Sociological Transition and Breast Cancer in the Arab World: the Experience of Lebanon

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Abstract

Background: Breast cancer is the leading cause of cancer death among females in Lebanon. This study aimed at analyzing its epidemiology in the country over time. Methods: Data were extracted from the Lebanese National Cancer Registry (NCR) for the years 2004 through 2010. Age-standardized and age-specific incidence rates for cancers per 100,000 population were calculated. Results: Breast cancer ranked first, accounting for an average of 37.6% of all new female cancer cases in Lebanon during the period of 2004-2010. Breast cancer was found to have been increasing faster than other hormone-related women’s cancers (i.e. of the ovaries and corpus uteri). The breast cancer age-standardized incidence rates (world population) (ASRw) increased steadily from 2004 (71.0) to 2010 (105.9), making the burden comparable to that in developed countries, reflecting the influence of sociological and reproductive patterns transitioning from regional norms to global trends. The age-specific incidence rates for breast cancer rose steeply from around age 35-39 years, to reach a first peak in the age group 45-49 years, and then dropped slightly between 50 and 64 years to rise again thereafter and reach a second peak in the 75+ age group. Five-year age-specific rates among Lebanese women between 35 and 49 years were among the highest observed worldwide in 2008. Conclusion: Breast cancer is continuously on the rise in Lebanon. The findings of this study support the national screening recommendation of starting breast cancer screening at the age of 40 years. It is mandatory to conduct an in-depth analysis of contributing factors and develop consequently a comprehensive National Breast Cancer Control strategy.

Keywords: Breast neoplasms- Lebanon- developed countries- registries- incidence

Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females worldwide, accounting respectively for 25.2% of total cancer cases (excluding non-melanoma skin cancers) and 14.7% of cancer deaths in 2012 (Ferlay et al., 2010a; Ferlay et al., 2010b; Ferlay et al., 2015). The highest incidence of breast cancer is in Western and Northern Europe (Age-standardized incidence rates (world population) (ASRw): 89.9 and 84.0 respectively), followed by Australia/New Zealand (ASRw: 85.5), and Northern America (ASRw: 76.7); while the lowest incidence is in Eastern Africa (ASRw: 19.3), Middle Africa (ASRw: 21.3), South-Central Asia (ASRw: 24.0) and Central America (ASRw: 26.0) (Ferlay et al., 2015).

Lebanon is a small developing country in the Middle East with an estimated population of around 5 million in 2013 (World Health Organization, 2015). Lebanon has health indices that are almost comparable to those of more developed countries, with a reported Infant Mortality Rate of 8 per 1000 live births in 2012, Maternal Mortality Ratio of 16 per 100,000 live births in 2013, and Life Expectancy at Birth of 80 years in 2012 (83.2 for females and 79.6 for males) (World Health Organization, 2015; World Health Organization, 2016a; World Health Organization, 2016b). The Lebanese National Cancer Registry (NCR) was officially restarted in 2002, and is believed to be an almost absolute count of all incident cases in Lebanon (Adib et al., 2008). The NCR has completed its cancer incidence data for the years 2004 through 2010 and published the data on the official website of the Ministry of Public Health (MoPH). The estimated age-standardized incidence rate per 100,000 (ASRw) for female breast cancer in Lebanon was 71.0 in 2004 (Lakkis et al., 2010). This rate was higher than those estimated for Arab nations but lower than those observed in North America, West Europe and Israeli Jews (Lakkis et al., 2010). The Lebanese NCR showed that the five-year age-specific rates among Lebanese women in 2004 were among the highest observed worldwide for the age groups 35–39, 40–44 and 45–49 years (Lakkis et al., 2010). The MoPH in Lebanon recommends screening for breast cancer yearly starting at the age of 40 years (Adib et al., 2009); whereas most Western countries recommend
starting the screening at the age of 50 years (Forouzanfar et al., 2011; Youlden et al., 2012).

The main aim of this study is to analyze the 7-year incidence rates for breast cancer and study the related trends, and to compare it to regional and Western countries. The results of this study would contribute to the national strategy to control breast cancer in Lebanon including current screening recommendations. This study will also discuss different possible contributing factors.

Materials and Methods

The age-standardized incidence rate was computed using the WHO standard world population of 2001 (ASRw) (Hill and Menhamou, 1995). The ASRw and the age-specific incidence rates were obtained from the Lebanese NCR figures for the years 2004 to 2010 (Ministry of Public Health, 2010) and were expressed as per 100,000 population. The age-standardized incidence rate (ASR) is a summary measure of a rate that a population would have if it had a standard age structure. Standardization is necessary when comparing several populations that differ with respect to age structure. The most frequently used standard population is the World Standard Population (Hill and Menhamou, 1995). The age-specific incidence rate is the number of new cancer cases happening during a specific period, in a population of a specific age and sex group, divided by the number of midyear population of that age and sex group (Centers for Disease Control and Prevention, 2014). The NCR does not include data on non-invasive precancerous lesions and in-situ lesions and non-melanoma skin cancer.

The calculated ASRw and age-specific rates were subsequently compared with rates from selected regional and Western countries as published online or from Globocan 2008 (Figures 1, 2).

Results

Breast cancer has been the leading cancer among Lebanese females since the 1960s (Abou-Daoud, 1966). Over a seven-year period (2004-2010), breast cancer ranked as the first most common cancer in women and it represented an average of 37.6% of all new female cancer cases in Lebanon. Other hormonal-related women’s cancers were also common, namely ovarian cancer that ranked fifth and corpus uteri cancer that ranked sixth. However, breast cancer has been increasing at a faster rate than both ovarian and corpus uteri cancers (figure 1). Breast cancer ASRw rose steadily from 2004 (71.0) through 2010 (105.9) with an increase of 49.2% in 7 years. An increase in the ASRw of the other female hormone-dependent cancers, which share many similar risk factors (Jemal et al., 2011; Cramer, 2012), was also noted during the same period even though their total caseloads remained much smaller than that of breast cancer. Corpus uteri cancer incidence rose from 6.3 in 2004 to 8.5 in 2010 (an increase of 34.9% in 7 years) and ovarian cancer incidence rose from 8.3 in 2004 to 8.8 in 2010 (an increase of 6.0% in 7 years).

Throughout the years of 2005 to 2010, the age-specific incidence rates for female breast cancer rose steeply at around the age group of 35-39 years, to reach a first peak in the age group 45-49 years, and then drop slightly between 50 and 64 years to rise again thereafter and reach a second maximal peak in the 75+ age group (figure 2 and table 1). The age-specific incidence rates for ovary and corpus uteri cancers in Lebanon for the years 2005-2010 are showed in figure 2 as well.

Breast cancer in Lebanon accounted for 37.9% of all new female cancer cases in 2008 compared to 30.2% in the Middle East and Northern Africa (MENA) region and 22.9% in the world (Ferlay et al., 2010a). This proportion was even higher than in some European nations such as Belgium and Denmark (35.4% and 28.5% respectively in 2008) (Ferlay et al., 2010a; Belgian Cancer Registry, 2011; Engholm et al., 2013; UNECE, 2013).
The breast cancer ASRw in Lebanon (95.7 in 2008) was lower than the ASRw reported in Western countries such as Belgium (106.0 in 2008) and Denmark (99.9 in 2008), but higher than the ASRw in the United Kingdom (UK) (91.9 in 2008-2010) and the United States (US) SEER (89.4 in 2006-2010) (United States Census Bureau, 2008; Ferlay et al., 2010a; Belgian Cancer Registry, 2011; Cancer Research UK, 2013; Engholm et al., 2013; Howlader et al., 2013; UNECE, 2013) (table 2). This rate was almost comparable to that of the Israeli Jewish women (ASRw: 94.3) (Ministry of Health, 2008). However, it remained higher compared to other MENA region (32.7) (Ferlay et al., 2010a; Ferlay et al., 2010b) countries (table 3) (Chouchane et al., 2013).

Ovarian ASRw in Lebanon (9.3 in 2008) was higher than the one estimated for the world (6.3 in 2008) and for MENA region (4.8 in 2008) (Ferlay et al., 2010a). It was comparable to the one estimated in developed countries (9.4 in 2008) (Jemal et al., 2011) and Israeli Jewish (8.9 in 2008) (Ministry of Health, 2008).

Corpus uteri ASRw in Lebanon (8.8 in 2008) was almost similar to the one estimated for the world (8.2 in 2008) and higher than the one estimated for MENA region (3.9 in 2008) (Ferlay et al., 2010a). But, it was lower than the one estimated in developed countries (12.9 in 2008) (Jemal et al., 2011), and Israeli Jewish (14.7 in 2008) (Ministry of Health, 2008).

### Table 2. Breast Cancer Age-Standardized Incidence Rates (World Population) and Age-Specific Rates per 100,000 Females in Lebanon Compared to Non-MENA* Countries

| Breast | Lebanon | Iran | Malaysia | Japan | USA | England | Denmark | Finland | Sweden | Belgium |
|--------|---------|------|----------|-------|-----|---------|---------|---------|--------|---------|
| 2004   | 95.7    | 23.2 | 29.1     | 52.0  | 89.4| 90.3    | 99.9    | 85.5    | 79.6   | 106.0   |
| 20-24y | 2.6     | 0.8  | 1.6      | 1.6   | 1.6 | 2.0     | -       | 0.6     | 0.7    | 3.5     |
| 25-29y | 9.9     | 5.9  | 5.7      | 5.6   | 8.6 | 10.1    | 8.3     | 4.3     | 8.1    | 8.8     |
| 30-34y | 19.3    | 14.7 | 16.0     | 22.6  | 26.2| 27.2    | 31.4    | 20.0    | 27.4   | 35.0    |
| 35-39y | 78.7    | 33.1 | 29.6     | 55.4  | 59.1| 61.2    | 56.6    | 45.6    | 51.6   | 75.4    |
| 40-44y | 203.6   | 47.9 | 54.9     | 113.0 | 122.2| 122.1   | 115.5   | 100.8   | 103.6  | 165.5   |
| 45-49y | 338     | 74.0 | 95.1     | 171.4 | 187.7| 202.2   | 175.3   | 183.0   | 175.5  | 265.9   |
| 50-54y | 276.5   | 74.3 | 90.6     | 155.5 | 222.8| 274.2   | 258.1   | 274.0   | 219.2  | 304.1   |
| 55-59y | 271.1   | 69.3 | 100.4    | 155.1 | 268.3| 273.3   | 353.3   | 301.4   | 245.7  | 347.5   |
| 60-64y | 259.2   | 69.1 | 85.7     | 157.6 | 346.2| 358.4   | 450.0   | 391.5   | 321.8  | 394.3   |
| 65-69y | 320.5   | 48.6 | 82.2     | 144.0 | 413.2| 391.8   | 528.6   | 369.0   | 374.1  | 402.2   |
| 70-74y | 303.2   | 43.7 | 63.1     | 141.0 | 424.6| 302.8   | 408.6   | 287.5   | 337.7  | 360.1   |
| 75+y   | 267.0   | 47.2 | 53.7     | 110.0 | 405.7| 388.6   | 371.3   | 295.0   | 291.0  | 365.2   |

The symbol *"* = 0-2 cases; *MENA, Middle East and North Africa region; §Age-standardized incidence rate world population; References, Lebanon (Ministry of Public Health, 2010); Iran (World Health Organization, 2008); Malaysia (Malaysia Ministry of Health, 2011); Japan (Matsuda et al., 2013); US-SEER (United States Census Bureau, 2008; Howlader et al., 2013); England (Office of National Statistics, 2009; Office of National Statistics, 2010); Denmark (Engholm et al., 2013); Finland (Engholm et al., 2013); Sweden (Official Statistics of Sweden, 2009); Belgium (Belgian Cancer Registry, 2011; UNECE, 2013)
| Age Group | Lebanon | Cyprus | Jordan | Saudi Arabia | Oman | Egypt (Aswan) | Egypt (Damietta) | Egypt (Minia) | Algeria | Morocco (Rabat) | Morocco (Casablanca) | Israeli Jewish | Israeli Arabs |
|-----------|---------|--------|--------|-------------|------|-------------|-----------------|-------------|---------|----------------|------------------|----------------|-------------|
| 20-24y    | 2.6     | 6.1    | 7.3    | 5.6         | 4.6  | 4.2         | 1.7             | 4.2         | -       | -                | -                | 0.5            | -           |
| 25-29y    | 9.9     | 3.0    | 7.3    | 5.6         | 4.6  | 13.7        | 5.7             | 14.0        | 3.3     | 6.8             | 6.9               | 3.3            | 6.3        |
| 30-34y    | 19.3    | 29.9   | 17.3   | 14.0        | 11.0 | 28.9        | 29.5            | 28.3        | 38.5    | 27.6            | 18.1             | 21.8          | 22.4       |
| 35-39y    | 78.7    | 53.1   | 44.4   | 24.2        | 24.2 | 57.2        | 49.6            | 42.5        | 66.7    | 25.9            | 26.3              | 81.5          | 26.3       |
| 40-44y    | 203.6   | 111.3  | 93.0   | 47.8        | 50.0 | 140         | 78.2            | 56.0        | 163.6   | 100.0           | 96.8              | 131.3         | 82.7       |
| 45-49y    | 338.0   | 180.8  | 139.6  | 69.1        | 48.0 | 99.1        | 116.7           | 83.1        | 184.1   | 107.2           | 106.1             | 205.5         | 145.1      |
| 50-54y    | 276.5   | 224.7  | 154.1  | 62.1        | 71.0 | 220.7       | 107.8           | 109.7       | 181.9   | 88.3            | 108.2             | 237.4         | 199.2      |
| 55-59y    | 271.1   | 226.4  | 157.7  | 61.0        | 70.8 | 99.1        | 116.7           | 83.1        | 197.2   | 108.5           | 108.5             | 263           | 228.6      |
| 60-64y    | 271.4   | 316.4  | 193.3  | 74.8        | 35.0 | 184.4       | 127.1           | 142.3       | 181.7   | 85              | 103.2             | 365.1         | 225.5      |
| 65-69y    | 267.2   | 324.7  | 198.3  | 62.7        | 58.0 | 220.6       | 142.3           | 112.2       | 197.2   | 143.7           | 106.5             | 434.9         | 317.3      |
| 70-74y    | 303.2   | 324.7  | 198.3  | 62.7        | 58.0 | 220.6       | 142.3           | 112.2       | 197.2   | 143.7           | 106.5             | 434.9         | 317.3      |
| 75+y      | 267.0   | 271.4  | 147.1  | 43.8        | 111.0| 296.9       | 151.7           | 89.9        | 83.5    | 55.4            | 53.2              | 343.5         | 170.2      |

Table 3. Breast Cancer Age-Standardized Incidence Rates (World Population) and Age-Specific Rates per 100,000 Females in Lebanon Compared to MENA* Countries

The symbol "-" means < 3 cases; MENA, Middle East and North Africa; §Age-standardized incidence rate world population; References: Lebanon (Ministry of Public Health, 2010); Cyprus (Pavlou et al., 2011); Jordan (Tarawneh et al., 2008); Saudi Arabia (Al-Eid et al., 2012); Oman (Sultanate Oman Ministry of Health, 2008); Egypt (Egypt National Cancer Registry, 2009); Algeria (Ministère de la Santé et de la Population, 2007); Morocco (Registre des cancers de Rabat, 2005; Association Lalla Salma, 2012); Israel (Ministry of Health, 2008).
Discussion

Breast cancer remains by far the leading cancer among women in Lebanon. ASRw remains higher compared to the other MENA countries but still lower than non-MENA countries reflecting possibly the influence of sociological and reproductive patterns transitioning from regional norms to global trends. Another particularity is the presence of relatively high age specific incidence rates at age groups younger than 50 years in Lebanon, which supports the current national recommendation of starting screening at the age of 40 years.

Several factors have been reported in the literature to be associated with the international variation in breast cancer incidence rates; these include: differences in reproductive, hormonal and lifestyle factors; differences in population size and age structure; and availability of early detection services (Jemal et al., 2011; Youlden et al., 2012). The rise of female breast cancer incidence rates in Lebanon between 1998 and 2010, in general and across all broad age groups (Table 1 and Figure 1), might be attributed to the following factors:

Improved breast cancer screening rates and improved technology in Lebanon

The awareness campaigns held annually by the Lebanese MoPH since 2002, recommending yearly screening starting at the age of 40 years, led to higher rates of mammography screening and improved awareness of early signs of breast cancer among Lebanese women (Adib et al., 2009).

Organized screening programs in developed countries are associated with improved diagnosis of breast cancers (Paci et al., 2004; Svendsen et al., 2006; Youlden et al., 2012). The incidence rates from several Western countries increased sharply in the late 1980s and 1990s (Jemal et al., 2011) mainly due to the introduction of population screening (Jurgensen and Gotzsche, 2009; Jemal et al., 2011; Youlden et al., 2012) and to changes in reproductive factors such as the increased use of postmenopausal hormone replacement therapy (HRT) (Jemal et al., 2011). Since the beginning of the millennium, the overall incidence rates remained significantly higher than expected worldwide, despite a decrease in several developed countries, partly due to lower use of combined postmenopausal HRT (mainly in age group 50-59), a plateau in participation rates for mammographic screening and a decline in the pool of cases diagnosed by screening prior to becoming symptomatic (Jurgensen and Gotzsche, 2009; Forouzanfar et al., 2011; Jemal et al., 2011; Youlden et al., 2012; Hou and Huo, 2013). In Lebanon, breast cancer incidence rates did not reach a plateau yet and the rates of participation in breast cancer screening are still increasing particularly in the age group 50-59 compared with the age group 40-49 or ≥ 60 (Haddad et al., 2015). Moreover, and in view of the limited use of postmenopausal HRT in Lebanon (Obermeyer et al., 1999), its effect on the sharp rise in incidence rates was not obvious between 1998 and 2006, even among women in the age group 50-59, contrary to what happened in Western countries such as US, UK, France and Australia (Center et al., 2011).

Furthermore, the introduction of advanced breast cancer screening methods such as digital mammography, to the Lebanese market improved cancer detection rates, hence contributing to the rise in incidence rates. Digital mammography is significantly more accurate than regular film mammography in detecting cancer in women under the age of 50 years, women with dense breasts, and premenopausal or perimenopausal women (Pisano et al., 2005; Pisano et al., 2008; Hou and Huo, 2013).

In Lebanon, the trends by age group show clearly that the steeper increase in breast cancer incidence between 2004 and 2010 was largely confined to women above the age of 40 corresponding to the target population of the national awareness campaign. The aforementioned factors contributed to the high incidence rates for the age group 40-49 years. Moreover, the elevated ASRw in the age group 35-39 years may be attributed to an improved awareness of breast cancer early signs since the initiation of the annual national breast cancer awareness campaigns in 2002, particularly among those who have a family history of breast cancer.

The low rates in Arab countries might be due to limited screening and incomplete reporting (El Saghir et al., 2007; Forouzanfar et al., 2011; Youlden et al., 2012; Chouchane et al., 2013).

Lebanese women demographics

The overall worldwide number of new breast cancer cases in 2008 were almost similar in more developed and less developed countries, but the different population size and age structure resulted in a lower ASRw in the latter (71.7/100,000 and 29.3/100,000 respectively) (Ferlay et al., 2010a; Ferlay et al., 2010b). The proportion of women younger than 50 years in Lebanon (77.6% in 2007) is higher than the ones reported in Western countries such as the USA (67.7% in 2008) (United States Census Bureau, 2008), UK (64% in 2009) (Cancer Research UK, 2013), Australia (69% in 2009) (Center et al., 2011) and Denmark (62.7% in 2008) (Engholm et al., 2013). This may partly explain the highest age specific rates among women below 50 years in Lebanon.

Moreover, the changes in the Lebanese women demographics since 1998 may contribute to the high rate of breast cancer in elderly women. These demographic changes were mainly related to a steady increase in life expectancy at birth for both sexes (80.0 years in Lebanon compared to 68.0 years in the WHO Eastern Mediterranean region in 2012) (Central Administration of Statistics, 2007; World Health Organization, 2015).

Changes in reproductive, hormonal and lifestyle factors

Breast cancer risk factors that are more prevalent in more developed countries than less developed ones including having children (if any) at an older age, inappropriate breastfeeding, use of oral contraceptives and postmenopausal HRT, obesity (body fatness), poor physical activity, and excessive alcohol consumption (Jemal et al., 2011; American Cancer Society, 2014) are also prevalent in Lebanon, with the exception of alcohol consumption (Sibai et al., 2009), use of oral contraceptives...
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Female reproductive factors in Lebanon are different than the regional Arab countries and are more similar to Western developed countries: The total fertility rate per woman in Lebanon (year 2011) was 1.5 compared to a regional average of 3.2 and a global average of 2.4 (World Health Organization, 2015); the median age of marriage among females was reported to be 28.9 years; the number of single nulliparous women in Lebanon is relatively high (Central Administration of Statistics, 2007; World Health Organization, 2015), and the age at natural menopause in Lebanon is comparable to median ages reported for women in industrialized countries (49.3-51.4) (Reynolds and Obermeyer, 2001). Although different contraceptive methods are easily accessible at low prices and without a prescription, Lebanon’s 58% contraceptive-use rate is relatively low compared to some Arab countries (e.g. Morocco: 63%) regional countries (e.g. Iran: 73.8%) and to Western countries (e.g. France: 81.8% and US: 72.8%) (World Health Organization, 2014), with only around 15% of Lebanese women using oral contraceptives (Sikimic, 2010).

Physical activity: In their national representative sample of household survey, Sibai et al. found that a good percentage of adult female respondents had sedentary lifestyle, with the percentage increasing with age from 25.4% for the age group 18-39 years to 31.8% and 47.3% for the age groups 40-59 and 60+ years respectively (Sibai et al., 2009).

Excess body weight: Is associated with an increased risk of breast cancer among postmenopausal women (Lahmann et al., 2004; Ligibel, 2011; American Cancer Society, 2014), and a poor prognosis in obese women diagnosed with early-stage breast cancer (Ligibel, 2011). A national population-based study in Lebanon in 2009 showed high prevalence rates of excess weight in women aged 40 to 59 years (76.9%; overweight: 40.3%; obesity: 36.6%) and ≥ 60 years (84.4%; overweight: 35.1%, obesity: 49.3%), with the rates approaching those observed in developed countries such as the US (Nasreddine et al., 2012).

Smoking, active or passive: Suspected to increase breast cancer risk (California Environmental Protection Agency, 2005; Luo et al., 2011; Xue et al., 2011; Gaudet et al., 2013), is on the rise among Lebanese females of different age groups (Sibai et al., 2009; Nakkash et al., 2010; World Health Organization, 2013). Lebanon has one of the weakest tobacco control regulatory environments in the Middle East region, and smoking is socially accepted even among teen girls unlike other Arab countries. The average rate of tobacco use in females aged ≥ 15 years in Lebanon is 30.0% compared to 4% in the region (World Health Organization, 2013).

Genetic factors

Genetic factors may also account for a small part of the worldwide variation in the incidence of breast cancer (Parkin and Fernández, 2006; American Cancer Society, 2014). About 5% to 10% of breast cancer cases in the US are thought to be due to inherited gene mutations mostly the BRCA1 and BRCA2 genes (American Cancer Society, 2014). The prevalence of BRCA1 and BRCA2 mutations in Lebanese women with breast cancer and at high risk of carrying inherited gene mutations (young age at presentation and/or positive family history of breast and/or ovarian cancer) and recruited at the American University of Beirut-Medical Center between 2009 and 2012 (n=250) turned out to be 5.6% (El Saghir et al., 2015). Further population-based study is recommended to evaluate different breast cancer genetic mutations.

Conclusion and Recommendations

Breast Cancer among Lebanese women is in continuous rise across all age groups especially in younger age compared to Western countries. Lifestyle modernization, reproductive changes, environmental and genetic factors should be further evaluated and addressed in an effort to control and halt this increase in breast cancer incidence. Establishing a comprehensive National Breast Cancer Control strategy can be of great help in this respect. The results of this study support the current national screening recommendation of starting breast cancer screening at the age of 40 years; yet, a cost-effectiveness study of this screening recommendation is still needed. Moreover, the Lebanese NCR which has had an excellent case update of cancer 2003 [Online]. Beirut, Lebanon: Ministry of Public Health, National Cancer Registry. Available: http://www.moph.gov.lb/Prevention/Surveillance/Pages/Cancer.aspx [Accessed 7 2014].

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