan, Lebanon and Egypt are included).

Methodology

In 2009 a comprehensive breast cancer information system database was designed by the Principal Investigator under direct supervision of IARC/Screening Unit to document the demographic characteristics, clinico- pathological presentations and treatment outcomes in Iraqi patients complaining of breast cancer. Following the development and installation of that data base another shorter proforma was devised in consultation with IARC for a "Comparative Regional Breast Cancer Research Program". The main objective is to collect information on critically important clinical, pathological and risk factors from consecutive breast cancer patients attending major cancer facilities in selected countries within the EMR for comparative studies. The recorded clinical data include tumor size, nodal status, stage distribution at presentation, hormonal receptor status, proportion of women presenting with distant metastases, prevailing treatment modalities and survival rates.

A focal representative from each of the four participating countries has been nominated. The criteria for selection comprised being a well known specialist in the field of breast cancer management, preferably directing a major national cancer

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facility. Country representatives, who will work collaboratively in that program, should have a keen interest in cancer research and should express a serious intention to deliver sincerely on that dedicated effort. Each focal country representative will be in charge of nominating five different specialists from his/her local cancer facility, who should actively participate in the research program through the various disciplines of breast cancer management (including registration, diagnosis and treatment), i. e. , pathologists, radiologists, surgeons, statisticians and oncologists.

Currently, the "online information system data base", supervised by the Screening Group of IARC, is operating in a major cancer facility within each of the four countries participating in that project; i. e. , Iraq (Iraqi National Breast Cancer Research Center), Egypt (National Cancer Institute of Cairo), Jordan (King Hussein Cancer Center) and Lebanon (Lebanese Cancer Society). Data are collected systematically from consecutive breast cancer patients diagnosed and treated in those targeted breast cancer centers. Follow-up of the recorded cases will be sustained for 3-5 years.

The **Objectives** of the Regional Comparative Breast Cancer Research Program are presented in Table 1.

The 1st international consultative meeting of the regional comparative breast cancer research program (Sharm Al-Sheikh, Egypt, 21-22 January 2012)

The World Health Organization Regional Office for the Eastern Mediterranean (EMRO) in collaboration with the "Iraqi National Cancer Research Program", "Susan G Komen for the Cure Organization", IARC and IAEA/PACT organized a Consultative Meeting to discuss the plan of action for the implementation of the "Regional Comparative Breast Cancer Research Program".

In addition to representatives from the aforementioned international collaborating agencies, participants in that multidisciplinary meeting included focal representatives and expert statisticians/ epidemiologists from the four participating EM countries.

The main objectives of the first consultative meeting were to discuss the plan of action of the proposed research program, to endorse the devised breast cancer information system and to agree on the collaborative process of data collection and overall analysis. Following the endorsement of the proposed questionnaire, the online data base was installed by IARC/Screening Group, and is currently operating in the targeted cancer centers.

The monitoring and training activities of that regional project are supervised technically by IARC and WHO/EMRO.

Roles of the international collaborating agencies

WHO / EMRO:

World Health Organization / Eastern Mediterranean Regional Office:

- Supervise and coordinate communication between the various stakeholders, focal country representatives and collaborating agencies.

- Collaborate in facilitating funding support to the proposed activities including the international meetings and workshops.

- Collaborate in enhancing publications, dissemination and exchange of relevant documentations and results of the research studies.

- Coordinate regional breast cancer research activities in collaboration with the concerned collaborative agencies.

IARC :

International Agency for Research on Cancer / Screening Group, Early Detection and Prevention Section:

- Plan, develop, install and train in the use of the breast cancer information system to support information collection.

- Provide technical assistance on the utilization and application of the online data base.

- Facilitate and supervise the regional training workshops.

- Supervise the overall process of data collection, analysis and reporting of results.

- Enhance publications, dissemination and exchange of relevant documentations and results of the research studies.

Susan G. Komen for the Cure Organization:

- Promote advocacy to empower breast cancer research grassroots; incorporating targeted community outreach and public awareness.

- Participate in supporting funds required to implement the program particulars including sponsoring the training workshops.

- Cover the requested expenses needed for advertisement, media exposure issues and health education materials.

IAEA/PACT:

International Atomic Energy Agency / Program of Action for

Table 1: Objectives of the regional breast cancer research program.

1. Promoting the process of accurate documentation of clinical findings in medical records of breast cancer patients; facilitating proper collection of data.
2. Supporting and facilitating national cancer registries in the participating countries through providing vital breast cancer statistics including stage distribution, age-specific incidence and survival rates.
3. Comparing the demographic characteristics, clinicopathological presentations and management outcomes of breast cancer patients inhabiting selected countries in the EMR .
4. Enhancing the advancement of cancer research in the region through conducting properly designed analytical and descriptive studies on the impact of putative risk factors and clinical profile of patients with the disease.

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Table 2: Potential outcomes of the regional breast cancer research program.

1. Highlighting the clinical patterns of breast cancer in different EMR countries and the current opportunities to control the disease in LMC.
2. Promoting the dissemination and exchange of accurate information required for breast cancer control in the region.
3. Advancement of cancer research through establishing a regional mechanism for obtaining up to date clinical data.
4. Advocating the development of prompt diagnostic and optimum treatment technologies for breast cancer.
5. Generating the evidence base to emphasize the need for the availability and accessibility of feasible options for early detection and treatment of breast cancer in EMR.
6. Facilitating the development of evidence based, cost-effective, low technology approaches for early detection and multimodality treatment of loco-regional breast cancer in EMR.
7. Documenting the profile of prognostic and predictive factors in breast cancer patients within the EMR.
8. Correlating survival outcomes with known prognostic and predictive factors in LMC in general and EMR in particular.
9. Facilitating the establishment of a resource virtual library on breast cancer control required for sharing data across local and regional boundaries in LMC.

Cancer Therapy; as WHO partner defined in the WHO/IAEA Joint Cancer Control Program:

- Provide technical assistance in radiation medicine related activities including radiology (mammography/quality assurance), nuclear medicine and radiotherapy.

- Collaborate in promoting the utilization of recommendations for improving breast-health and cancer care in Low- and Middle- income countries (LMC).

- Contribute in supporting resource mobilization to ensure implementation of the plan of action in relevant areas.

- Support the implementation of the recorded program activities in collaboration with its partner organizations (i. e. , WHO, IARC and Komen G for the Cure Org.) especially in PMDS (PACT Model Demonstration Sites).

- Include experts in collaboration with its partners to address needs assessments as part of the imPACT missions to related countries. The Potential Outcomes of Regional Comparative Breast Cancer Research Program are displayed in Table 2.

ACKNOWLEDGEMENT

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