Clinico-pathological Features of Breast Cancer in Pakistan

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Abstract

Objective: To obtain information about presenting features of women with breast cancer in Pakistan, to compare these data with information on patients with breast cancer in the United States and to highlight the differences.
Methods: Patients referred to the National Cancer Institute, Karachi, Pakistan between January 1, 1994 and February 28, 1999 who had been recently diagnosed with breast cancer were prospectively evaluated. A printed questionnaire was used as an interview guide. Information was obtained about demographic features/ clinical characteristics, stage of the disease and previous therapy.
Results: Five-hundred sixty-six patients were evaluated. Mean age was 47.7 ± 11.8 years. Risk factors for breast cancer were observed in a minority. Mean number of pregnancies was 4.4. Eighteen percent had positive family history mostly in first-degree (64%) relatives. The vast majority (93%) discovered the lump accidentally. Average size was 5.7±2.3 cm. Over half had used unconventional therapies before receiving standard medical care. Most patients had undergone modified radical mastectomy and only 5% had conservative surgery done. Almost one third had locally-advanced disease. Seventeen percent had metastases at the time of diagnosis.
Conclusion: Despite significant advances made in cancer care in the United States, patients in Pakistan still present at an advanced stage. Antecedent use of unconventional therapies before seeking any medical advice is widespread. There is a great need for public education to enhance awareness about cancer and other health habits (JPMA 52:100;2002).

Introduction

Considerable progress has been made in the fight against cancer. Prevention, early detection and better therapeutic management have resulted in a decline in the incidence of cancer and its related mortality[1,2]. This is attributable to the tremendous efforts made by the governmental agencies, non-governmental organizations and societies, general public and health professionals, particularly in the technologically advanced countries. Cancer, however, is a worldwide problem. More than half of all cancer patients live in developing countries where resources to combat this disease are meager[3]. Budgetary restrictions, general illiteracy, poverty, poor hygienic conditions, environmental pollution, lack of awareness about etiology and pathogenesis of cancer, scarcity of well-equipped oncology institutions, trained health professionals and lack of sustained efforts by the government, general public and societies, have created an extremely dreadful situation. If not already, this problem will reach epidemic proportions. Its impact on

global health care resources will be enormous.
Breast cancer is an excellent example of the contrast between the progress made in the developed countries and difficulties associated with cancer care in the developing countries. It is the most common cancer in women worldwide3. Breast cancer is a model for successful strategies that can be employed to fight against cancer, Public education and increased awareness have resulted in early detection of this disease in the United States[4], Furthermore, significant therapeutic advances have been made with considerable improvement in disease-free and overall survival[4]. More recently, prevention of this disease has become a reality[5]. Mortality rates are declining. Against this very optimistic background, a clinico-pathological study of breast cancer cases observed in Pakistan is presented.

Patients and Methods

All patients referred to oncology service at the National Cancer Institute, Karachi, Pakistan between January 1,1994 and February 28, 1999 for the management of breast cancer were subjects of this study. Eligibility criteria included histologically confirmed diagnosis of carcinoma of breast made within the last 6 months. Patients were also required to have an ability to understand the study objectives and willingness to provide the required information. Verbal consent was obtained in all cases. Males were excluded. A printed questionnaire was used as a guide and patients were interviewed for an average of 30 minutes. Study objectives were explained to the patients. They were promised complete confidentiality with absolutely no consequences on subsequent medical care. This institution provides oncology services primarily to middle and upper socio-economic groups. A governeyta1 institute in the city handles most of the indigent patients. Socio-demographic features were assessed on the basis of information obtained from the patient which, when possible, were corroborated with factual information such as monthly salary, etc. Clinico-pathological features and stage of disease were, however, objectively assessed from patients' medical records.
Epi Info statistical package (Center for Disease Control, Atlanta, Georgia) was used for data analysis.

Results

Five hundred and sixty-six patients were accrued. All were analyzed. Demographic features, menstrual history and reproductive findings are presented in Table 1.

Table 1. Demographic features, menstrual history and reproductive behavior.

	No.	%
Total no. of patients	566	
Mean age in years (SD)	47.7	11.8
Socio-economic status (%)		
High	113	20
Middle	356	63
Low	97	17
Educational level (%)		
Illiterature	164	29
High school or less	306	54
College or above	96	17
Menstrual status (%)		
Pre	266	47
Post	300	53
Mean age at menarche in years (SD)	13.1	1.4
Early menarche (< 11 years) (%)	44.7	7.9
Nulliparity (%)	86.0	15.2
Mean number of pregnancies (SD)	4.4	2.5
Age at first full-term pregnancy (SD)	21.8	4.6
Lactation done (%)	385	68
Lactation done at each pregnancy (%)	345	61
Mean duration of lactation in months (SD)	13.7	9
Age in years at menopause (SD)	42.6	13.8
Late menopause (> 51 years) (%)	54.9	9.7

Mean age pf the patients was 47.7 years. Ethnic distribution was Mohajirs 54%, Gujrati Memon 16%, Punjabi 11%, Aga Khani 8%, Sindhi 6%, Pathan 4% and Parsi 1%. Most (94%) were married and belonged to the middle class. Due to the referral bias, there were fewer patients in the lower socio-economic group. Eighty-four percent were homemakers and only 16% were gainfully employed. Twelve percent had history of previous breast

disease. Very few (3.7%) were smokers and hardly any (0.7%) consumed alcohol. Eighty patients (14%) had received exogenous steroids- mostly oral contraceptives. Family history was positive in 18% of the patients (Table 2).

Table 2. Personal and family history of cancer.

Personal history of cancer	No.	%
None	541	95.5
Ca. Ovary	22	3.8
Ca. Breast	2	0.4
Ca. Cervix	1	0.2
Family history of breast cancer	103	18.2
Relationship to the relative with cancer		
1st degree	66	64.5
2nd degree	28	26.9
3rd degree	9	8.6
Menopausal status of the relative when cancer was diagnosed		
Premenopausal	45	43.5
Post-menopausal	58	56.5
History of bilateral breast cancer in the relative		
Yes	14	14.0
No	83	80.6
Unknown	6	5.4

Most of them were first degree relatives. The breast lump was discovered accidentally in the majority of the cases and it was not part of a routine self-examination or use of mammographic screening. More than half used un-conventional therapies before visiting a physician (Table 3).

Table 3. Perception of the lump, time to presentation and resons for delay.

	No.	%
How was the lump found		
Self accidentally	526	93.0
Self, as part of regular physical examination	17	2.9
Routine physical examination	20	3.5
Mammographic screening	2	0.4
Unknown	1	0.2
Time since perception and first visit to doctor in months (SD)	14.0	38.5
Treatment undertaken before diagnosis		
None	235	42
Use of homeopathy	280	49
Use of traditional healers	51	9

The most common surgical procedure was modified radical mastectomy, which was even done in some cases with documented metastatic disease (7%). In many cases, mastectomy followed a previous lumpectomy with clear margins (11%). Pathological features are provided in Table 4.

Table 4. Physical findings and clinico-pathological features of the study patients.

	No.	
Average size of the lump at diagnosis (SD)	5.7	2.3
Physical findings at presentation (%)		
Nipple retraction (%)	110	19.4
Bloody discharge (%)	39	6.9
Palpable axillary lump (%)	121	21.4
Fixation to overlying skin (%)	136	24.0
Fixation to the underlying muscle (%)	75	13.2
Erythema of skin (> 50% of breast) (%)	7	1.3
Peau d' orange (%)	48	8.4
Satellite nodules (%)	24	4.2
Abscess (%)	23	4.0
Type of local therapy done		
Modified radical mastectomy (%)	447	78.9
Radical mastectomy (%)	35	6.1
Lumpectomy with clear margins (%)	29	5.2
Total mastectomy (%)	6	1.0
Biopsy only (%)	49	8.8
Histology of the cancer		
Infiltrating ductal (%)	515	91
Intraductal (%)	34	6
Lobular (%)	17	3
Degree of differentiation		
Well differentiated (%)	68	12
Moderately differentiated (%)	300	53
Poorly differentiated (%)	198	35
Mean number of nodes removed (SD)	13.4	6.9
Mean number of nodes positive (SD)	6.9	6.6
Stage of disease at diagnosis		
I (%)	75	13
II (%)	230	41
III (%)	164	29
IV (%)	97	17

Most were infiltrating ductal carcinomas. Vascular invasion was observed in 41% and lymphatic invasion in 59% cases.
Estrogen receptor status was done on 55% of cases. one percent were ER negative. Very few patients presented with stage I disease. Most had stage II disease. Seventeen percent had metastatic disease time of diagnosis.

Discussion

Demographic features of the study patients present some interesting findings. Diagnosis of breast cancer at a relatively earlier age has previously been reported by investigators from several other developing countries[6-11]. Thirteen percent of our patients were less than 30 years of age. This is in marked contrast to American women with breast cancer[4]. Many risk factors well documented in American women, such as early menarche, nulliparity, advanced age at first full-term pregnancy and late menopause, etc were infrequently observed. Most of the patients were multiparous. Similarly, the majority carried out lactation.
One interesting aspect of this cohort was family history of breast cancer observed in 18% of the patients. Most of these relatives were first degree, were perimenopausal, and 14% had bilateral disease. This study, however, was not specifically designed to ascertain familial aspects of breast cancer. Specific questionnaires to obtain family history were not used and pedigree analysis was not performed. Furthermore, it is not a case-control study. Hence, it is difficult to draw any conclusions. North American investigators with special interest in familial breast cancer have described positive family history (first or second-degree relatives) in up to one-third of the patients[12,13].
transmission
Consanguinity plays an important role in the of genetic disorders. Consanguineous marriages are common in Pakistan[14,15]. One can expect a higher incidence of familial breast cancer in Pakistani patients. Patients with familial breast cancer, particularly those with genetic mutations, are significantly younger than the sporadic cases[12,13,16]. Could that account for the young age of our patients? More research is needed to study the familial aspects of breast cancer in Pakistan and the role played by consanguinity in these cases. Furthermore, genetic analysis of patients may provide important information. Such studies, in collaboration with investigators at University of Toronto, are in progress.
The most important finding of this study is the demonstration of advanced stage of disease at the time of diagnosis. This is in marked contrast to American women with breast cancer[4]. Almost one-third of our patients had locally advanced disease. Other investigators in the region have observed similar findings[6-11,17]. Most of these women presented with large masses in the breast. These massçs were discovered accidentally and only a rare patient carried out regular self-examination or underwent screening mammography. Many delayed seeking medical advice. Previous studies have identified ignorance, fear and fatalistic attitudes, poor socioeconomic conditions, and illiteracy as important factors resulting in delay[18-22]. In this study, we identified the use of unconventional therapies as another important reason. Although use of unconventional therapies is widespread, reasons behind their use and relationship to conventional therapy vary considerably in different regions of the world. In the United States, 6 to 23% of

cancer patients have been observed to practice alternative medicine at one time or another[23-26]. In the vast majority of cases, these methods are used as an adjunct to conventional medical care or at times when other therapeutic options have been exhausted. In the developing countries, on the other hand, besides the widespread use, these therapies are often employed as the initial line of treatment. They are practiced for a fairly long time, resulting in significant delay in diagnosis and treatment. Use of these therapies in Pakistan is widespread[27,28]. Further studies are needed to evaluate the influence of this delay on clinical presentation and therapeutic outcome of the patients with breast cancer.

An alternate explanation for advanced stage of disease at the time of presentation may be aggressive biologic behavior of breast cancer in Pakistani women. Racial differences in biology of breast cancer have been well described. Japanese women tend to have less aggressive and Afro-American women, more aggressive disease[29-33]. Such differences in biologic behavior of breast cancer have not been described from the developing countries. Further work is needed. The most common surgical procedure performed on these patients was modified radical mastectomy. Breast conservation was infrequent. In most cases, this was due to the advanced stage of disease at the time of diagnosis. However, many patients had mastectomy done even after a margin negative lumpectomy. Furthermore, several patients underwent surgery even in the presence of metastatic disease. None received neo-adjuvant chemotherapy. There is a clear need for educating health professionals in the management of breast cancer, particularly since fear of mastectomy may be an important reason behind the delay in seeking medical advice.

Socioeconomic factors play an important role in the provision of health care. Lack of awareness, inaccessibility of medical care, non-affordability of drugs and other medical therapies, fear of disease and associated death, and lack of social acceptance of cancer in Pakistan are important factors influencing the outcome of the patients. These factors may have contributed to late presentation of our patients with breast cancer.

One drawback of our study is under-representation of patients in the low socioeconomic group. This is due to the referral bias, since most of the indigenous patients in the city are referred to governmental institutions. Hence our findings may not be reflective of all breast cancer patients in Pakistan. It is likely that our findings under-estimate the intensity and enormity of the problem. A unique feature of cancer care in Pakistan is patients' lack of awareness of the diagnosis[28,34-36] There is a significant effort on part of the family to "protect" the patient and not divulge the diagnosis. Family members often feel that awareness of diagnosis will adversely influence the psychological and physical well being of the patients. Patients, under these circumstances, describe their cancer in terms of "tumor", "growth", "infection", "germs", etc. Physicians often go along with the families' desire to do so. It is primarily to avoid losing the patient altogether. This, unfortunately, results in a major communication gap between the patient and the physician[28,34-36]. Consequently, there is lack of dissemination of knowledge and building of trust that could occur when the disease and its treatment are frankly discussed with the patient. In conclusion, our study suggests that Pakistani patients with breast cancer, in contrast to their Western counterparts, still present at a relatively advanced stage of disease at the time of diagnosis. In order to improve the outcome of these patients, it is essential to understand reasons behind delayed presentation and taking appropriate remedial measures. There is great need to investigate all possible means to achieve results

similar to those obtained in the Western countries. Efforts at public education to enhance awareness may be most rewarding.

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