

## “Incidence and Prognosis of Breast Cancer among the Females of Islamabad”

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### Abstract

*Breast cancer is the most common cancer in women worldwide. It is estimated that more than 1.7 million new cases of breast cancer occurred among women worldwide. The disease occurs almost entirely in women, but men can get it, too. For men the life time risk of getting breast cancer is 1 in 1000.*

*A cross sectional study on Breast cancer was carried out in the medical center of Oil and Gas Development Company Islamabad. The purpose of this study was to find out the incidence of breast cancer in different age groups of females and its response to the available treatment in Pakistan. The period of study was from July 2017 to June 2018.*

*Total numbers of 210 females screened were between the ages of 25-65 years; with different complaints related to their breast. 29 females (14%) were found having breast cancer. 10 patients were with stage 4. Five of them were between the ages of 30-40 years, one was 28 years and four patients were between the ages of 41-65 years. Stage 3 patients were 5 (17.2%), two (40%) were between the ages of 30-40 years and three patients (60%) were between the ages of 41-65 years. However stage 2 patients were 13 (44.8%). Among the 13 stage 2 patients seven (54%) were between the ages of 30-40 years and six (46%) were between the ages of 41-65 years.*

### Introduction

Among the Asian countries Pakistan has highest age standardized incidence rate (ASIR) of Breast cancer [1,2]. The Karachi Cancer Registry (KCR) is the first population based cancer registry in Pakistan shows results of 99% morphologically verified cancers [1,2]. The ASIR of 50.3/100,000 was estimated by GLOBOCAN in 2012 [3]. The population-based Punjab Cancer Registry (PCR), of Lahore district with a population of 15 million, has shown an ASIR of 47.6/100,000 for 2010-2012 [4]. The five-year survival rate for breast cancer varies worldwide. The data of 5,486,928 women with breast cancer from 279 population-based cancer registries from 67 countries around the Globe was analyzed by Concord 2 study on Global Surveillance of survival 1995-2009 [5].

In 34 countries during 2005-2009 the age standardized five year survival in women diagnosed with breast cancer was 80% or higher. However survival of breast cancer patients was lower than 70% in countries such as Malaysia (68%), India (60%), and low in Mongolia (57%) and South Africa (53%) [3]. In North America and Oceania, survival from breast cancer was high (84-89%). In Europe, the survival was generally lower than in North America and Oceania. The difficulties in assessing the incidence and progress of disease are with countries such as Africa because of lack of data available and in Pakistan too proper data is missing since there is no national population based cancer registry system. In low and middle income countries like Pakistan follow up of patients is not

practiced. Therefore the country has no primary mortality data on breast cancer. However for Pakistan the Age Standardised Mortality Rate (ASMR) assessed through (GLOBOCAN 2012 estimates) was 25.2/100,000 which is the highest among all Asian Countries. The biggest reason for having high (ASMR) is late diagnosis because patients reach at medical facility with advance stage of cancer due to lack of awareness and access to care, delayed clinical evaluation, and staging and absence of timely access to optimum treatment [3]. The prognosis of breast cancer depends on how early it is detected. Early detection through screening has reduced the mortality rate in developed countries. In USA for localized disease five year survival is 99%, for regional 85%, and for distant 27% [6]. Stage distribution of breast cancer is very important in breast cancer cases and very little data is available on staging of breast cancer in Pakistan. There are studies carried out on staging of breast cancer in two tertiary care hospitals in Pakistan, SKMH and INMOL Lahore [7]. From SKMH 179 biopsy and stage proven patients and from INMOL 470 patients, Stage 3 and 4 were 71% and 63% respectively, 36% Patients at SKMH and 25% patients at INMOL presented with stage 4 metastatic. In a recently published descriptive, retrospective study conducted at the Liaquat National Hospital, Karachi, Pakistan, records of 8,291 breast cancer patients (all biopsy-proven) registered from 1994-2014, were analysed [8]. The number of patients with stage 1 increased from 53 (0.64%) in 1994 to 847 (10.21%) in 2014.

ASIR, high ASMR, and advance stages at presentation, all point to

an alarming situation in Pakistan.

Although many epidemiological studies shows that age is not directly related to prognosis of breast cancer, however this dispute is now consider debatable. It has been renowned through studies that breast cancer is more aggressive in young women such as triple negative or Her 2 positive breast cancer are more commonly seen in young adults. Another reason for having bad prognosis in young females could be late diagnosis because of less suspicion about the disease in young age. This interprets to more loco-regional recurrences as well as distant metastasis which could be the possible cause of poor prognosis in young women with breast cancer.

Since HER 2 positive cases are less benefited by chemotherapy, therefore hormonal therapy mostly Herceptin is providing good results by reducing the chances of relapse. Although the breast cancer cases are increasing worldwide but due to early detection especially in developed countries the prognosis is getting better [9]. Mammography is still a primary method of detecting the disease but MRI and CT scan are also used especially if suspecting metastasis [9].

In country like Pakistan the biggest barrier in diagnosing the disease in early stages is lack of awareness about the disease and the consequences of late diagnosis. Many women remain in denial stage and not ready to accept the presence of disease in their body. Nevertheless during the last decade educated women in big cities like Karachi, Lahore and Islamabad do participate in seminars and campaigns design to spread the message stressing more on early detection of disease leads to good prognosis.

The epidemiology of breast cancer disease is difficult to define in Pakistan because of lack of data available [10]. Less resources and less budgets available for health services is one of the barrier.

### Literature Review

Breast cancer in young women is associated with adverse pathological factors, including high grade tumors, hormone receptor negativity, and HER2 overexpression. This has a significant negative impact on the rate of local relapse and overall survival. Moreover, younger women often tend to present with breast cancer at a later stage than their older counterparts, which further explains worse outcome. Regardless of these factors, age is still being supported as a self-determining role player in the prognosis. This involves more aggressive treatment modalities and the need for closer intensive care and follow-up [11].

The incidence of early onset breast cancer has increased moderately and the survival rate has not improved during the last 35 years. When young women are diagnosed with breast cancer their tumors are larger, their lymph nodes more often involved, and the median grade higher than in older with 64% having grade 3 tumors. Lymph node status was the strongest sole prognostic indicator but the use of NPI gave more accurate prognostic information than node status alone [12].

According to GLOBOCAN, it is the most common cancer in women, accounting for 25.1% of all cancers. Breast cancer incidence in developed countries is higher, while relative mortality is greatest in less developed countries. Education of women is suggested in all countries for early detection and treatment. Plans for the control and

prevention of this cancer must be a high priority for health policy makers; also, it is necessary to increase awareness of risk factors and early detection in less developed countries [13].

Racial variation did not have any impact on the prognosis of the TNBC [14].

Chemotherapy or hormonal therapy reduces the risk of distant metastases by approximately one-third; however, 70–80% of patients receiving this treatment would have survived without it. None of the signatures of breast cancer gene expression reported to date allow for patient-tailored therapy strategies [15].

Half of elderly patients with breast cancer are undertreated, with strongly decreased specific survival as a consequence. Treatments need to be adapted to the patient's health status, but also should offer the best chance of cure [16].

Breast cancer patients younger than 35 years have a worse prognosis than older patients. This difference is only partially explained by a higher frequency of adverse pathologic factors seen in younger patients [17]. Adjuvant chemotherapy therapy has a dual effect on metachronous cancer: it reduces the risk, while at the same time it seems to worsen the prognosis [18]. Women who developed bilateral cancer within 5 years and at age younger than 50 years were 3.9 times (95% CI, 3.5 to 4.5) more likely to die as a result of breast cancer than women with unilateral cancer [19].

The combination of increasing incidence and improved survival rates implies that the number of prevalent cases will continue to increase considerably in the next 10 years [18]. Axillary status is a better prognostic factor than response of the primary tumor to primary chemotherapy [20].

The lower breast cancer incidence in minority women and higher breast cancer mortality in African American women than in white women are largely unexplained [21]. Together, the currently available evidences suggest that BRCA1 mutation and E-ER signal together, contribute to breast tumor genesis by providing the metabolic support for cancer cell growth and even may directly be involved in promoting the de-differentiation of cancer-prone epithelial cells [22]. Breast cancer (BC) is highly heterogeneous with ~ 60–70% of estrogen receptor positive BC patient's response to anti-hormone therapy. Estrogen receptors (ERs) play an important role in breast cancer progression and treatment [23]. Postmenopausal, tamoxifen treated patients with estrogen receptor (ER) positive; PR-A-rich tumors have much faster disease recurrence than patients with PR-B-rich tumors [24]. PR-A and PR-B both inhibit cell growth and provoke resistance to Taxol-induced apoptosis. PR-A:PR-B ratios, even in the absence of P, influence the biology and treatment response of ER+ tumors, that PR-A isoforms are functionally dominant in P deficient states, and PR-A rich tumors are especially aggressive [24].

Estrogen receptor  $\alpha$  (ER $\alpha$ ) has an established role in promoting breast cancer. Transcriptional activation by ER $\alpha$  is a complex and multistep process, and it is influenced by co-activator and co-repressor proteins that can either positively or negatively modulate ER $\alpha$ -mediated transcriptional activity [25]. TNBCs exhibit fairly aggressive local growth and rapid progression and account for a high rate of early metastases, most commonly to visceral organs and the central nervous system. TNBCs are also characterized by

diagnosis at a later stage and the poorest survival of patients as compared with cases of any other breast cancer types [26]. The risk factors associated with this cancer varies with respect to other cancers, genetic predisposition, most notably mutations in *BRC1* or *BRC2* gene, is an important causative factor for this malignancy [9].

### Methodology

Studies were included by searching PubMed, Google Scholar, and Scopus. Detailed search was done to include the relevant studies in the literature. Patients between the ages of 25 to 65 years were screened and great care was taken to include patients only with complaints related to their breast. Some problems arose during collection of data such as lack of cooperation from patient's side, delay in follow up visits of patients living in remote areas and refusal of patients for surgery, but all of these matters were dealt very diligently to minimize the delay in getting the histo-pathological reports. While taking the history patients were calm down by counseling and assuring about their recovery from the disease. Data was gathered together and transferred to excel sheets.

### Findings

Modified Radical Mastectomy was performed in all patients. Chemotherapy was given to 26 patients. Radiations were given to 16 patients. Those 3 patients who were not fit for chemotherapy were given hormonal therapy. Herceptin was administered to 1 patient who was Her 2 positive.

Stage 2 patients responded well with surgery and chemotherapy. Two of the stage 3 patients who were between the ages of 30-40 years developed bone metastasis during chemotherapy period. Prognosis was very poor in stage 4 patients, whereas 3 of them died during the study period. They were of the ages 28 years, 35 years and 64 years respectively.

Histopathology of all cases showed the tumor was infiltrating ductal carcinoma. Three patients of stage 2 between ages 25-40 were triple negative. Only one patient of age 55 was triple negative with stage 2. Among the stage 3 one patient of age 32 years was triple negative. Four patients between the ages of 25-40 years of stage four were triple negative. Among these four 2 died during the study period.

**Table 1: Showing the results**

S.NO	Stages	Total	Sub -Total	Percentage	Age	Treatment	Prognosis
1.	Stage 1	Nil	Nil	Nil	Nil	Nil	Nil
2.	Stage 2	13	7 patients (25-40yrs) 3 TNBC	54%	25-65	13 patients underwent MRM	Prognosis Satisfactory
			6 patients(41-65yrs) 1TNBC	46%			
					25-65	13 patients received Chemotherapy	Prognosis satisfactory
					25-40	6 patients received Radiation	Prognosis satisfactory
					41- 65	4 patients received Radiations	Prognosis Satisfactory
3.	Stage 3	6	2 patients(25-40 yrs) 1 TNBC	40%	25-65	5 patients underwent MRM	2 patients between the ages of 30-40 develop bone metastasis during chemotherapy.
			3 patients(41-65 yrs)	60%		6 patients received Chemotherapy	
					25-65	2 patients received radiations	
4.	Stage 4	10	6patients (25-40yrs) 4 TNBC	60%	25- 40	10patients underwent MRM	3 patients died during the study period ages 28 years, 35 years, and 64 years.
			4 patients (41-65 yrs)	40%	25-65	7 received Chemotherapy	
					25-40	4 received radiation	
					25-40	3 Harmon therapy	
					41-65		

### Discussion

Breast cancer is the most frequently diagnosed cancer in Pakistani females [27]. Breast cancer incidence is increasing tremendously in Pakistani population among the Asian countries [28]. This current trend of increase in incidence of breast cancer in Pakistan has created a need for preventive measures [29]. This is a fact that age is an important factor in the increase incidence of breast cancer [30-32]. Most of the breast cancer cases are seen in ages <40, 40s, and 50s. In our present study more the younger patients were diagnosed with advance stage, the reason for this delay could be unsuspected cases because of young age, lack of knowledge about the disease, social barriers and taboos. Obesity is one of the factors responsible for increased incidence of breast cancer. Patients with normal BMI has a longer survival rate as compare to patients with higher BMI [33-36]. Many studies support this fact that obesity is one of the major factors in the increase incidence of breast cancer, which may be mainly due to higher levels of free estrogen produced by excess

aromatase activity in the peripheral adipose tissue [37,38]. Increase in BMI is seen mostly in women which in turn is due to change in eating habits and sedentary life style.

In the current study we screened 210 patients with different complaints of breast. We found 13.8% having breast cancer. The alarming situation is that not a single patient is diagnosed at stage 1 while stage 4 patients are 34.4%. Late diagnosis is a leading cause of poor prognosis. 60% of stage 4 patients are young. This means 60% are not curable which indicates failure of efforts in reducing the mortality rate especially among young patients. On the other hand 44.8% patients were diagnosed with stage 2. This explains the need for active treatment in 44.8% of patients. This is actually the disease burden. We need to have more cancer hospitals and available chemotherapy medicines. Since there are (24.1%) young patients with stage 2, our efforts should be towards early diagnosis in young that is at stage 1 so that they can live as much

longer as possible. At older age the possibility of all types of cancers increases, therefore older patients should have regular screening and checkups to rule out the presence of cancer in any part of their body. In our study stage 3 patients are 17.2%. Young patients between the age of 25-40 are (6.9%) while between the age 41- 65 are (10.3%). Previously there was a concept that only older patients get this cancer disease but now we have seen many young patients with cancer. This study shows (48.2%) young patients having breast cancer. The change in this trend has many factors involved and the top most factors are change in the dietary habits, stressful and sedentary life style. Breast cancer is also explained in obese patients and obesity is also included in the risk factors of breast cancer over the fact that excessive adipose tissues are responsible for release of estrogen hormone which in turn a major factor involve in causing breast cancer [39-41]. Total 9 patients are triple negative (TNBC) and 2 of them died during the study. TNBC patients are mostly young 25-40 years of age, only patient was 55 years. Prognosis of Breast cancer mostly depends on stage of the disease and also on estrogen progesterone receptors and Her 2.

### Conclusion

Breast Cancer incidence is increasing tremendously therefore it has become one of the commonest malignancies not only in Pakistan but all over the world. Since it is the widely occurring cancer in women there are many causative factors that are being associated with its occurrence especially in young women, but variation do occur therefore do not rely on these factors alone. However these factors may predict the chances of occurring breast cancer to some extent. The most frequent and major risk factors include age, family history, socio economic status, high BMI, age at menarche, contraceptive pills, alcohol consumption, night shift working, smoking, HRT and use of medicines are labeled as risk factors. The factors that are protective against breast cancer are successful and full term pregnancies at young age, breast feeding, eating healthy food, regular exercise and physical activities, and a happy lifestyle may reduce the risk of breast cancer.

### Implications

1. Avoid radiation and environmental pollution.
2. Do not continue hormone therapy for a longer duration and in high dose.
3. Breast feed your baby.
4. Remain physically active and exercise regularly.
5. Avoid junk food, artificial flavors, colors and sugary drinks.
6. Eat green leafy vegetables, fruits, fish, beans and legumes.
7. Don't smoke.
8. Don't drink alcohol, the more you drink alcohol the more the risk of developing breast cancer.
9. Avoid stress.
10. Sleep well.

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