

From the editor

Dear Readers,

The Journal of Breast Health has received increasing number of articles from you, and become one of the peer review journal in Turkey with your supports. In order to be an international journal, we funded an international editorial board, and invited very well known experts from the world on breast health. There will be a professional redaction department of the journal, to review submissions in english. As you know, our journal has both an electronic and hard copies, being reached to more than 2.000 readers(<http://www.memesagligi.dergisi.org>). And, it has been accepted by The Scientific and Technological Research Council of Turkey (TUBITAK) and EBSCO Publishing to site last year. Our next step is to site by Pub-Med and SCI Expanded. For this reason, we would like to have your submissions both Turkish with english abstract and also in english. We will do redaction for your papers writing in english. Turkish Federation of National Breast Societies will also support you for this aim.

In our new issue, I would like to give you some information on breast cancer incidence, screening, stages in the world. As a member of The Breast Health Global Initiative (BHGI), results of previous three Global Summits will be given in this paper. National Breast Cancer Registry Program has reached more than 11.000 patients, and new statistical results of the program will be shared with you.

With my warm regards,

Prof. Dr. Vahit Özmen
Editor-in Chief

BREAST CANCER IN THE WORLD AND TURKEY

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Abstract

Background: Breast cancer is the most common cancer of women, comprising 23% of all female cancers around the globe, with an estimated 1.15 million cases diagnosed in 2002. Of the 411,000 breast cancer deaths around the world, 221,000 (54%) occurred in low- and middle-income countries (LMCs). However, in most low- and middle-income countries (LMCs), incidence rates are increasing at a more rapidly than in areas where incidence rates are already high. Breast cancer incidence and prevalence in western part of Turkey in 1992 was 24.4/100.000 in 1992 and 0.3% respectively. Distribution of breast cancer incidence in 2000s changes in different regions of Turkey due to geographic, economic, social, cultural factors. Breast cancer incidence in western part of Turkey (50/100.000) is more than two times in eastern part of Turkey (20/100.000) due to "Westernizing life" (early menarche, late menopause, first birth >30 years, less breast feeding, etc.), and other related factors.

Methods: Established in 2001, Turkish Federation of National Breast Societies has National Breast Cancer Registry Programme

including more than 11.000 breast cancer patients. These patients were evaluated in February 2008, and statistical results will be presented in this paper. The Breast Health Global Initiative (BHGI) created an international health alliance to develop evidence-based guidelines for LMCs to improve breast health outcomes. The BHGI held three Global Summits in October 2002 (Seattle), January 2005 (Bethesda) and, October 2007 (Budapest) using an expert consensus, evidence-based approach developed resource-sensitive guidelines that define comprehensive pathways for step-by-step quality improvement in health care delivery.

Results: Most of 11.208 breast cancers in the registry program diagnosed at stage II (52.8%). Only 4.28% of patients had opportunistic screening and non-palpable breast cancer, and 90% of patients admitted to clinics with a complaint of mass in the breast. Breast conserving surgery was applied in 35% of patients. Five years mean overall survival was 86% in Istanbul Medical Faculty, The Breast Unit. Half of the patients had a pathologic diagnosis with fine needle aspiration or tru-cut biopsy, and diagnosis was performed by excisional biopsy in 29.5% of patients. The BHGI guidelines stratify resources into four levels (basic, limited, en-

hanced, and maximal), making the guidelines simultaneously applicable to countries of differing economic capacities. The BHGI guidelines provide a hub for linkage among clinicians and alliance among governmental agencies and advocacy groups to translate guidelines into policy and practice.

Conclusions Breast cancer incidence has been increased in Turkey in last decades, and there is not nationwide screening program. Its frequency, stage at diagnosis, and treatment have heterogeneity in different regions of Turkey (earlier diagnosis and higher incidence in western Turkey), due to social, cultural, educational economic factors. These problems can be improved through practical interventions that are realistic and cost-effective. Early breast cancer detection and comprehensive cancer treatment play synergistic roles in facilitating improved breast cancer outcomes. The most fundamental interventions in early detection, diagnosis, surgery, radiation therapy, and drug therapy can be integrated and organized within existing health care schemes in Turkey and other LMCs. The BHGI will study what implementation strategies can most effectively guide health care system reorganization to assist countries that are motivated to improve breast cancer outcome in their populations.

Key words: breast cancer, incidence, Turkey, The BHGI, risk factors, low-middle income countries

Breast cancer is the most common cancer of women, comprising 23% of all female cancers around the globe, with an estimated 1.15 million cases diagnosed in 2002¹. There is marked geographical variation in incidence rates, being highest in the developed world and lowest in the developing countries in Asia, Middle East, and Africa. The age-standardized incidence in North America is the highest, at 99.4 per 100,000, while the lowest is in central Africa where it is 16.5 per 100,000¹. However, in most low- and middle-income countries (LMCs), incidence rates are increasing at a more rapidly than in areas where incidence rates are already high. Global breast cancer incidence rates have increased by about 0.5% annually since 1990, but cancer registries in China are recording annual increases in incidence of 3-4%. (1)

Incidence

A population-based cancer registry, covering the province of Izmir (population 2.7 million, 1993-1994) in Western Turkey was established in 1992 (2). Overall cancer incidence was higher in males than in females (age-standardised rates 157.5 and 94.0 per 100,000, respectively), as in previous non-population-based series. The principal cancers in males were tobacco-related - lung (age-standardised incidence rate (ASR) 61.6), bladder (ASR 11.0) and larynx (ASR 10.6), consistent with the high prevalence of smoking, and use of traditional high-tar tobaccos. In women, Breast cancer incidence and prevalence are 24.4/100,000 in 1992 and 0.3% respectively; cervical cancer was relatively rare (ASR 5.4) (2). Distribution of breast cancer incidence changes in different regions of Turkey due to geographic, economic, social, cultural factors. Breast cancer incidence in western part of Turkey (50/100,000) is more than two times in eastern part of Turkey (20/100,000) due to "Westernizing life" (early menarche, late menopause, first birth >30 years, less breast feeding, etc.).

Table 1. Estimated number of breast cancers (Females)

Years	Number of Breast Cancer Cases
2007	44.253
2008	45.696
2009	47.205
2010	48.809
2011	50.399
2012	51.990

To the estimations of the Health Ministry resources (Tuncer, 2006, www.saglik.gov.tr), the number of breast cancer patients in the period of 2007-2012 has been seen in Table 1.

Prognosis

Prognosis from breast cancer is rather good, although globally it still ranks as the leading cause of cancer mortality among women. Very favorable breast cancer survival rates in the United States and other developed countries have been attributed to early detection by screening, and by timely and effective treatment (3). For example, women diagnosed with breast cancer between 1990 and 1992 and reported in the population-based case series from the Surveillance, Epidemiology, and End Results (SEER) program (13,172 women) had an 89% 5-year survival rate (4). By contrast, age-adjusted survival rates for breast cancer in developing regions average 57% and are as low as 46% in India and 32% in sub-Saharan Africa. (4) In addition to heterogeneity in incidence of breast cancer in Turkey, breast cancer mortality also shows differences in different regions depending on breast health awareness, diagnostic and therapeutic infrastructures. In a study evaluating 1841 breast cancer patients from Istanbul Medical Faculty, 5 years breast cancer mortality rate was similar to rates for developed countries (86% and 85% for patients with breast conserving surgery, and mastectomy respectively, median follow up 76 months) (5). This rate was low in Diyarbakir and other cities in East Anatolia (around 60%) due to advanced stage at diagnosis, lack of breast cancer awareness, and other social, educational, cultural and economic barriers to early diagnosis and effective treatment. Surgical procedure was MRM in 66%, and breast conserving surgery in 34% of patients (5).

Breast cancer screening and early detection

There is solid evidence supporting the value of diagnosing cancer early, and guidelines on early detection are available (6,7). The only screening method that has been demonstrated to reduce mortality from breast cancer is mammographic screening (8,9). However, mammography is expensive and requires manpower and technical expertise that is not affordable in most Low-Middle income Countries (LMCs). As a result, BHGI guidelines recommend that breast health awareness (BHA) should be promoted to all women at the basic level (10). In addition to this basic facility, further development will require training of relevant staff to perform clinical evaluation, including taking a history and performing a clinical breast examination (CBE) for both symptomatic and asymptomatic women. Higher-level early-detection programs may include opportunistic screening with CBE, trials of organized screening using CBE and/or

breast self-examination (BSE), and finally feasibility studies of mammography screening. There are sociocultural, educational, economic barriers to breast cancer detection that need to be overcome among women in Turkey. In some cultures, the woman's decision and actions are controlled by men who may be unaware of breast screening as an effective, life-saving modality. According to Turkish Breast Cancer Registry, breast cancer stages at diagnosis were 27% (Stage I), 53% (Stage II), 9% (Stage III), and 6% (Stage IV) respectively (<http://www.mdkk.org/memekanseri/register.php>). 90% of patients admitted to the clinics with a complaint of a painless mass in the breast, only 4.28% of patients had an opportunistic screening mammogram and non-palpable breast cancer.

The breast health global initiative

Evidence-based guidelines outlining optimal approaches to breast cancer detection, diagnosis, and treatment have been well-developed and disseminated in several high-resource countries (11,12). Even in some developing countries, there have been attempts to develop clinical practice guidelines for the treatment of breast cancer based on the resources available (13). Most guidelines define optimal practice, which have limited utility in developing countries where resources are poor. Optimal practice guidelines may be inappropriate to apply in LMCs for numerous reasons, including poverty, infrastructure constraints, drugs, and cultural barriers. Hence, there is a need to develop clinical practice guidelines oriented toward countries with limited financial resources (14). For these reasons, the Breast Health Global Initiative (BHGI) was established in 2002. Cosponsored by the Fred Hutchinson Cancer Research Center in Seattle, Washington, and the Susan G. Komen For The Cure in Dallas, Texas, the BHGI is a program that strives to develop, implement, and study evidence-based, economically feasible, and culturally appropriate guidelines that can be used in LMCs with the aim of improving breast health outcomes. The first evidence-based guidelines were developed at the 2002 BHGI Global Summit, creating guidelines for (1) early detection, (2) diagnosis, and (3) treatment. These guidelines, published in 2003, are free and available on the internet (<http://www.fhrc.org/science/phs/bhgi/>). They outline general principles for programmatic improvement in breast health services as applied to LMCs (15-18). The first BHGI Global Summit adopted two axioms as principles for guideline development: 1. All women have the right to have access to health care, although considerable challenges exist in implementing breast health-care programs when resources are limited, and 2. All women have the right to education about breast cancer, but it must be culturally appropriate and targeted and tailored to the specific population.

At the 2005 BHGI Global Summit, the guidelines were updated and expanded into a flexible, fully comprehensive framework for improving the quality of health-care delivery based upon outcomes, cost, cost-effectiveness, and use of health-care services. Held January 12-15, 2005, and hosted by the Office of International Affairs of the U.S. National Cancer Institute in Bethesda, Maryland, the 2005 BHGI Global Summit convened 67 international experts representing 33 countries and 5 continents to define specific "best practices with limited resources" and was expanded to include medical ethics, international health, medical economics, and sociology. Twelve national and international groups (includ-

ing Breast Surgery International, International Union Against Cancer, International Atomic Energy Agency, International Society of Breast Pathology, and World Society for Breast Health) joined the BHGI as collaborating organizations. In addition, the BHGI established affiliations with three WHO programs: The Cancer Control Programme, Health System Policies and Operations, and the Alliance for Health Policy and Systems Research. The 2005 guidelines addressed (1) early detection and access to care (19), (2) diagnosis and pathology (20), (3) cancer treatment and allocation of resources (21), and (4) health-care systems and public policy (22).

The 2005 BHGI guidelines can be used to communicate programmatic needs to hospital administrations, government officials, and/or health-care ministries. The thesis of the BHGI is that these guidelines create a framework for change by defining practical pathways through which breast cancer care can be improved in an incremental and cost-effective fashion (23,24). However, guidelines do not in and of themselves improve outcomes for women. Implementation is the critical step by which the value of the guidelines can be measured. The results of pilot research projects and demonstration projects need to be studied and reported to determine the effectiveness of the guidelines and to create evidence that will guide and facilitate guideline implementation in other settings.

The Breast Health Global Initiative (BHGI) held its 3rd Global Summit in Budapest, Hungary from October 1-4, 2007, bringing together internationally recognized experts to address the implementation of breast health care guidelines for early detection, diagnosis and treatment in low- and middle-income countries (LMCs). A multidisciplinary panel of experts addressed specifically the implementation of BHGI breast cancer guidelines for early detection of disease as related to resource allocation for public education and awareness, cancer detection methods and evaluation goals. Public education and awareness is a key first step, because early detection cannot be successful when the public is unaware or has adverse misconceptions about the value of early detection. The approach and scope of any screening program will determine both the success of any early detection program as measured by cancer stage at diagnosis, and will also drive the breadth of resource allocation needed for program implementation. The effectiveness and efficiency of screening modalities including screening mammography, clinical breast examination (CBE) and breast self-examination were reviewed in the context of resource availability and population-based need. Social and cultural barriers to breast cancer early detection must be considered in any context where early detection programs are being established. For each early detection category and tool, the use of well-developed, methodologically sound quality indicators is important to determine the effectiveness of early detection program implementation success.

Breast cancer risk factors in Turkish women

In a survey conducted by Ozmen et al., breast cancer risk factors in Turkish women were studied (25). The survey was prospectively conducted among women admitted to clinics of Istanbul Faculty of Medicine for examination and/or treatment by using a questionnaire. The women were selected from the waiting area of different clinics without breast cancer by convenience sampling (n=

Tablo 2. Symptoms of patients with breast cancer admitted to clinics.

Symptoms	Number of patients (n)	Per cent (%)
Pain	157	2,60
Mass in the axilla	57	0,94
Breast skin/nipple areola changes	73	1,21
Mass in the breast	5426	89,91
Discharge from nipple	64	1,06
No symptoms		
Opportunistic screening and menopause clinics	258	4,28
Total	6035	100,00

2167) whereas patients with breast cancer were either selected from patients visiting our Breast Clinic for follow-up, or from our breast cancer database (n=1492). The results suggested that, being greater than or equal to age 35 years old, having induced abortion, multiparity (≥ 1), late age at first birth (≥ 35 years old), late age at menopause (≥ 50 years old), body mass index (BMI) ≥ 25 and having first-degree family history of breast cancer were risk factors for breast cancer in Turkish women. Higher educational level (high school), having miscarriages, cigarette smoking, oral contraceptive usage, breast feeding more than one child (unrelated to total period of breast feeding) reduced breast cancer risk. Factors including use of hormone replacement therapy for 5 years or more and alcohol consumption are not found to be associated with breast cancer risk.

Breast Cancer Patients' Characteristics in Turkey

National Federation of Breast Societies of Turkey funded in 2001 and has a Breast Cancer Registry Programme since June 2005 (<http://www.mdck.org/memekanseri>). In this registry programme, 11.208 breast cancer patients were recorded till February 2008 (26). Patients' registrations came from 13 breast centers localized in 8 cities (Istanbul, Izmir, Ankara, Bursa, Kocaeli, Aydin, Diyarbakir, and Adana) in Turkey.

According to statistical analyses of National Breast Cancer Registry Programme (26), mean age of breast cancer was 51.5 (12 to 97), and 20.2% of patients was ≤ 40 years of age. Breast cancer in women under 35 years of age has been reported in the West to account for 2%–4% of all breast cancer cases (27), and only 6.5% of all breast cancers are detected in women under the age of 40 (28). Our rate is similar to other Middle East, Asian countries (29). Although this finding may be partially due to the age structure of the population in Turkey, age-adjusted incidence still found that a higher proportion of young women who present with breast cancer in this locality. There is also documentation that, although the Asian population has a lower incidence of breast cancer, they have an earlier age at maximal risk and less increase after menopause (30). The full rea-

Tablo 3. Clinical stages of patients with breast cancer at the first presentation

Stages	Number of patients (n)	Per cent (%)
I	1262	26,86
II A	1532	32,62
II B	949	20,20
III A	411	8,75
III B	299	6,37
III C	20	0,43
IV	224	4,77
Total	4697	100,00

son for the peak of onset of breast cancer at the age of 40 is still unclear. This may be attributed in part to a more Westernized lifestyle, reflected by a significant difference in the mean age at first live birth and mean age of menarche in this cohort (31). Further studies on the predisposition and gene-environmental interaction in this age group may increase this understanding.

Breast cancer in Turkish women between 41-50, 51-70, and ≥ 70 years of age were 31%, 40.7%, and 8.2% respectively. 14.5 per cent of patients had family history of breast cancer. Mean age of menarche, and first birth were 13.2 and 22.5 respectively. Mean number of deliveries and breast feeding duration in patients with breast cancer were 2.67 and 18.5 months, respectively. History of previous hormone replacement therapy and oral contraceptive usage were positive in 9.3% and 11% of patients. The rate of menopausal patients was 57%. All patients with breast cancer had diagnostic mammography, and in 7% of patients, magnetic resonance imaging was added to mammography and breast ultrasound.

Only 4.28% of patients with breast cancer and without any symptoms came to the clinics with opportunistic screening or from menopause clinics. A painless mass in the breast was only symptom in 90% of patients (Table 2). Duration of symptoms was less than 1 month in 40% of patients, but more than 6 months in 23.5%. This delaying to admission is mostly related with the belief of Turkish women that a painless mass in the body is not cancer.

Fine needle aspiration biopsy (FNAB) and excisional biopsy were performed in 39% and 29.5% of patients for histopathologic diagnosis, respectively (Table 4).

If we look at the surgical procedures, modified radical mastectomy was the most common surgery (63%), and breast conserving surgery was the second(36%). Only 1% of patients had radical mastectomy. Histopathologic diagnoses were invasive ductal (70.7%), invasive lobular(7.1%), and mixed type invasive cancer(5.8), respectively. Medullar(2%), mucinous(2%), tubular(1.5), and papill-

Table 5. Pathologica tumor size of patients with breast cancer.

<i>Tumor size (T)</i>	<i>Number of patients (n)</i>	<i>Per cent (%)</i>
≤ 10 mm	348	9,5
10 < T ≤ 20 mm	1272	34,7
20 < T ≤ 50 mm	1810	49,4
T>50 mm	234	6,4
Total	3664	100,0

er(0.9%) types were other less frequently seen cancers. Tumor sizes in 3664 patients were seen in Table 5. Only 9.5% of patients had tumor size less than 10 mm.

Estrogen, progesteron, and HER-2 receptors were positive in 67.4%, 51.9%, and 17.5% of patients. Only 4.5% of patients had Nuclear grade 1 tumor (55.8% Grade 2, 39.7% Grade 3). Lymphovascular invasion was positive in 52.3% of patients. Sentinel lymph node biopsy was performed in 1233 patients, and sentinel lymph node was positive 54.7% of patients. Blue dye (busulphan or methylen blue) alone or combined technique (blue dye + radioisotope) was used in 62% and 38% of patients.

Conclusions

Breast cancer is the most common female malignancy, and consists of 24% of cancers in women. Incidence rate and prevalence have increased three times in last decades in Turkey. There are big differences regarding stage at diagnosis, and effective treatments between eastern and western part of

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Table 4. Methods performed for histopathologic diagnosis in patients with breast cancer.

<i>Diagnostic method</i>	<i>Number of patients (n)</i>	<i>Per cent (%)</i>
FNAB	1396	39,18
Excisional biopsy	1051	29,50
Tru-cut biopsy	383	10,75
Incisional biopsy	366	10,27
Frozen section	280	7,86
Mammography/ultrasound guided biopsy	51	1,43
Cytology from nipple discharge	36	1,01
Total	3563	100,00

Turkey. Poorer survival in eastern part of Turkey is largely due to late presentation of the disease which, when coupled with limited resources for diagnosis and treatment, lack of breast health awareness, social, cultural, and educational factors leads to particularly poor outcome. The BHGI guidelines can be used to communicate programmatic needs to hospital administrations, government officials, and/or health-care ministries in LMCs. The thesis of the BHGI is that these guidelines create a framework for change by defining practical pathways through which breast cancer care can be improved in an incremental and cost-effective fashion.

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