RESEARCH COMMUNICATION

Clinicopathologic Profile of Breast Cancer Patients in Pakistan: Ten Years Data of a Local Cancer Hospital

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Abstract

   Breast cancer is the most frequent cancer of women worldwide, with considerable geographic and racial/ethnic variation. Data are generally derived from population based cancer registries in the developed countries but hospital data are the most reliable source in the developing countries. Ten years data from 1st Jan 2000 to 31st Dec 2009 of a cancer hospital in Pakistan were here analyzed by descriptive statistics to evaluate the clinicopathologic profile of local breast cancer patients. Among 28,740 cancer patients, 6,718 were registered as breast cancer. The female to male ratio was 100:2. Breast cancer accounted for 23% of all and 41% of female cancers. Some 46% were residents of Lahore, with a mean age of 47±12 years. Less than 1% were at Stage 0 and 10%, 32%, 35% and 23% were at Stage I, II, III and IV respectively. Histopathology was unknown in 4% while 91%, 2% and 1% had invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC) and mucinous carcinoma respectively. Rare carcinomas accounted for the rest. Tumor grade 1, 2 and 3 was 11%, 55% and 34% among the known. Profile of breast cancer patients in Pakistan follows a pattern similar to that of other developing countries with earlier peak age and advanced disease stage at presentation. The male breast cancer accounts for higher proportion in the local population. Local women have higher frequency of IDC and lower frequency of ILC and DCIS, owing probably to a different risk profile. Use of hospital information systems and establishment of population based cancer registry is required to have accurate and detailed local data. Promotion of breast health awareness and better health care system is required to decrease the burden of advanced disease.

Keywords: Breast cancer clinicopathologic profile - gender dependence - cancer hospital data - Pakistan

Introduction

   Breast cancer is the world's most common cancer of females accounting for nearly a quarter of all cancers in the women (Ferley et al., 2010). Women of all geographic areas, races and ethnicities are affected. However ethnicity and region based variations in breast cancer biology is an established feature (Echeverria et al., 2009; Jemal et al., 2009; Bhikoo et al., 2011). The incidence, clinical presentation and survival rates vary in different geographic areas and among different races and ethnicities within the same geographic region (Merkin et al., 2002; Gorin et al ., 2006; Stead, 2009). Higher incidence and lower mortality rates have been reported from developed countries, with 45% of all cases and 55% of all deaths occurring in the low and middle income countries. Late stage presentation of biologically aggressive disease in relatively younger population is the characteristic feature reported from these countries (Igene, 2008). Genetic, economic, cultural and life style differences are the main attributing factors. These factors and the poor access to adequate treatment are the causes of the higher mortality rates in spite of lower incidence rates in these regions.

   Population based cancer registries do not exist in the developing countries including Pakistan. Most of the available figures from these countries are estimates based on data from small sections of population (Velsecchi and Steliarova-Foucher, 2008). Hospital and Institution based data is therefore an important source of information in these regions. The patient clustering provides easy and reliable data for pattern of disease and highlights key issues for local research and corrective strategies (Gress, 2002). There are only a few dedicated cancer hospitals in Pakistan. Institute of Nuclear Medicine and Oncology Lahore (INMOL) is a tertiary care nuclear medical centre and dedicated cancer hospital in Punjab, Pakistan. It is a public sector cancer hospital providing cancer care services in this region since 1984. At INMOL hospital computer based data have been maintained to record some information of all newly registered cancer cases since 1998. The data from year 2000 to 2009 were analyzed in the present study to evaluate the clinicopathologic features of breast cancer patients in the local Pakistani population, primarily from Lahore.

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Materials and Methods

The computer based hospital data maintained in Microsoft Excel format was obtained from year 2000 to 2009. This had some basic information about all the cancer cases registered in a year chronologically. The data was sorted depending on the "organ" of origin of cancer. The data of patients registered as "Breast" being the organ of cancer was analyzed by applying descriptive statistics to further evaluate the clinical and pathologic features of breast cancer patients.

Results

During the 10 year period from 1st January 2000 to 31st December 2009, a total of 28,740 patients with diagnosis of cancer were registered at INMOL. Among these patients 6,718 had breast cancer. Table 1 shows the year wise distribution of these patients along with the relative frequency of breast cancer among all, as well as among females only. The frequency of breast cancer patients among all registered patients, in the ten years was 23% (21.5% in the first five years and 26% in the later five years period). The frequency of breast cancer among females in this time period was 41% (38% in the first five years and 42% in the later five years).The female to male ratio was 100:2. Majority of patients (46%) were residents of Lahore and a small proportion were from nearby cities. Only 7% patients were residents of Gujranwala, 6% of Sialkot, 4% each of Sargodha and Sheikhupura and 3% each were from Kasur, Okara, Sahiwal, Faisalabad and Gujrat. Patients from far off cities and other provinces of

Table 1. Year-wise Distribution of Breast Cancer Patients

Year	Total Patients	Breast Cancer Patients	Total Females	Breast Cancer Females
2000	2,361	511 (22%)	1,301	502 (39%)
2001	2,284	481 (21%)	1,245	465 (37%)
2002	2,224	479 (22%)	1,199	463 (39%)
2003	2,620	560 (21%)	1,453	550 (38%)
2004	2,988	638 (21%)	1,627	621 (38%)
2005	2,830	643 (23%)	1,620	641 (40%)
2006	3,136	759 (24%)	1,788	743 (42%)
2007	3,514	815 (23%)	1,985	793 (40%)
2008	3,545	926 (26%)	2,097	908 (43%)
2009	3,238	906 (28%)	1,945	894 (46%)
Total	28,740	6,718 (23%)	16,220	6,580 (41%)
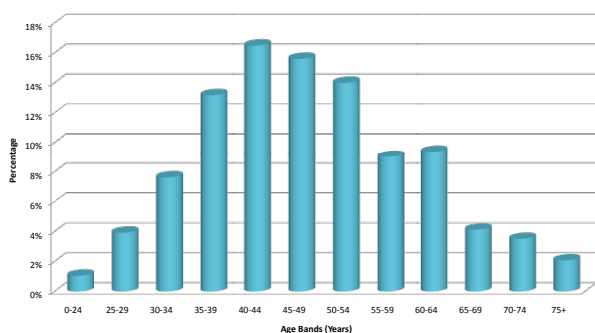
Figure 1. Age Distribution of Women with Breast Cancer in Lahore, Pakistan

Pakistan accounted for only 18% of all.

The mean age of females with breast cancer was 47±12 years and the age ranged from 18 to 90 years. The median age was 45 years and mode was 40 years. Peak age of incidence was 40-44 years followed by 45-49 years. Figure 1 shows the age distribution of these patients.

Stage was recorded in 5,939 patients. Less than 1% (20 patients only) was registered at Stage 0 having In Situ Carcinoma while 10% were at Stage I at the time of registration. The stage distribution for Stage II, III and IV was 32%, 35% and 23% respectively. Vast Majority (91%) of patients had Invasive ductal Carcinoma while histology was unknown in 4% of patients. Only 2% had Invasive Lobular carcinoma and 1% had mucinous carcinoma. All other known categories of histology accounted for less than one percent each. These consisted of mucinous carcinoma (42 patients), medullary carcinoma (31 patients), squamous cell carcinoma (28 patients), ductal carcinoma *in situ* (20 patients), Papillary carcinoma (15 patients), Sarcoma (9 patients), cystosarcoma phylloides (10 patients), mixed lobular and ductal carcinoma (6 patients), Pagets carcinoma (5 patients), spindle cell sarcoma (5 patients), papillary intracystic carcinoma (4 patients), Lymphoma (3 patients) and metaplastic carcinoma (3 patients). Two patients each were registered with the histopathology of, adenoid cystic carcinoma, colloid carcinoma, basal cell carcinoma, fibrosarcoma and metastatic carcinoma. One patient each had histological diagnosis of Ewings sarcoma, leiomyosarcoma, liposarcoma, malignant melanoma and neuroendocrine carcinoma. Tumor grade was recorded only in 447 patients. Among these 11% (49) were Grade 1, 55% (246) were Grade 2 and 34% were Grade 3.

Discussion

The 10 years institutional data of the present study with 6,718 patients of breast cancer, provides one of the largest series of breast cancer patients from Pakistan for evaluation of the clinicopathologic features of local patients. This type of hospital based cancer registry data is an important public health tool to provide useful information for the researchers of developing countries (Gress, 2002). In these countries institution based data is the only reliable source of information to identify pattern of disease and areas of need in the local community. The biggest limitation of this data is that the population from which the cases are registered is not known and the incidence rates cannot be calculated. In addition the present study is limited because of the few parameters of the recorded data and incomplete data entry. As the hospital based data is currently the only reliable source of cancer related information of the local patients, there is an urgent need to have hospital information systems in the local cancer hospitals. The best strategy however to develop comprehensive nationwide cancer data base is to establish and maintain a population based cancer registry.

Breast cancer is the most frequently diagnosed cancer in the women worldwide. Globally it accounted for 23% of all cancer cases and 14% of all cancer deaths in year 2008 (Jemal et al., 2011) with about five fold variation in different regions. There is no national population

based cancer registry in Pakistan, therefore the precise incidence and mortality rates of breast cancer are not known. Karachi Cancer Registry was established in 1995 and currently it is the only source for the estimate of breast cancer burden through a sample population of the country (Bhurgri et al., 2006). The available population based cancer registry data from South Asia shows that Pakistan has the highest Age Standardized Rate at 69 per 100,000, of breast cancer in this region (Moore et al., 2009). The 23% frequency of breast cancer patients among all cancer patients and 41% among females, registered at INMOL from the year 2000 to 2009 is higher than that cited in the global cancer statistics (Parkin et al., 2005; Jemal et al., 2011). A recently reported frequency of breast cancer in 21.5% among all and 45.9% among female patients (Badar et al., 2011) from Shaukat Khanum Memorial Cancer hospital (SKMCH) is quite similar to the data from INMOL hospital.

Breast cancer is rare among males accounting for about 1% of all cases only (Giordano et al., 2004). Although the incidence and prevalence data is scanty because of the rarity of male breast cancer, geographic variations have been noted (O'Malley et al., 2002). The 2% proportion of male breast cancer in the present study is twice that of the overall 1% incidence in the world. Significantly higher rates (6% to 15% of all breast cancer cases) have however been reported from some countries in Africa like Tanzania and Zambia (Ihekwaba, 1994, Contractor et al., 2008). A recent population based study however reports only 0.6% male patients among 4,62,511 patients of breast cancer in the cancer registry data of Denmark, Finland, Geneva, Norway, Singapore and Sweden (Miao et al., 2011). The studies from developing countries are hospital based, like ours and therefore can provide only rough estimates on the pattern of local disease. True comparisons with the developed countries can only be made with population based cancer registry data.

Studies from Pakistan have consistently shown breast cancer to be the most frequent cancer of the women (Bhurgri et al., 2006; Jamal et al., 2006). Data from Karachi Institute of Radiotherapy and Nuclear Medicine (KIRAN) from the year 2000 to 2008 (Hanif et al., 2009) and Jinnah hospital Lahore from 1997 to 2001 (Aziz et al .,2003) also show breast cancer to be the commonest cancer of women accounting for 38% of all. This is similar to some other developing countries like Egypt where 35% of female cancers were found to have breast cancer (El Saghir et al., 2007). The developed countries like United Kingdom, Australia and USA have 30%, 27% and 26% patients of breast cancer among all female cancers (Jemal et al., 2009; AIHW 2010; Barrett, 2010).

The data from INMOL shows tendency for increasing proportions from 22% frequency of breast cancer among all and 39% among females in the year 2000, to 28% among all and 46% among females in the year 2009. The tendency for increasing proportions is very sharp and obvious after the year 2005. During this year a dedicated breast clinic with female experts was established at INMOL. The sharp trend of increasing proportion of breast cancer patients at INMOL may be explained by the improved facilities for breast cancer diagnosis and treatment locally or by the rising incidence of breast cancer in the local population in general. The former may be a contributing factor however a rising incidence of breast cancer in the local population is another possible explanation. The latter is likely because a rapidly rising incidence rate of breast cancer at 3 to 4% per year compared to 0.5% per year of global rise, has been reported from the Asia Pacific region (Parkin et al 2005). Only a well maintained local population based cancer registry can tell the actual time scaled increase in the incidence of breast cancer in the local population.

Profile of breast cancer patients is fairly similar within the developed countries like UK, USA and Canada etc. Similar is the case with the developing countries in Asia, Africa and Arabian regions (El Saghir et al., 2007; Leong et al., 2010). The clinical data of women with breast cancer in the present study is different from that of the developed world with regard to the age of the patients and the stage of the disease at diagnosis. The presentation however is in consistence with the previous reports from Pakistan and is similar to the other developing countries (Malik, 2002; Gilani et al., 2003; Aziz et al., 2008; Agarwal et al., 2007). The most striking difference between the developing and the developed world is in terms of an early peak age at presentation, which is 40 to 50 years in the former compared to 60 to 70 years in the latter (Leong et al., 2010). The mean age of 47±12 years (Median =45 years and mode=40 years) of breast cancer patients in the present study is considerably younger than that reported by the developed countries. This is about one and a half decade earlier than that of the patients in the developed countries like United States and Australia. The average age of breast cancer patients is reported as 61 years (SEER 2005, American Cancer Society 2007) and 69 years respectively (AIHW, 2010) in these countries. A report of a database from 1998 to 2006 of a diverse population with invasive breast cancer at Boston University Medical School (Stead et al., 2009) had median age of 58 years compared to 47 years in our study. The age distribution of breast cancer patients in the present ten years data report from INMOL hospital however is similar to that reported in small series of patients from other institutions of Pakistan. Mean age has been reported as 48 years by Malik (2002) in 566 patients, Siddiqui et al. (2000) in 572 patients, Bhurgri et al. (2007) in 680 patients and Sharif et al (2009) in 535 patients. The data (average age=47.6±12, range=18-102, median=46 and mode=45 years) of SKMCH in Lahore (Badar et al., 2011) is also similar to the age pattern of patients presenting at INMOL.

Data on the proportion of young patients in various other countries and societies shows that 7.4% American patients (Shavers et al., 2000), 8% of Australian patients and 12.6% of patients in Singapore are under 40 years of age (Foo et al 2005). Among the patients from diverse population at Boston University Medical School, 30% were less than 50 years in age. This is in sharp contrast to our local patients, among whom 58% were younger than 50 and 26% were younger than 40 years in age. A similar proportion of 60% patients being younger than 50 years (Bhurgri et al., 2007) and 32% patients younger than 40 years (Badar et al., 2011) has been reported in studies from Pakistan and other developing countries. In a recent

report on breast cancer profile of patients in Cameroon, 66% were younger than 50 years and 32% were younger than 40 years (Ngowa et al., 2011).

The younger age at presentation is a feature of breast cancer patients in most of the developing countries like India (Dinshaw et al., 2005; Saxena et al., 2005; Agarwal et al., 2007), SriLanka (Lokuhetty et al., 2009) and Cameroon (Ngowa et al., 2011). The younger age range of patients in Pakistan and the other developing countries may be explained by the younger age structure and the lower life expectancy of their women. Pakistan hosts one of the largest proportions of young population in the world. Only 4.2% of the population in Pakistan is 65 years or older compared to 12.8% in USA. The average life expectancy of women in Pakistan (66 years) on the other hand is far lower, compared to 82-84 years of the women in America, Australia and Sweden (Wikipedia, 2011).

Ductal carcinoma in situ (DCIS) is a preinvasive variant of breast cancer. The patients diagnosed with DCIS are assigned stage 0 according to TNM classification. About 80% to 85% DCIS is detected by mammography and the rest are detected as a lump. Moreover upto 34% of mammographically diagnosed cases are DCIS (Ernster et al 2002). Only 26 patients among 6,718 in our study were registered as DCIS during the ten years. This is in sharp contrast to the scene in the developed countries like United States, where about 20% to 25% of all newly diagnosed cases are DCIS (Kerlikowski 2010). The major reason of this discrepancy is the absence of population-based mammographic screening program in Pakistan and the limited availability of mammography machines in the local hospitals.

Breast cancers are classified into biologically and clinically distinct subgroups according to the histological grade, histological type and the receptor status. Data about the tumor Grade of breast cancer was available in only a small fraction (7%) of patients in the present study. Moreover there was no record of hormone receptor status. No conclusions can therefore be drawn about the biological aggressiveness of the disease in the local population. However the grade distribution in the present study (11, 55, 34% respectively of Grade 1, 2 and 3) is similar to previous report (12, 53 and 35%) from Pakistan (Malik, 2002) and other countries like Turkey reporting, 4, 56, 40% respectively of Grade 1, 2 and 3 (Ozmen, 2008) and Malaysia reporting, 13, 47, 40% patients with these grades respectively (Pathy et al., 2011).

The various histologic types of breast cancer have distinct clinical, prognostic and biological features. Invasive ductal carcinoma (IDC) is the most frequent followed by invasive lobular carcinoma (ILC) and some rare variants. The 91% frequency of IDC in our patients is higher and 2% frequency of ILC is lower than that found in the developed countries. About 70% to 80% patients had IDC and 5% to 15% had ILC in the developed countries (Li et al., 2005; Ozmen, 2008; Pestalozzi et al., 2008) while 90% to 92% IDC and 1% to 3% ILC has been reported from Pakistan (Malik, 2002; Bhurgri et al., 2007; Sharif et al., 2009). These differences can be attributed to the reproductive practices (early age at birth of first child, high parity and prolonged lactation), low frequency of

hormone replacement therapy and early peak age of breast cancer incidence of the local women, as all these factors are known protective factors for ILC (Li et al., 2006; Albreksten et al., 2010).

Majority of breast cancer patients present with advanced disease in Pakistan. The stage at presentation of breast cancer is a major determinant of patient's survival after treatment. Socioeconomic status, geography and race have been found to have an interactive effect in the risk of advanced stage presentation of breast cancer in large and diverse populations (Merkin et al., 2002; Gorin et al., 2006; Stead et al., 2009). In a study of breast cancer cases presenting at two cancer hospitals in Lahore (Gilani et al., 2003), 63% and 71%, presented at advanced stages (TNM Stage III and IV). The present 10 years data report of INMOL shows that 58% of patients presented at these late stages. A similar picture has been reported in various other studies from Pakistan (Malik, 2002; Hanif et al., 2007; Aziz et al., 2008; Khokher et al., 2010; Malik et al., 2010) and other developing countries (Chopra, 2001; Hebert et al., 2006; El Saghir et al., 2007; Lim et al., 2007). The stage wise distribution of breast cancer patients is far better in the developed Asian countries. Only 10% patients in Hong Kong and 27% in Malaysia had advanced disease at presentation (Agarwal et al., 2007). In a review of breast cancer databases of two hospitals in Malaysia, about 25% patients presented at Stage III and IV (Pathy et al., 2011). This picture is however in sharp contrast to the developed countries with established screening programs. During the year 2006, about 9% of breast cancer patients were diagnosed at preinvasive stage and among the invasive cancers, 56%, 37%, 5% and 2% were diagnosed at stage I, II, III and IV respectively in Stockholm, Sweden (Leong et al., 2010). In a state specific breast cancer data analysis of United States, including 811,652 patients, Stages III and IV collectively accounted for only 10% of patients while 57 to 61% patients presented at Stage I (Sariego, 2009). The striking difference in the stage distribution of breast cancer patients in the developing and developed countries has been largely attributed to the lack of screening facilities, delays in seeking medical attention, poor socioeconomic status, poor health care systems and poor diagnostic and therapeutic facilities. There is an urgent need to adopt corrective strategies best suited to local culture and resources for early diagnosis and affordable appropriate treatment of breast cancer in these countries. Population based mammographic screening program is neither affordable nor feasible in the current scene (Badar et al., 2011) as a recent review shows that it is not associated with decrease in the incidence of advanced breast cancer (Autier et al., 2011).

In conclusion, the profile of breast cancer patients in Pakistan follows a pattern similar to that of other developing countries with earlier peak age and advanced disease stage at presentation. Higher frequency of breast cancer among all cancers is registered at local hospitals. Very few women are diagnosed at Stage 0 having DCIS. Limited availability of mammography machines in local hospitals is the main reason. The local women have higher frequency of Invasive Ductal Carcinoma and lower frequency of Invasive Lobular Carcinoma. This difference

is attributed to the low prevalence of the risk factors for ILC in the local population. Incidence of male breast cancer is twice that of the world in general. Introduction of hospital information systems in the local cancer hospitals and population based cancer registry at the national level is required for accurate and reliable local cancer data base. Promotion of breast health awareness and better facilities for earlier diagnosis and appropriate treatment is required to improve the present clinical scenario.

Acknowledgements

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