

Breast cancer in women suffering from serious mental illness

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Abstract

Background: Breast cancer is a major public health concern and the most common cause of cancer-related mortality among women. Compared with the general population, schizophrenia patients have been reported to have lower or similar rates of breast cancer despite several risk factors such as excess smoking, obesity and hyperprolactinemia. However, it has been argued that psychiatric morbidity itself may be the confounding factor that affects cancer incidence and not particularly schizophrenia.

Objective: To evaluate the frequency of breast cancer in a large cohort of female schizophrenia patients utilizing tertiary psychiatric care and to compare it with that of female inpatients with other serious mental illness (SMI).

Method: Data were analyzed from a cohort of 2011 female schizophrenia patients and 6243 female SMI patients. All patient's records in the database were meshed with records of the Israeli National Cancer Registry to identify pathologically confirmed cancer comorbidity. Cancer incidence rates among patients were compared with the expected incidence in age matched general population for the same time interval.

Results: Among 2011 female schizophrenia patients, 51 (2.5%) developed breast cancer vs. 83 (1.3%) breast cancer cases amongst SMI patients. The standardized incidence ratios (SIR) for breast cancer were low for both patient groups; 0.63 (95% CI, 0.47–0.83) and 0.54 (95% CI, 0.43–0.67) (schizophrenia and SMI respectively).

Conclusions: The findings emphasize that reduced risk of breast cancer is found in a tertiary care cohort of female schizophrenia patients. Yet, breast and ovarian cancer screening for all women who are on long term drugs that induce weight gain or hyperprolactinemia should not be neglected. Our study emphasizes the probable contribution of environmental factors to the mechanisms responsible for this lower risk.

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1. Introduction

Breast cancer is one of the leading causes of morbidity and mortality among women worldwide. Multiple and complex factors influence its epidemiology including age, race ethnicity, parity, lifestyle, environment,

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socioeconomic status, genetic risk factors, and access to medical services (Hortobagyi et al., 2005). The identification of potentially modifiable risk factors for breast cancer such as dietary intake, alcohol use, physical activity, obesity, ethnicity, history of pregnancy and breast feeding and possibly exposure to hormonal replacement provides opportunities for intervening in breast cancer prevention (Brewster and Helzlsouer, 2001).

Female schizophrenia patients are a vulnerable group as they are exposed to several factors associated with breast cancer. On the one hand neuroleptic induced hyperprolactinemia, resulting in low estrogen levels — protective for breast cancer, and on the other hand obesity, smoking, alcohol abuse and low parity are risk factors. In addition, the limited access and use of medical care are all characteristics of schizophrenia and may be modifiable.

We have previously reported that there was no increase in breast cancer amongst female schizophrenia patients (Barak et al., 2005). This was in line with the report by Lichtermann et al. (2001) as well as the findings of Dalton et al. (2003) and Cohen et al. (2002). Yet, this issue is controversial as illustrated by another study undertaken in Israel reporting mixed findings (Grinshpoon et al., 2005). The SIRs for aggregated sites for Jewish patients with schizophrenia was below 1.0 while the risk was marginally higher for breast cancer in women. Halbreich et al. (2003) in the USA stated that incidence of pathologically documented breast cancer is higher among psychiatric inpatients than that reported for the general population.

The effects of lifestyle habits and particularly heavy smoking (de Leon et al., 1995; Zammit et al., 2003) combined with less than optimal medical care (Dickerson et al., 2003; Druss and Rosenheck, 1997) for this vulnerable section of the population suggest that cancer ought to be increased amongst schizophrenia patients and that the diverse reports in the published literature may reflect a variety of methodological limitations. Pandiani et al. (2006) have recently emphasized that important questions about the relationship between serious mental illness (SMI) and cancer need be answered and that future research should consider the effect of lifestyle factors, exposure to antipsychotics and heredity. In order to control for lifestyle, exposure to psychotropic compounds and under-use of medical care comparison of cancer frequency amongst schizophrenia patients to that of patients with SMI is warranted.

The aim of the present study was to compare frequency of breast cancer between a large cohort of women suffering from SMI and those suffering from schizophrenia both utilizing tertiary psychiatric services.

2. Method

The present study focused on evaluating cancer risk amongst women suffering from severe psychopathology. In line with Pandiani et al. (2006) but more restrictively, we defined SMI patients as non-schizophrenia patients who were hospitalized in our center. Excluded were patients treated only in ambulatory settings in our catchment area.

We compared two inpatient groups: schizophrenia patients and women suffering from other SMI. All had been admitted to a large university affiliated mental health center. The Abarbanel Mental Health Center serves an urban catchment area with a population of 850,000 subjects. It is the referral center for the greater Tel-Aviv area. In accordance with the Israeli Ministry of Health's regulations, all HMO's in the center's catchment area refer patients for admission as there is no charge for psychiatric inpatient treatment. This emphasizes that there is no referral bias in the present sample.

2.1. Subjects

We utilized the Abarbanel Mental Health Center, Bat-Yam, Israel, computerized patients database to identify all adult (18 years and older) women who had been inpatients (lifetime). The sample thus acquired was divided into two sub-groups; women suffering from schizophrenia (DSM-IV) and women suffering from all other SMI. The database of women patients was linked to the National Cancer Registry of Israel for calculating cancer rates. We compared cancer incidence rates in this cohort of women patients with rates in the Jewish population of Israel. Cancer incidence rates among patients were compared with the expected incidence in age matched (and age adjusted) general population for the same time interval (1960 to 2005). In order to provide a useful context for the breast cancer data we also compared SIRs of all cancers and other types of female genitalia cancers.

Patients' records were meshed with records of the Israeli National Cancer Registry within the Israeli Center for Disease Control (ICDC) to identify pathologically confirmed cancer co-morbidity. The reporting of cancer cases to the ICDC since 1960 is mandatory in Israel.

We thus identified all female patients with pathologically confirmed cancers (in accordance with the International Classification of Diseases, 9th Revision, CM), diagnosed from 1960 through December, 2005. Information was available on patient age, ethnicity, age at cancer onset and type of cancer, if any. The Israeli Ministry of Health Ethical Committee approved the study.

2.2. Statistical analysis

To compare cancer incidence rates in women patients suffering from severe psychiatric disorders with the general population, standardized incidence ratios (SIR) were based on the Jewish population of Israel. SIRs were corrected for age. In the analysis, patients were at risk until the earliest of cancer onset, death or end of follow-up on Dec. 2005.

3. Results

Of the 8254 women patients' records analyzed, 2011 (24.4%) were schizophrenia patients and 6243 (75.6%) had been diagnosed as suffering from other psychiatric disorders, namely SMI. Mean age at diagnosis of cancer for the schizophrenia group was 53.9+13.1 years while mean age at diagnosis of cancer for the SMI group was 52.6+12.8 years. The ethnic composition of both patient groups is similar to that of the general Israeli population, as published previously (Brewster and Helzlsouer, 2001; CBS, 2002).

Amongst the 6243 SMI female patients 257 (4.1%) had developed cancer. The overall frequency of cancer at any site for female schizophrenia patients was 139 (6.9%). Both patient groups had SIRs that were significantly lower than expected frequency for the general population; 0.49 (95% CI=0.43–0.55) and 0.56 (CI=0.47–0.66) for SMI and schizophrenia respectively, $p<0.05$. Of the 6243 SMI female patients 83 (1.3%) had developed breast cancer. The overall frequency of breast cancer for female schizophrenia patients was 51 (2.5%). Both patient groups had SIRs that were significantly lower than expected frequency for the general population; 0.54 (95% CI, 0.43–0.67) and 0.63 (95% CI, 0.47–0.83) for SMI and schizophrenia respectively, $p<0.05$.

It is of note that the frequency of developing cancers in female genitalia was as follows: ovary — reduced for both

patient groups. However, the reduction in ovarian cancer was significant only for the SMI patients. Cervical uteri cancer was increased amongst schizophrenia patients, albeit not significantly. Amongst the SMI patients the frequency of cervical uteri cancer was similar to that expected for the general population (see Table 1).

Calculating the differential relative risk (RR) of developing cancer between SMI patients and schizophrenia patients, the resulting RR was for all cancers was 0.86 (CI=0.7–1.04) and for breast cancer it was 0.85 (CI=0.72–1.1). The RRs were not statistically significant thus reflecting reduction of risk regardless of diagnostic group.

4. Discussion

The major finding of the present study is the reduction in occurrence of breast cancer in both female schizophrenia patients and other SMI patients. The common denominator for both patient groups in our study is their use of tertiary psychiatric services. The use of SMI as a concept is gaining attention amongst researchers and service providers (Folsom et al., 2007). The relative incidence of cancer among adults with SMI other than schizophrenia or bipolar disorder patients has been little dealt with in the medical literature. In the one study that focused specifically on this issue, Pandiani et al. (2006) extended this line of inquiry by examining the incidence of cancer diagnoses in a population of adults with serious mental illness in Vermont, USA. In this work, SMI was defined as “individuals served by community programs for adults with serious mental illness”. The group reported that the incidence of cancer for adults with mental illness was more than twice that of the general population. In our study, the definition of SMI employed was more restrictive and included only women who had been admitted to a psychiatric hospital. This may explain in part the different findings we herein report.

Table 1
Standardized incidence ratios and 95% Confidence Intervals by cancer site and diagnostic group

	SMI					Schizophrenia				
	N=6243					N=2011				
	Observed	Expected	SIR	Lower CI	Upper CI	Observed	Expected	SIR	Lower CI	Upper CI
Breast	83	153	0.54*	0.47	0.67	51	81	0.63*	0.47	0.83
Cervix uteri	16	16.6	0.97	0.55	1.57	12	10.4	1.15	0.60	2.02
Ovary	12	23	0.51*	0.27	0.90	6	11.5	0.52	0.19	1.14
All sites	257	530	0.49*	0.43	0.55	139	247	0.56*	0.47	0.66

Legend:

SIR=Standardized Incidence Ratios.

CI=95% Confidence Interval.

SMI=Serious Mental Illness.

*= $p<0.05$.

There is no agreement as to the association between breast cancer and severe mental illness. A marginal increase in risk of breast cancer among women with schizophrenia has been reported by some authors (Dalton et al., 2005; Halbreich et al., 1996; Gulbinat et al., 1992) but not in all studies which have generally found no difference (Lichterman et al., 2001; Dalton et al., 2003; Mortensen, 1994; Goldacre et al., 2005) or a reduction in risk (Barak et al., 2005). There have been suggestions that an increase in risk of breast cancer could be mediated by a prolactin-releasing effect of neuroleptic medications (Halbreich et al., 2003), but a recent study failed to confirm this (Dalton et al., 2006). Risk factors which tends to be associated with an increased risk of breast cancer and may confound the relationship between schizophrenia and cancer include obesity, use of oral contraceptives, hormonal replacement and the observed lower parity among women with schizophrenia.

One of the earlier assumptions regarding the lower frequency of cancer in psychiatric patients was stated by Fox and Howell (1974) suggesting that prolonged hospitalization wherein smoking is curtailed and diet controlled is a protective factor. This is in line with the present findings that hospitalized patients had a lower frequency of cancer compared to the general population. It is conceivable that utilizing tertiary care psychiatric services may be an epiphenomenon indirectly reflecting a variety of factors that are related to cancer risk. Our findings draw attention to the possible contribution of environmental factors to the mechanisms responsible for the lower cancer rates.

There are several limitations that need be acknowledged when discussing this work. Several risk factors such as parity and obesity are not adjusted for. Recent publications report the fact that weight gain increases the risk of breast cancer mediated through higher estrogen levels (Ahn et al., 2007). We were unable to obtain data as to weight in our sample albeit patients suffering from schizophrenia and SMI have a high proportion of obesity. The distribution of psychotropic compounds between groups is also a possible confounder. Other confounding factors related to lifestyle and parity could not be corrected for. Finally, the group of SMI patients is heterogeneous and may thus introduce additional bias.

This analysis focuses on female patients. It is of note that while breast cancer rates were reduced in both patient groups, other gender associated cancers presented a different pattern. Ovarian cancer was reduced significantly only in the SMI group while cancer of the uterine cervix was non-significantly increased amongst schizophrenia patients. Thus, hormonal driven cancers in this analysis do not seem to behave identically. This further underlines the importance of the findings herein reported

for breast cancer being not merely “hormonal-related” but unique. Focusing on the study of breast cancer may thus reveal specific epidemiological patterns important for prevention. It may be inferred that the fact that the SMI group also had reduced rates of breast cancer may suggest a cohort effect.

It is conceivable that in the minority of patients low incidence rates of breast cancer may be due to less than optimal medical care.

However, all State owned mental health facilities are required to employ a specialist in internal medicine amongst their regular staff. Physical examinations are mandatory upon admission and at least once every six months. In addition, the national psychiatric case register was used by Levinson et al. (2003) to follow four cohorts of all new admissions in 1960, 1970, 1980 and 1990 diagnosed with schizophrenia or affective disorders. The overall accumulated length of stay decreased by 50% between 1960 and 1980 with the largest reduction observed among long-stay patients with schizophrenia. Thus, nowadays most schizophrenia patients receive routine medical care in the community similar to that of the general population.

The potential benefits in the understanding of the relative contribution of environmental factors in the evolution of breast cancer are enormous. The low rate of breast cancer in hospitalized psychiatric patients is encouraging. Yet, promoting breast and ovarian cancer screening for all women who are on long term drugs that induce weight gain or hyperprolactinemia is called for. Whether lifestyle, exposure to psychotropics or characteristics of the psychiatric system drive the mechanism responsible for reduced cancer rates these need be further elucidated so that practical recommendations as to their modification be devised.

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Contributors

Authors YB and DA designed the study and wrote the protocol. Author AA and TL managed the literature searches. Authors YB and DA wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare no actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three (3) years of beginning the work submitted that could inappropriately influence, or be perceived to influence, their work.

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