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A decreasing incidence of ovarian carcinoma in Israel

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The aim of the present study was to assess the incidence trend of invasive epithelial ovarian carcinoma in Israel. We assessed the incidence rate of invasive epithelial ovarian cancer in Israeli Jewish women during the 10-year period from 1993 to 2002 based on data obtained from the population-based Israel National Cancer Registry. There was a gradual significant decrease in the incidence of ovarian cancer from 9.64 in 1993 to 6.55 in 2002. The decrease in incidence was evident in all ethnic groups except those born in Asia and in all the age groups older than 35 years. The decrease in incidence of ovarian carcinoma is gratifying, but its reason remains obscure.

KEYWORDS: epithelial ovarian carcinoma, incidence, Israel.

Determination of incidence trends of malignant tumors is of great importance. A change in incidence may indicate alterations in risk factors and lead to clues to etiology and to a better understanding and possible identification of modifiable risk factors.

Ovarian carcinoma is one of the most common gynecological malignancies and one of the leading causes of cancer mortality in women. It was for many years the most common gynecological malignancy in Israeli Jewish women[(1)]. Its etiology is unknown, but several risk factors have been identified.

The aim of the present study was to assess the incidence trend of invasive epithelial ovarian carcinoma in Israel.

Materials and methods

The study is based on data obtained from the Israel National Cancer Registry established in 1960. This population-based central tumor registry is notified by all medical institutions of all newly diagnosed malignancies in Israel, and reporting to it is mandatory. After document copies are obtained, the person is identified, through computer linkage, in the Central Population Registry, and the diagnosis is coded according to the International Classification of Diseases—Oncology (ICDO-3).

We assessed the incidence rates of invasive epithelial ovarian cancer during the 10-year period from 1993 to 2002.

The number of non-Jewish women with invasive ovarian cancer throughout the entire study period ($n = 90$) was too small for meaningful analysis. The present study is therefore restricted to Israeli Jewish women ($n = 2258$).

The age-standardized rates (ASR) were computed per 100,000, standardized to the "World Standard Population," and calculated for each year of the study period. The Israeli population data by age were retrieved from the Central Bureau of Statistics. For the purpose of analysis, four age group categories were considered. Age-specific rates were calculated for each age group. The standardized incidence ratio (SIR) was calculated using as a reference the entire Israeli population. In order to avoid a bias introduced by yearly variations, the SIR of the first 3 years (1993–1995) was compared to that of last 3 years (2000–2002) of the study period in the entire study group and according to place of birth and age. Separate data for women born in the former Soviet Union are not available prior to 1996. In order to assess the effect of the mass immigration from the former Soviet Union, the SIR among

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these women diagnosed from 1996 to 2002 was compared to that of women born in Europe–America diagnosed during the same period.

Trend analysis was computed by linear regression. Tests of significance used 95% confidence intervals (CI), and a significant result was when $P < 0.05$.

Results

Table 1 presents the number of new cases and the ASR of ovarian carcinoma in Israeli Jewish women by year of diagnosis. There was a gradual decrease in ASR from 9.64 in 1993 to 6.55 in 2002. The SIR decrease from 1993–1995 to 2000–2002 was highly significant (95% CI 0.66–0.77; $P < 0.0001$).

Table 2 presents the ASR according to place of birth. A decrease in ASR is observed in women born in Europe–America, in Israel, and in Africa. The SIR decrease from 1993–1995 to 2000–2002 for those born in Africa was significant (95% CI 0.54–0.98; $P < 0.02$) and for those born in Europe–America and in Israel was highly significant (95% CI 0.59–0.72 and 0.60–0.81, respectively; $P < 0.0001$). No statistically significant change was observed in those born in Asia.

Table 3 presents age-specific rates according to age group. Ovarian cancer was most prevalent in the 55–69 and 70+ age groups, while its prevalence was very low in the <35 age group. Between 1993–1995 and 2000–2002, there was a significant decrease for the age group 35–54 (95% CI 0.78–1.00; $P = 0.03$) and highly significant decrease for age groups 55–69 and 70+ (95% CI 0.66–0.86 and 0.64–0.86, respectively; $P < 0.001$).

An excess of SIR of borderline significance was found among women born in the former Soviet Union compared to women born in Europe–America (SIR 1.12; 95% CI 0.99–1.24).

The incidence of borderline ovarian tumors over the study period remained stable, and their proportion ranged between 12% and 17%, with an average of 14% of epithelial ovarian tumors.

Survival data were available only till 1996. During the 4-year period between 1993 and 1996, no change in the 5-year survival of women with invasive ovarian cancer was observed.

Table 1. The ASR of invasive epithelial ovarian cancer in Israeli Jewish women by year of diagnosis

Year of diagnosis	No. of new cases	ASR
1993	243	9.64
1994	234	8.88
1995	238	9.02
1996	251	9.06
1997	215	7.50
1998	218	7.30
1999	199	6.35
2000	219	6.77
2001	234	7.39
2002	207	6.55

Table 2. The ASR of invasive epithelial ovarian cancer in Israeli Jewish women by year of diagnosis and place of birth

Year of diagnosis	ASR			
	Israel	Europe–America	Asia	Africa
1993	9.97	12.99	4.98	5.77
1994	7.88	11.99	6.58	3.43
1995	9.13	11.10	6.83	3.82
1996	9.01	10.64	8.07	3.30
1997	6.82	9.62	5.36	3.76
1998	8.59	8.13	6.20	3.99
1999	5.81	7.59	4.79	5.48
2000	6.39	7.43	7.52	3.21
2001	8.08	8.20	5.82	3.13
2002	6.21	7.75	3.03	3.03

Discussion

Our population-based data indicate a significant incidence decrease of epithelial ovarian carcinoma in Israeli Jewish women during a 10-year period from 9.64 in 1993 to 6.55 in 2002. The decrease was observed in women of all ethnic groups except those born in Asia as well as in all age groups except those 34 years old or younger.

Several main risk factors are known to play a role in the etiology of invasive epithelial ovarian cancer: incessant ovulation uninterrupted by pregnancy and breast-feeding, environmental factors, and genetic factors.

Pregnancy and breast-feeding exert a protective effect[2]; therefore, variation in parity might influence

Table 3. Age-specific rates of invasive epithilial ovarian cancer in Israeli Jewish women by age group

Year of diagnosis	Age-specific rates			
	0–34 years	35–54 years	55–69 years	70+ years
1993	0.98	13.92	37.76	35.21
1994	1.04	13.10	34.52	32.81
1995	1.10	15.23	31.47	29.11
1996	0.23	14.95	38.23	29.84
1997	0.23	12.22	31.38	25.17
1998	0.23	13.8	28.09	26.65
1999	0.07	11.17	26.29	22.23
2000	0.18	13.36	25.03	25.63
2001	0.65	11.97	28.41	27.90
2002	0.43	12.36	25.48	18.91

incidence. There are no data indicating an increase in the birth rate in Israeli women[3]. The use of oral contraceptive pills is known to reduce remarkably the risk of ovarian cancer[4]. Data from Wales have shown that cohorts with increased exposure to oral contraceptives had a marked decrease in the incidence of ovarian cancer[5]. The widespread use of contraceptive pills began in the 1960s. Women who were in their reproductive years in the 1960s had reached during the period of our study the age at which ovarian carcinoma is prevalent. A recent nationwide Israeli population–based case-control study of ovarian carcinoma[6] found that about 22% of the women in the control group used contraceptive pills. It is therefore possible that this quite frequent use of oral contraceptives may have contributed to the decrease in invasive epithelial ovarian carcinoma in our population. A decreased incidence in younger women has been reported in some studies[7–9] and attributed to trends in birth rates and use of oral contraceptives. The incidence decrease in our population was evident in all but the 0–34 age group.

With the exception of Japan, the incidence rates of ovarian carcinoma are high in Western industrialized countries such as in Europe and in North America and low in developing countries such as in North Africa and in Asia[10]. Migrational studies have shown that for women who emigrate from low-risk countries of origin to high-risk areas, there is a gradual increase in incidence of ovarian cancer to rates expected for native-born women[11]. Thus, ovarian cancer rates in Japanese women who immigrated to the United States are rapidly approaching the rates for the white local population[12]. These findings support the notion that environmental factors affect the incidence of ovarian cancer. The decrease in incidence in our study population was evident in all ethnic groups except those born in Asia. No verified answer can be given with regard to a change in environmental factors such as dietary habits or a change in ecologic conditions that might explain the decrease in incidence of ovarian cancer in the other Israeli ethnic groups. Several ecologic studies suggest that sunlight may protect against several malignancies including ovarian cancer[13].

Increased sunlight exposure may have contributed to the decreasing incidence among some women born in Europe–America but does not explain the decrease in those born in Africa.

The association between socioeconomic status and ovarian cancer is controversial. Nevertheless, Liu *et al.*[14] reported that socioeconomic status is positively associated with ovarian cancer. As in other Israeli studies[15], the incidence of ovarian cancer in the present study was higher in women born in Europe–America and in Israel than in women born in Asia or in Africa. Over the years, there was an improvement in the socioeconomic status of women who immigrated from Africa and Asia to Israel. But a decrease in incidence was observed only in those born in Africa.

The genetic risk factor is associated with BRCA1 and BRCA2 mutations. These mutations are known to be more frequent in the Jewish population as well as among Jewish ovarian cancer patients[16,17]. This important risk factor pertains only to a small proportion of ovarian cancer patients, and a sudden decrease in the frequency of these mutations that might have affected incidence is unlikely over the relatively short period our study covers.

Pelvic surgery reduces the risk of ovarian cancer[18]. There is no indication that there is a higher trend for hysterectomy in our population. The advent of ultrasound and its routine use in gynecology may detect ovarian cysts previously unrecognized by clinical examination. It is therefore possible that there has been an increase in the frequency of cystectomy or adnexectomy. The protective effect of these procedures could have affected the incidence in younger women in our population, who were more exposed to this imaging modality. Interestingly, the incidence decrease in the 35–54 age group, though significant, was less prominent than in the older age groups.

Although highly controversial[19], the use of ovulation-inducing drugs is considered by some to be a risk factor. In spite the increased use of these drugs in our population, the incidence of ovarian carcinoma has decreased.

The decreasing incidence could have also been caused by the mass immigration from the former Soviet Union that started in 1990. However, the excess cancer rate in this population should have had an opposite effect.

Incidence trends of ovarian carcinoma vary in different populations. Similar to the trend in our population, a recent report from the United States also revealed a significant decline for all races combined, as well as for white and Hispanic women between 1992 and 1998[20]. In contrast, no change in overall incidence rates from 1967 to 1996 have been observed in South East England, but the rates in women aged more than 70 years have increased[7]. No change in incidence rates from 1982 to1998 has also been found in Australia[8]. On the other hand, the low incidence in Japan has markedly increased since 1970[21,22]. A significant incidence increase in Alexandria, Egypt, from 1988 to 1999 has also been reported[23].

The main disadvantage of our study is that the diagnosis of invasive epithelial ovarian cancer is based on

the original pathology report. It should however be noted that the diagnosis of a malignant disease is signed out by two certified pathologists.

A reporting bias during the study period that could have contributed to the decreasing incidence is highly unlikely since notification to the Israel Central Cancer Registry has improved over the years. The decrease in incidence can also not be explained by a more frequent diagnosis of borderline malignancies since their proportion remained stable. Data with regard to survival were available for only a part of the study period, and the 5-year survival did not change until 1996.

Most of the ovarian cancer patients are diagnosed at an advanced stage of the disease, and their survival is poor. Therefore, the decrease in incidence of this lethal disease in Israel is extremely gratifying, but its exact reason remains obscure.

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