A comparison of trends in incidence and mortality rates of breast cancer, incidence to mortality ratio and stage at diagnosis between Arab and Jewish women in Israel, 1979–2002

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In Israel, breast cancer is the most common malignancy in women, but there are large intra-population differences. The aim of this study was to compare the incidence and mortality, incidence to mortality rate ratio and stage at diagnosis of breast cancer between Arab and Jewish women in Israel. Data on all cases of breast cancer, stage at diagnosis and mortality were obtained from the National Cancer Registry and the Central Bureau of Statistics. Trends in age-specific and age-adjusted incidence and mortality rates, rate ratios and stage at diagnosis were examined for Arab and Jewish women during 1979–2002. Five-year survival rates for 1995–1999 were compared by stage. Among Arab women, age-adjusted incidence rates increased by 202.1%, from 14.1 per 100 000 in 1979–1981 to 42.6 in 2000–2002. Among Jewish women, the rates increased by 45.7%, from 71.1 per 100 000 women in 1979–1981 to 103.6 in 2000–2002. Incidence to mortality rate ratio increased for both population groups, but it is still lower among Arab women. In every age group, Arab women were more likely to be diagnosed at a more advanced stage of the disease. The rise in breast cancer incidence and mortality rates and the later stage of diagnosis among Arab women emphasize the urgent need for increasing early detection of breast cancer in the Arab population by improving rates of compliance with screening mammography. ***European Journal of Cancer Prevention*** **16:36–42 © 2007 Lippincott Williams & Wilkins.**

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Introduction

Excluding cancers of the skin, breast cancer is the most common cancer among women (American Cancer Society, 2005). Breast cancer incidence varies widely between countries and between populations. In Israel, as in most developed countries, breast cancer is the most common form of malignancy in women, with high incidence and mortality rates [Israel Center for Disease Control (ICDC), 1999; Israel National Cancer Registry (INCR), 2000]. This differs with ethnic background, however. The incidence of breast cancer has previously been reported to be considerably higher among Jewish women than among Arab women (ICDC, 1999). In general, incidence rates are higher in developed countries such as the United States, Canada and Western Europe, and lower in less developed countries in Africa and East Asia (Ferlay *et al.*, 2001). Within countries, ethnic differences have been reported. For example, in the United States, among women above the age of 40 years, white women are more likely to be diagnosed with breast cancer than black women [National Cancer Institute (NCI), 2004; American Cancer Society, 2005]. Under the age of 40 years, the incidence tends to be slightly higher among black women than among white women (NCI, 2004; American Cancer Society, 2005).

The stage of breast cancer at diagnosis is an important prognostic factor and early-stage disease can be treated with good chances of cure (Paci *et al.*, 2005). In the United States, black women with breast cancer are diagnosed at a later stage of the disease than are white women (Wells and Horm, 1992). This has partly been explained by socioeconomic variables. The percentage of cases with metastatic disease decreases with increasing educational level or income among women of both racial groups in the United States (Richardson *et al.*, 1992). Differences in socioeconomic status and use of preventive health services in Jewish and Arab women could affect the stage at diagnosis of breast cancer in the two population groups in Israel.

With improvements in sanitation and water supply, increased vaccination coverage and better control of malnutrition, many of the developing countries have been

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undergoing what is called the 'epidemiological transition'. Such populations are characterized by an increasingly older population, increasing life expectancy, decreasing infant mortality, and a shift of the burden of mortality and morbidity from infectious diseases to chronic diseases such as cardiovascular diseases and cancer (Omran, 1971). Usually these changes are related to demographic changes and socioeconomic development within a modernization process (Caldwell, 2001). As a result of this transition, non-communicable diseases such as cardiovascular disease and malignancies, have emerged as some of the leading causes of morbidity, disability and mortality in many of the developing countries (Wahdan, 1996; Alwan, 1997). The Israeli Arab population is undergoing epidemiological transition, and is adopting a more western lifestyle with a decline in fertility rates. More Arab women are part of the labor force than in the past when the majority were home-makers [Israel Central Bureau of Statistics (ICBS), 2003]. Socioeconomic indicators have improved during the years (education and family income) (ICBS, 2003, 2005a). This is likely to impact on the epidemiology of breast cancer in this population.

The aims of this study are to compare trends in breast cancer incidence and mortality rates between Arab and Jewish women, to compare the incidence to mortality ratio and the stage at diagnosis of the disease.

Methods

Sources of data

The current analyses are based on the data files of the INCR, which was established in 1960, and is located in the Ministry of Health. Information on diagnosed cancer cases in Israel is reported to the Registry by hospitals, pathology and cytology laboratories and oncology clinics. In addition, copies of death certificates are received from the public health district offices. From 1960 to 1982, reporting to the Registry was on a voluntary basis. Since 1982, all new cases of cancer must be reported by law. In a nationwide quality control survey conducted in 1995–1996 for the 1991 Cancer Registry Database, the completeness in case finding for invasive solid tumors was found to be 94.2% (ICDC, 2003a). The register contains information on sex, age, country of birth, population group (Jewish/Arab), primary site, morphology, tumor size and stage at diagnosis. New cases of cancer are coded according to the appropriate version of the International Classification of Diseases for Oncology (ICD-O) (WHO, 2000) and classified following the current Surveillance, Epidemiology and End Results (SEER) program summary staging manual (SEER, 2000). All invasive and in-situ female breast cancer cases diagnosed during the period of 1979–2002 registered in the INCR were included in the analysis. Incidence cases include codes C50.0–C50.9 (morphology behavior codes 2 or 3) (ICD-O). Data on mortality for the years 1979–2000 were extracted from the cause of death files of the Central Bureau of Statistics (ICBS, 2005b) and include codes 174.0–174.9, 233.0 (ICD-9) (International Statistical Classification of Diseases, 1979). Staging analysis includes cases diagnosed during 2000–2002. Staging was based on the summary staging manual, 2000 (SEER, 2000). The SEER staging codes are as follows: stage 0 includes *in situ*, stage 1 includes localized only, stage 2 includes regional spread by direct extension only, stage 3 includes regional spread by lymph nodes only, stage 4 includes regional spread by both direct extension and lymph node, stage 5 includes regional spread not otherwise specified and stage 7 includes distant involvement. Owing to the small number of cases in stages 0 and 1, mainly among Arab women we present the cases with these stages together. The unknown stage of breast cancer in 2000–2002 was 35.7% among Jewish women and 31% among Arab women.

Statistical methods

Incidence and mortality rates (rates per 100 000) were calculated for Arab and Jewish women separately and were directly age-adjusted using the world population standard, in order to control for the different age structures of the Arab and Jewish populations (the Arab population is considerably younger). Mean 5-year age-specific rates per 100 000 for ages 20–39, 40–49, 50–64, and 65 years and above were calculated by population group. The 5-year means of incidence rate ratios and mortality rate ratios between Jewish and Arab women, as well as 95% confidence intervals, were calculated. Trends of age-specific incidence rates (3-year means) are presented separately for Arab and Jewish women, by age group. The distribution of breast cancer cases by stage at diagnosis is presented separately for Arab and Jewish women in each age group.

The Kaplan–Meier method was used for calculating the 5-year survival rate of breast cancer cases by stage at diagnosis for all cases diagnosed during the years 1995–1999 in Jewish and Arab women. The INCR staging procedure at these years was as follows: stage 0 includes *in situ*, stage 1 includes organ confined, stage 2 includes lymph nodes metastasis, stage 3 includes spread to adjacent tissue and stage 4 includes spread to distant metastasis. Our survival analysis by stage is based on the 'old' staging system that was used up to the year 2000.

Results

Trends in incidence and mortality rates

Age-adjusted incidence rates of breast cancer in Arab women were considerably lower than those in Jewish women. During the period 1979–2002, age-adjusted incidence rates among Arab women increased by 202.1% (14.1 per 100 000 in 1979–1981 compared with 42.6% in

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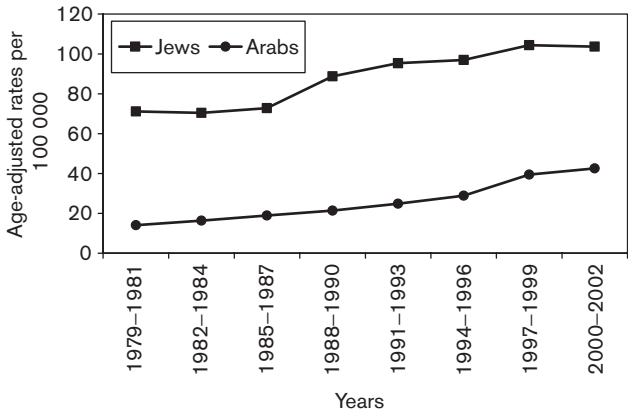
2000–2002). Age-adjusted incidence rates in Jewish women increased by 45.7% between 1979 and 2002 (71.1 per 100 000 in 1979–1981 compared with 103.6 in 2000–2002). During 1979–1981, the age-adjusted incidence of breast cancer in the Jewish population was about five times higher than that in the Arab population, whereas during 2000–2002, the age-adjusted incidence of breast cancer in the Jewish population was about 2.4 times higher than that in the Arab population (Fig. 1).

The incidence rate ratio of breast cancer between Jewish and Arab women declined during the years from 4.82 in 1979–1984 to 3.05 in 1995–2000. The mortality rate ratio between Jewish and Arab women also declined during the years (from 2.63 in 1979–1984 to 1.98 in 1995–2000), particularly owing to an increase in mortality rates among Arab women with no change in mortality among Jewish women (Table 1).

Incidence to mortality rate ratio

Among Arabs, although incidence rates of female breast cancer are generally low, mortality rates are close to the incidence rates. During the 1970s, the two rates were similar (data are not presented) and in the 1980s and 1990s, incidence rates gradually surpassed the mortality rates. Among Jewish women, there has been a substantial difference between incidence and mortality rates of breast cancer since the 1970s, which increased during the 1990s as the incidence rates increased more steeply than the mortality rates. The incidence to mortality rate ratio among Arab women was 1.6 during 1979–1984, whereas among Jewish women the ratio was about 2.7 during the same period. In 1995–2000, the ratio was 2.2 in Arab women and 3 in Jewish women (Table 1).

Fig. 1



Trends in incidence rates of breast cancer in Jewish and Arab women in Israel, 1979–2002 (age-adjusted rates per 100 000).

Age-specific rates

Among Arab women, 45.6% of total breast cancer cases diagnosed in 2000–2002 were aged 50 years and younger compared with 23.3% among Jewish women. Among Arab women, only 18.6% of total breast cancer cases were diagnosed at the age of 65 years and older, compared with 39.5% among Jewish women (data not presented). Age-specific rates, however, are higher among Jewish women than among Arab women in all age groups. In younger women (ages 20–39 years), the incidence ratio between Jews and Arabs in 2000–2002 was 1.8, and the absolute difference of incidence rates was 12.3 per 100 000, and at the age of 65 years and above the incidence ratio was 2.8, and the absolute difference of the incidence rates was 255.2 per 100 000 (Table 2).

Since the beginning of the 1980s, among Arab women, in contrast to Jewish women, the highest rates of breast cancer have been among those aged 50–64 years and not in the older age group (above 65 years). The age-specific incidence rates for the age group 20–39 years among Arab women increased steeply during the period 1979–2002 (from 5.4 per 100 000 in 1979–1981 to 14.6 in 2000–2002) Among Jewish women, age-specific incidence rates increased during the years 1979–2002 mainly among women above 50 years. Below 50 years of age the increase is not pronounced (Fig. 2a and b).

Stage at diagnosis

Stage at diagnosis was analyzed for the years 2000–2002 in both population groups. A higher percentage of Jewish women were diagnosed at an early stage than Arab women (53.5 and 36.7%, respectively, were diagnosed at in-situ and localized stage). Arab women were more likely to be diagnosed with advanced stage of the disease (27.5% were diagnosed at stages 4 and 7 compared with 16.9% among Jewish women) (Fig. 3).

Table 1 Age-adjusted incidence, mortality and incidence to mortality rate ratios (RRs) for breast cancer among Jewish and Arab women in Israel, 1979–2000 (age-adjusted rates per 100 000)

	Incidence		Mortality			Incidence/mortality RR		
Years	Jews	Arabs	RR (95% CI)	Jews	Arabs	RR (95% CI)	Jews (95% CI)	Arabs (95% CI)
1979–1984	70.6	15.4	4.82 (4.80–4.83)	24.7	9.1	2.63 (2.61–2.64)	2.7 (2.7–2.8)	1.6 (1.3–1.8)
1985–1989	77.2	19.4	4.45 (4.43–4.46)	24.1	10.4	2.03 (2.01–2.04)	3.0 (2.9–3.1)	1.8 (1.5–2.0)
1990–1994	95.9	25.3	4.24 (4.23–4.25)	24.8	14.1	2.08 (2.06–2.09)	3.5 (3.4–3.6)	2.0 (1.8–2.2)
1995–2000	102.1	35.7	3.05 (3.04–3.06)	24.6	14.0	1.98 (1.97–2.0)	3.0 (2.9–3.0)	2.2 (2.0–2.4)

CI, confidence interval.

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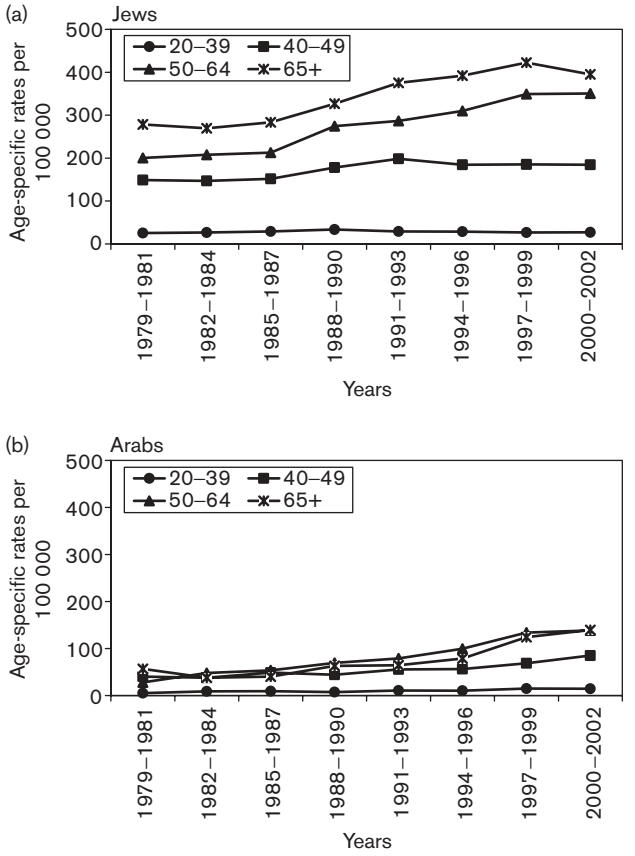
Table 2 Age-specific incidence rates (per 100 000) and incidence rate ratios of breast cancer in Jewish and Arab women in Israel, 2000–2002

Age group (years)	Incidence in Jews	Incidence in Arabs	Incidence rate ratio (Jews/Arabs)
20–39	26.9	14.6	1.8
40–49	184.6	85.2	2.2
50–64	350.3	138.5	2.5
65+	394.8	139.6	2.8

Fig. 2



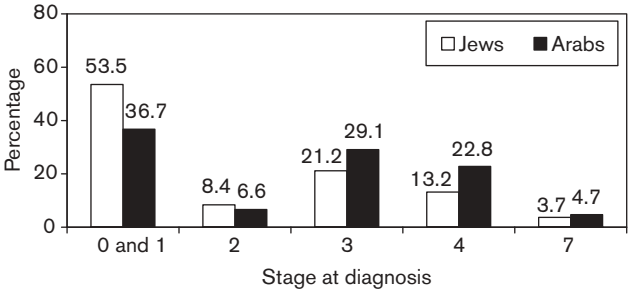
Trends in age-specific incidence rates of breast cancer by population group, 1979–2002: (a) Jews; (b) Arabs.

Among women aged 20–39 years, 34% of breast cancer cases in Arabs were diagnosed at stages 4 and 7 (30.2 and 3.8%, respectively) compared with 19.9% among Jews (17 and 2.9%, respectively). Among women aged 50–64 years diagnosed with breast cancer, 40% of the Arab women were diagnosed with early-stage (in-situ and localized stages) disease compared with 57.1% Jewish women. In all age groups, a higher percentage of Arab women were diagnosed with advanced stages (4 and 7) of breast cancer (Fig. 4).

Survival

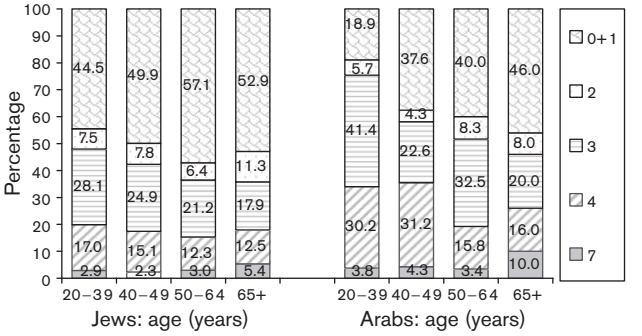
Differences in rates of 5-year survival of breast cancer (among cases diagnosed during 1995–1999) were

Fig. 3



Distribution of breast cancer cases by stage at diagnosis and population group (percentage), 2000–2002. 0, *in situ*; 1, localized only; 2, regional spread by direct extension only; 3, regional spread by lymph node involvement only; 4, regional spread by both direct extension and lymph node involvement; 7, distant site(s)/node(s) involvement.

Fig. 4



Distribution of breast cancer cases by stage at diagnosis, age (years) and population group (percentage), 2000–2002. 0, *in situ*; 1, localized only; 2, regional spread by direct extension only; 3, regional spread by lymph node involvement only; 4, regional spread by both direct extension and lymph node involvement; 7, distant site(s)/node(s) involvement.

reported between Arab and Jewish women by stage at diagnosis. The survival rate among breast cancer cases at stage *in situ* and localized combined (0 and 1) was similar for Jewish and Arab women (91.5 and 89.9%, respectively); among cases diagnosed at stage 2 (lymph node metastasis), the survival rates were 82 and 75.9%, respectively; among cases diagnosed at stage 3 the rates were 67.2 and 61.9%, respectively; and among cases diagnosed at stage 4 (distant metastasis), survival rates were 16 and 14.9%, respectively (unpublished data).

Discussion

During the last 24 years (1979–2002), incidence rates of breast cancer increased among both Jewish and Arab women. Although during this period incidence rates remained lower in the Arab population, the increase in

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incidence was considerably steeper and the difference between the two groups has narrowed.

Some of the differences between the two population groups are due to a higher prevalence of the mutations in BRCA1 and BRCA2 genes related to breast and ovarian cancer in the Jewish population (Levy-Lahad *et al.*, 1997). Family history, however, has also been found to be an important risk factor among Arab women in Israel: the odds ratio for breast cancer in Arab women with first-degree relatives with breast cancer was found to be 3.4 (95% confidence interval: 1.06–10.7) (Aghassi-Ippen *et al.*, 2002). Variations in the prevalence of other risk factors for breast cancer may explain, at least in part, the differences in incidence rates of breast cancer in Jewish and Arab women. Other than age and genetic factors, known risk factors for breast cancer include early age at menarche, late age at menopause, lower fertility rates, obesity, use of hormone replacement therapy, smoking, alcohol consumption and possible environmental exposures (Lubin *et al.*, 1985; Brinton *et al.*, 1988; Hsieh *et al.*, 1990; Brinton and Schairer, 1993; John and Kelsey, 1993; Kelsey *et al.*, 1993; Palmer and Rosenberg, 1993; Hunter and Willett, 1994; Morabia *et al.*, 1996; Alberg *et al.*, 2000; Colditz *et al.*, 2004). In the 2003–2004 Israel National Health Interview Survey (INHIS), conducted as part of the cross-national EUROHIS (European Health Interview Survey) project, 15.3% of Arab women aged 21–64 years reported that their age at menarche was 12 years or younger, as compared with 35.3% of Jewish women (unpublished data). Arab women have higher fertility rates, smoke less, report less consumption of alcohol and use less hormone replacement therapy than Jewish women (Mitra *et al.*, 2004; ICBS, 2005a). On the other hand, Arab women are more obese than Jewish women (ICDC, 2003b).

Changes in the prevalence of risk factors for breast cancer may contribute to the increase in incidence in both ethnic groups. In terms of nutrition, occupation and physical activity, Arabs in Israel are adopting a western lifestyle because of the close coexistence with the Jewish population. Fertility rates have also decreased among Arab women (ICBS, 2003). In addition, environmental factors may play an important role in the etiology of female breast cancer (ICBS, 2005a). Changes in these risk factors may explain part of the increase in incidence of breast cancer.

The increase in breast cancer incidence during the 1990s may also be attributed to the increase in awareness of screening for early detection of breast cancer (mainly mammography). The increase in incidence that was observed at the end of the 1980s in the Jewish population and later in the Arab population, together with no corresponding increase in mortality among Jewish women, may indicate that the rise was due to an increase in early detection of breast cancer. Recent immigration of Jewish women mainly from western developed countries (Russia and Europe) can also explain a part of the increasing incidence rates of breast cancer among Jewish women since 1990.

The age distribution of women with breast cancer is different among Jewish and Arab women. We found that of all diagnosed breast cancer cases, in the Arab population young women comprise a larger proportion of the cases than young Jewish women (45.6 and 23.3%, respectively, were under 50 years of age). This phenomenon can be explained by the fact that Arab women are younger, in general. In 2003, 40.8% of the Arab women in Israel were under the age of 14 years and 3.5% were aged 65 years and above, compared with 24.2% and 13%, respectively, among Jewish women. The life expectancy of Arab women was 4 years lower than that of Jewish women (77.9 and 81.9 years, respectively) (ICBS, 2005a).

The potential for primary prevention of the disease is limited. Secondary prevention through screening appears to be the most promising intervention available in controlling the disease (Vahabi, 2003). Screening mammography is included in the basket of health services provided by the National Insurance Law, with no need for additional payment. The Ministry of Health and the Cancer Association in Israel recommend that women aged 50–74 years undergo mammography every 2 years, and women at high risk (family history) every year from the age of 40 years (Israel Cancer Association, 1995). The Ministry of Health requested that the four health maintenance organizations that provide services to all Israeli residents invite all women between 50 and 74 years of age to undergo mammography screening. Compliance with the recommendation to undergo mammography screening has been reported to be higher in the Jewish population than in the Arab population (Ifrah, 2000). In a survey conducted during 1998, Arab women aged 50–74 years were significantly less likely (24%) to have ever had a mammogram than were Jewish women of the same age group (52%) (Ifrah, 2000). Among 312 women operated on for breast cancer between 1994 and 1999 in Jerusalem, breast cancer was detected by screening mammography in 26% of Ashkenazi Jews, 13% of Sepharadic Jews and in only 9% of Arabs (Nissan *et al.*, 2004). Hagoel *et al.* (1999) studied Israeli women aged 50–74 years who were mailed an invitation to a prescheduled mammography screening. Three groups were compared: non-attenders, attenders and self-screeners. It was found that non-attenders were less educated, had a lower level of socioeconomic status and less frequently adopted other health behaviors.

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Differences in mammography attendance between population groups may be due to specific barriers to mammography screening such as socioeconomic status, employment status, rural compared with city residence, attitudes towards breast cancer and mammography, knowledge about early detection and cultural issues (Lannin *et al.*, 1998; Maxwell *et al.*, 2001; Lagerlund *et al.*, 2002). As socioeconomic status is an important predictor of stage at diagnosis (Schwartz *et al.*, 2003), it is possible that Arab women have less knowledge about the importance of early detection of breast cancer by mammography. They also may have more negative attitudes and beliefs regarding the technology, and a greater fear of negative outcomes (Baron-Epel *et al.*, 2004).

The low rate ratio of incidence to mortality among Arab women compared with Jewish women indicates higher case-fatality rates among Arab breast cancer patients. Two possible explanations for this phenomenon can be proposed. The first explanation is the existence of differences regarding early detection. Arab women are more likely to be diagnosed with breast cancer at advanced stages of the disease when the chances of survival are lower and Jewish women are diagnosed more frequently in the early stages of the disease when survival rates are higher (INCR, 2000). Therefore, case fatality is higher among Arab women (as indicated by their low incidence to mortality ratios). Similar findings have been reported by Nissan *et al.* (2004) in the Jerusalem area.

The second explanation for the higher breast cancer case-fatality rate in Arabs may be differences in the management and treatment process. Both Arabs and Jews are covered by the same National Health Insurance and receive the same services by law in the same facilities. Differences, however, may exist between Arab and Jewish patients with regard to compliance with the treatment protocol and there may also be differences in treatment with respect to the biology and the stage at diagnosis of the cancer. Nissan *et al.* (2004) reported that among women operated on for breast cancer in the Jerusalem area between 1994 and 1999, primary tumor size was significantly larger among Arab patients than among Jewish patients; 70.2% of Arab patients underwent modified radical mastectomy compared with 60.6 and 62.7% of Ashkenazi and Sephardic Jews patients, respectively (Nissan *et al.*, 2004). A further barrier lies in the relative accessibility of treatment centers: oncology departments and treatment centers in Israel are located in hospitals in the large cities, while the majority of the Arab population live in villages and smaller towns; there are hospitals only in the largest town (Nazareth). Patients living in other locations need to travel to the cities for treatment and follow-up, and this may well affect compliance. Our data regarding differences in survival rate between Jewish and Arab women by stage show no differences in this rate among cases diagnosed at early stage (91.5 and 89.9%, respectively). Among breast cancer cases at stages 2 and 3, the survival rate is 6.1 and 5.3% higher among Jewish women than among Arab women and at stage 4 (distant spread) the rate is similar (16 and 14.9%).

The trend of increasing incidence to mortality rate ratios for breast cancer among Arab and Jewish women may also be the result of the increase in incidence rates of breast cancer with no major increase in mortality rates. This may indicate some improvement in early detection and treatment of breast cancer in both populations.

Conclusions

An increase in incidence of breast cancer was observed in both population groups. In the Arab population, however, the relative increase is much larger, particularly in younger women. This may be due to changes in risk factors owing to a more western lifestyle. The higher percentage of breast cancers in Arab women that are diagnosed at more advanced stages of the disease than Jewish women, could explain the higher case-fatality rates among Arab patients than among Jewish patients. An urgent need arises to increase early detection of breast cancer in the Arab population by increasing compliance with screening mammography.

Limitations

For a relatively high percentage of breast cancer cases diagnosed in 2000–2002, stage at diagnosis was unknown (35.7% of cases among Jewish women and 31% among Arab women). The proportion of unknown stage breast cancer cases differ by age group: among Jewish women the proportion was 27.2% at ages 20–39 years, 29.5% among women aged 40–49 years, 31.2% among women aged 50–64 years and 43.8% among women aged 65 years and above. Among Arab women, these proportions were 34.6, 27.3, 26.8 and 41.2%, respectively. The relatively high proportion of cases with unknown stage is due to the fact that the INCR is a passive population-based cancer registry. Therefore, complete information for determining stage is not available for all the cases.

Acknowledgment

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