Primary research

Breast cancer mortality among Ashkenazi Jewish women in São Paulo and Porto Alegre, Brazil

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Abstract

Background: Increased *BRCA1* and *BRCA2* germline mutation rates have been reported in Ashkenazi Jewish women in North America, Europe and Israel, and have been mentioned as possibly related to a higher incidence of breast and ovarian cancer among these communities. The present study was carried out with the aim of obtaining evidence on the magnitude of breast cancer as a cause of death among Ashkenazi women in Brazil.

Methods: We reviewed all death certificates archived in the Jewish Burial Societies of São Paulo (1971–1997) and Porto Alegre (1948–1997), two of the main and oldest Jewish communities in Brazil. Breast cancer observed deaths were compared with expected deaths according to breast cancer mortality in the general population.

Results: The observed ratios were approximately quite close to unity, suggesting a similar breast cancer mortality pattern among the Ashkenazi population and the general population in both cities. These results maintain similar behavior regardless of whether analyzed before or after the mid-1980s, when mammography came to be increasingly performed in Brazil. Cancer proportional mortality ratios were 1.04 (0.83–1.29) in São Paulo and 1.16 (0.84–1.57) in Porto Alegre before 1985, and 1.17 (1.00–1.44) and 1.21 (0.81–1.79), respectively, between 1985 and 1997. Some evidence of the maintenance of protective risk factors such as high parity has been observed among Ashkenazi women in São Paulo.

Conclusion: A quite similar breast cancer mortality pattern was observed between Ashkenazi Jewish women and the general population in São Paulo and Porto Alegre, Brazil. These results may suggest an environmental role on germ mutation expression reported in this ethnic group.

Keywords: Ashkenazi, *BRCA1*, *BRCA2*, breast, cancer, mortality

Introduction

The understanding of the role of several cancer risk factors has been enhanced by the analysis of their distribution in different ethnic groups, as observed in several sites such as the brain, colon, breast, ovary and others. Despite the fact that some genetic differences have been identified, ethnic differences more often point out differences in the patterns of environmental exposures such as diet and other lifestyle-related factors.

Several studies carried out in the past decade have reported higher rates of *BRCA1* and *BRCA2* gene mutations (mainly 185 delAG, 5382insC and 6174delT) in Ashkenazi (Eastern and Central Europe ancestry) Jewish women than in the general population in different countries [1–6]. This fact has also been associated with a higher lifetime risk of developing ovarian and breast cancer among Ashkenazi women, the latter ranging from 38% by age 50 to 59% by age 70 [7].

CPMR = cancer proportional mortality ratios.

Different from the reported scientific literature about a higher breast cancer incidence among Ashkenazi women in North America and Europe than in the general population, breast cancer seems to present a moderate pattern of occurrence among Brazilian Ashkenazi women. The objective of this investigation is to evaluate evidence supporting this observation.

This paper presents preliminary results of a comprehensive ascertainment of cancer mortality in two main Jewish communities in Brazil, São Paulo and Porto Alegre, that was carried out by searching mortality and personal data archived in local Jewish burial societies (Chevra Kadisha).

Materials and methods

All death certificates archived from 1 January 1971 to 31 December 1997 in the unique São Paulo Jewish Burial Society and those from 1 January 1948 to 31 December 1997 in both Porto Alegre Burial Societies were reviewed. Data on gender, age, nationality, causes of death, and year of death were obtained for those death certificates that included any cancer site as a cause of death. Descendants (sons and daughters) were also compiled for all buried individuals regardless of gender and cause of death in selected years (1948–1949, 1980 and 1986). Country of birth, maternal family names and even surnames were used to further stratify deaths by origin such as Ashkenazi or Sepharad (those from North Africa and Mediterranean origin). The Sepharad usually maintain special characteristics according to used names and surnames, including those related to the nature, to feelings, or from cities and countries ever inhabited by their ancestors in the past, thus enabling identification of their origin.

Aiming to evaluate data completeness, we compared cancer mortality data obtained in the São Paulo Jewish Burial Society with that provided by the São Paulo population-based cancer registry. In a sample of 40 breast cancer death reports identified in the São Paulo Jewish Burial Society during selected years (1973–1974, 1983, 1988 and 1997), 38 (95%) could thus be retrieved by the cancer registry.

Age-adjusted (world population) breast cancer mortality rates regardless of Jewish origin (Ashkenazi or Sepharad) were ascertained using a census carried out in the Porto Alegre Jewish community during 1992 [8], and were further compared with those observed in the Porto Alegre general population. This census revealed that almost 95% of the Jewish families in Porto Alegre were Ashkenazi. Similar comparisons were not carried out in São Paulo, where any census of the Jewish community in the past 30 years could be traced.

Expected breast cancer deaths among Ashkenazi women according to breast cancer mortality patterns in the Brazilian general population in different age groups in both cities [9,10] were ascertained and further compared with observed breast cancer deaths. The expected number of breast cancer deaths was ascertained for two different time intervals: before 1985, when mammography use was quite unavailable in the country; and during the following years, when this radiologic procedure has become increasingly performed. The age-standardized breast cancer proportional mortality in the general population, either of São Paulo or Porto Alegre in 1980, was used to estimate the expected number of breast cancer deaths during the first interval (1971–1984 in São Paulo and 1948–1984 in Porto Alegre). Furthermore, breast cancer proportional mortality in the general population (according to all cancer site mortality among women of different age groups in those cities in 1994) was used to estimate expected deaths among the Jewish population during 1985–1997. Cancer proportional mortality ratios (CPMR) (observed versus expected breast cancer deaths) were therefore obtained in each city and time interval. Similar procedures were also carried out to ascertain CPMR for other cancer sites among women, such as ovary, stomach, colon and rectum, pancreas, uterus, leukemia and multiple myeloma.

Results

Proportional mortality

Of all cancer deaths among Ashkenazi women in São Paulo during 1971–1997, 211 (19.5%) were caused by breast cancer; 71 (22.7%) cancer deaths among Ashkenazi women occurred in Porto Alegre during 1948–1997. Younger than age 45, these proportions were 27.5% in São Paulo (27.3% among Sepharad women) and 23.5% in Porto Alegre. Cancer proportional mortality in São Paulo Ashkenazi women (1983–1987) was 17.8% (16.3% in the general population, 1993), and that among Porto Alegre Jewish women in 1991–1993 was 26.7% (20.7% in the general population, 1991–1993).

Mortality rates

The estimated breast cancer mortality rate in the Porto Alegre Ashkenazi community (1989–1995) was 108.6/100,000 women (95% confidence interval [CI], 29.5–278.0) at age 50–59 (56.5/100,000 in the general population, 1991–1993). At age 60–69, the rates were 77.6 (95% CI, 16.0–226.6) in the community and 98.3/100,000 in the general population, and the rates were 221.9 (95% CI, 95.6–437.0) and 154.7/100,000, respectively, among women aged 70 years or older. No breast cancer deaths were observed among Ashkenazi women younger than 50 years in Porto Alegre between 1989 and 1995. Age-adjusted breast cancer mortality rates were hence 24.1/100,000 (95% CI, 13.5–39.7) among Ashkenazi women and 22.3/100,000 women in the general population.

Table 1

Observed versus expected breast cancer deaths among Ashkenazi and Sepharad Jewish women in São Paulo (1971–1997) and Porto Alegre (1948–1997), Brazil

	São Paulo Ashkenazi				São Paulo Sepharad*				Porto Alegre			
Age group (years)	O	E	O/E	95% CI	O	E	O/E	95% CI	O	E	O/E	95% CI
Before 1985**												
20–29	–	1	0.00	–					–	–	0.00	–
30–39	3	4	0.75	0.15–2.19					4	3	1.33	0.36–3.41
40–49	9	8	1.13	0.52–2.15					6	5	1.20	0.44–2.62
50–64	31	26	1.19	0.80–1.70					20	18	1.11	0.68–1.71
65–79	31	32	0.97	0.65–1.39					11	8	1.38	0.69–2.47
> 79	11	11	1.00	0.50–1.79					1	2	0.50	0.01–2.79
Total	85	82	1.04	0.83–1.29					42	36	1.16	0.84–1.57
1985–1997												
20–29	–	1	0.00	–					–	–	0.00	–
30–39	2	2	1.00	0.12–3.61	2	1	2.00	0.24–1.72	–	1	0.00	–
40–49	5	7	0.71	0.23–1.65	6	4	1.50	0.55–3.50	–	2	0.00	–
50–59	15	14	1.07	0.60–1.77	11	5	2.20	1.10–3.94	5	7	0.71	0.23–1.65
60–69	29	25	1.16	0.78–1.67	10	9	1.11	0.53–2.04	8	5	1.60	0.69–3.15
70–79	40	26	1.54	1.10–2.09	13	6	2.17	1.15–3.71	8	6	1.33	0.57–2.62
> 79	34	30	1.17	0.82–1.63	2	3	0.67	0.08–2.42	8	3	2.67	1.15–5.26
Total	122	104	1.17	1.00–1.44	44	30	1.47	1.07–1.98	29	24	1.21	0.81–1.79

O, Breast cancer observed deaths; E, breast cancer expected deaths; O/E, ratio of observed versus expected breast cancer deaths; 95% CI, 95% confidence interval estimated by Poisson distribution. * 1971–1997; ** 1948–1997 in Porto Alegre and 1971–1997 in São Paulo.

Cancer proportional mortality ratios

Age-standardized breast cancer proportional mortality ratios (observed versus expected breast cancer deaths according to the general population all cancer site mortality) in Ashkenazi women before 1985 were 1.04 (95% CI, 0.83–1.29) in São Paulo and 1.16 (95% CI, 0.84–1.57) in Porto Alegre (Table 1). During 1985–1997, the ratios were 1.17 (95% CI, 1.00–1.44) and 1.21 (95% CI, 0.81–1.79), respectively. Low ratios between observed versus expected breast cancer deaths were verified in both time intervals for women younger than 50 years in São Paulo. A 47% excess of observed over expected breast cancer deaths was seen among Sepharad women in São Paulo in almost all age groups (Table 1).

Mean age of death

The breast cancer mean age of death among Ashkenazi women in São Paulo before 1980 was 62.0 years (standard error [SE], 1.5 years), and the mean was 57.7 years in the general population (1979). In the 1980s, the mean ages were 68.1 years in Ashkenazi women (1981–1989; SE, 1.5 years) and 59.8 years in the general population (1988), respectively, while in the 1990s observed means were 69.3 years among Ashkenazi women (1990–1997; SE, 1.4 years) and 65.0 years in the general population (1998).

Mean ages of death among Ashkenazi women in Porto Alegre were 55.5 years (SE, 2.0 years) before 1980, 65.4 years (SE, 2.3 years) between 1980 and 1989, and 73.4 years (SE, 3.1 years) in the 1990s. In the general population, the means were, respectively, 59.9 years (1979), 60.2 years (1988) and 65.6 years (1998).

Discussion

Burial societies have been organized almost everywhere following the settlement of Jewish communities in Brazil, and they usually have archived copies of all death certificates presented by relatives for funeral. Moreover, the strict rules on burial procedures carried out among Jewish communities make it feasible to accomplish a comprehensive data completeness, since almost all are buried by similar community burial societies, regardless of their previous compliance into observing religious rules.

Burial procedures are one of the most important and preserved rituals in Jewish tradition, being followed by those communities everywhere. Organization of such burial societies and cemeteries was one of the first goals accomplished by Jewish immigrants in Brazil and, indeed, their own communal cemeteries were created in 1908 in Porto Alegre and in 1923 in São Paulo. Records of all buried members have usually been archived since then, including some personal data collected for this study.

Considering that a comprehensive ascertainment on breast cancer incidence in Brazilian Jewish communities could not be easily accomplished, we first tried to evaluate breast cancer mortality in São Paulo and Porto Alegre, where two of the main Jewish communities in Brazil are situated.

A census of the studied communities enabling mortality rate ascertainment was only available in Porto Alegre [8]. Despite age-adjusted breast cancer mortality rates being similar between the Ashkenazi and the general populations (risk rate, 1.08), higher rates were observed among the Ashkenazi women at ages 50–59 and 70 years or older. The absence of reported deaths younger than age 50 years among Porto Alegre Ashkenazi women in 1989–1995 may perhaps reflect a comparatively longer survival of those affected in the 1980s, comparative with that observed in the general population.

Comparisons in São Paulo and Porto Alegre were further carried out using CPMR instead of rates to estimate the number of expected deaths among Ashkenazi women in both cities. Despite the fact that CPMR are more robust indicators than proportional mortality ratios, since variation on site-specific cancer proportions according to all cancer deaths is usually shorter than according to all causes of death, lack of accuracy on these estimates cannot be dismissed. Nevertheless, in support of such comparisons, high reliability and accuracy of reported causes of death from cancer in Brazil has been previously reported [11–13].

In the present study, we analyzed breast cancer mortality among Ashkenazi women, but not incidence, and the relatively low overall ratios of observed versus expected deaths could just reflect a better medical care offered to this group than to the general population. Nevertheless, this seems unlikely to explain the low ratios observed among younger affected women, usually presenting an aggressive clinical evolution. On the contrary, a better disease-free survival among Ashkenazi women than in the general population also seems to be unexpected for those affected until the mid-1980s, before mammography availability in Brazil. Origin misclassification (Ashkenazi versus Sepharad) could also yield data misinterpretation, but this seems improbable since the majority of reviewed death certificates were from women born in Eastern and Central Europe.

Hence, if the relatively low breast cancer proportional mortality ratios observed in São Paulo and Porto Alegre (even before the mammography era) could also be considered to indicate a pattern of low breast cancer incidence in these groups, which indeed was not ascertained in this study, this fact suggests that environmental exposures could perhaps act in modulating *BRCA1* and/or *BRCA2* penetrance, which was previously suggested worthy of investigation [14]. In other words, these results suggest that germ mutations seem insufficient to induce higher breast cancer risks by themselves, but environmental interaction would also be necessary to modulate gene expression related to familial breast cancer. This observation, if true, could offer an explanation for the different breast cancer mortality pattern among Ashkenazi women in North America and Europe comparative with that observed in São Paulo and Porto Alegre.

The ascertained CPMR for ovarian cancer, colorectal cancer and multiple myeloma revealed statistically significant increased ratios among Ashkenazi women in both studied cities (Table 2). Because antecedents of familial aggregation of those cancer sites have been reported to play an important role in their development, these results could be considered quite expected, taking into account the suggested or confirmed higher prevalence of related mutations among Ashkenazi women, comparative with the general population, according to such cancer sites [15–19]. On the contrary, and for the same reasons, a similar pattern of higher breast cancer mortality ratios would also be expected among Ashkenazi women, which indeed was not observed in this study.

In this sense, a protective role to breast cancer yielded by some lifestyle patterns should be further investigated to explain such unexpected distribution. A reproductive life pattern associated with low estrogen exposure (high parity or long breastfeeding duration) or the adoption of the typical Brazilian diet, richer in vegetable, beans and fresh fruit intake [20] than usually observed in North America, deserve to be analyzed in members of these communities. Future research should ascertain whether such an environmental profile could have played some role in delaying the breast cancer age of onset among Ashkenazi women in Brazil, or even could have inhibited phenotypic expression of *BRCA1* and/or other breast cancer associated genes.

In the case of the São Paulo Jewish Burial Society, information regarding relatives was available on reviewed files, and we could indeed estimate parity evolution along selected years. These data suggest that the São Paulo Jewish community seems to have maintained a pattern of high parity through the past decades. In this sense, observed parity among buried individuals in 1948–1949 was 3.2, and then it was 2.3 in 1985 and 2.5 in 1996. These data therefore suggest that parity among Ashkenazi

Table 2

Observed versus expected cancer deaths (selected sites) among Ashkenazi women in São Paulo (1971–1997) and Porto Alegre (1948–1997), Brazil

	São Paulo				Porto Alegre			
Cancer site	O	E	O/E	95% CI	O	E	O/E	95% CI
Ovarian	64	37	1.73	1.35–2.21	23	13	1.77	1.08–2.73
Stomach	51	81	0.63	0.47–0.83	15	15	1.00	0.56–1.65
Colon/rectum	128	90	1.42	1.18–1.70	49	28	1.75	1.30–2.31
Lung	79	71	1.11	0.89–1.39	17	29	0.59	0.34–0.94
Uterus (unspecified)*	19	51	0.37	0.22–0.58	5	10	0.50	0.16–1.17
Pancreas	36	31	1.16	0.81–1.61	8	11	0.73	0.31–1.44
Leukemia	43	25	1.72	1.03–2.29	8	10	0.80	0.34–1.58
Multiple myeloma	20	11	1.82	1.11–2.80	6	3	2.00	0.86–3.94

O, Breast cancer observed deaths; E, breast cancer expected deaths; O/E, ratio of observed versus expected breast cancer deaths; 95% CI, 95% confidence interval estimated by Poisson distribution. * Uterine cervix not included.

women in São Paulo, different to that reported in the USA [21], remained quite elevated during the past 50 years, perhaps as a consequence of several reasons, possibly including a relatively delayed engagement of those women in the labor force. If this hypothesis is true, trends on breast cancer incidence will probably change in the future as the Ashkenazi reproductive pattern seems to be changing into a similar distribution to that observed in the Brazilian general population (later age at first pregnancy, shorter parity and breastfeeding reduction).

Such a past breast cancer low-risk pattern among the Ashkenazi population, whether true and further confirmed, would be quite unexpected. Carrier rates of *BRCA1* or *BRCA2* germline mutations among Ashkenazi women may be similar wherever they live [22]. Germ mutation rates among those who immigrated to Brazil may probably therefore be identical, or very similar, to those observed among Ashkenazi families who also immigrated to North America in similar years, and from the same Eastern and Centro-European regions. In fact, among all reviewed death certificates from Ashkenazi women in São Paulo mentioning any cancer site as a cause of death, 807 (74.8%) were born in Central or Eastern Europe, and just 193 (17.9%) in Brazil. In relation to breast cancer, 22.9% were born in Brazil.

These preliminary results stimulate future data collection on breast cancer incidence and their joint analysis with mortality. Both could enhance our understanding of the possible different patterns of breast cancer development among Ashkenazi women in Brazil, comparative with those observed in other countries. Moreover, these results are suggestive that future research on the genetic aspects associated with breast cancer development should drive attention to explore the relationships between environmental exposures on carcinogenesis, including familial cancer aggregation. Such research could, perhaps, contribute to identifying selected risk factors triggering expression of tumor-related genes associated with breast cancer and other neoplasia.

Conclusions

Considering the reported higher frequency of *BRCA1* and *BRCA2* germline mutations related to breast and ovarian cancer among Ashkenazi women in different countries, the results presented in this study were interpreted as showing a relatively lower than expected breast cancer mortality pattern among Ashkenazi women in the studied Brazilian cities. If the breast cancer incidence among Ashkenazi women in Brazil, which was not evaluated in this study, has been showing a similar pattern to breast cancer mortality, a hypothesis can be raised that germ mutations previously reported among Ashkenazi women may be modulated by some environmental factors that perhaps could act as protective factors, delaying the mutation expression.

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