International Journal of Pharmacy
Journal Homepage: http://www.pharmascholars.com

Research Article **CODEN: IJPNL6**

INCIDENCES, SCREENING AND CHEMOTHERAPY OF BREAST CANCER

Sheikh Abdul Khaliq[1,*], Syed Baqir S. Naqvi[2], Anab Fatima[1]

[1]Department of Pharmaceutics, Faculty of Pharmacy, Hamdard University, Karachi
[2]Department of Pharmaceutics, Faculty of Pharmacy, University of Karachi, Karachi

***Corresponding author e-mail:** sheikh1974@gmail.com

ABSTRACT

Retrospective study in different ethnic groups determines the burden and patterns of breast cancers during the last eight years reported in Oncology wards of hospitals of Karachi, Pakistan and compares the pharmacotherapy/chemotherapy used with international guidelines, develops strategies for screening and evidence based pharmacotherapy/chemotherapy of cases. Every single one male & female case with histologically and cytologically established breast cancer was enrolled from January 2003 to December 2010. Data for all patients were collected retrospectively by patient's file & charts, which represents the population of Karachi, Interior Sindh & Balochistan. 847 female patients investigated for their diagnosis of cancer type, ethnicity, age & gender. The statistical analysis was performed for mean, standard error & proportions. Pharmacotherapy/Chemotherapy & screening employed by the hospitals was compared with international guidelines and evidences. Proportionately major ethnic groups female diagnosed with breast cancer in total female cases was Sindhi (25%), Urdu Speaking (48%), Baloch (6%), Pukhtoon (5%), Punjabi (11%), Siraiki (1%), Minorities & others (4%). Mean age at the time of diagnosis was 44.07±12.37 years, SE± 0.069. Screening strategies are implemented in <10% targeted population, however pharmacotherapy/chemotherapy was comparable with international guidelines. The study reveals that breast cancer incidences are highest among Urdu Speaking (17%) and then Sindhis (9%). Rests of the ethnic groups are in the range of 2-4%. There is a need to implement the screening strategies more extensively to the small/basic/rural health care centers for early diagnosis of the disease and new treatments like monoclonal antibodies are making revolution in the management of breast cancer.

Keyword: Ethnic groups, Breast Cancer cases, Incidences.

INTRODUCTION

Breast cancer is the cancer which is a major threat for developing countries health care system. Around the world it is major cancer occurring in women and a major cause of death. In 2008 only 1.3 million cases reported and 458,000 deaths occur.[1] The incidences of breast cancer are increasing and developing nations has to develop strategies for screening, early diagnosis and economic pharmacotherapy of breast cancer. In Pakistan, being developing state, the cost of management of these cancers, not only affect individuals those suffer from it but affect their families and society at large. Financial burden is not only the issue but emotional disaster is greater than former. Pakistan is one of the countries of diversified types of ethnic groups which include Sindhis, Urdu Speaking (migrated from India after 1947 and their descendents), Balochs, Pukhtoons, Punjabis, Kashmiris & others. Unfortunately, there is no single comprehensive data available to categorize the cancers and their types in these major ethnic groups. In countries where screening and reporting of cancer is excellent, they have made strategic alignment of their health resources to overcome the problem at earlier stage, which is not only reflected in their quality of life but also increased average life of individuals. In United States, 2.2% annual decline observed in the breast cancer cases after 1991 because of implementation of mammography and advancement of chemotherapy.[2]. Breast cancer is the

most common cancer among the females of Karachi and account 1/3rd of all cancers in women. In Asia, the incidences of breast cancer are highest except Israel. The risks factors may contribute in the development of breast cancer include early menarche, late menopause and use of reproductive hormones as well as obesity in addition to dietary factors and availability of breast cancer genes i.e. BRCA1 and BRCA2. During the last five years there is pronounced increase observed in the cases of breast cancer at Karachi. Strict implementation of screening and employment of pharmaco-economics principle not only reduces the financial burdens but also improve the health care system in Karachi.[3]

MATERIAL AND METHODS

This retrospective study conducted in Karachi, Pakistan, where material is collected from six different state of the art government and private hospitals located in Karachi and more than 1020 female patients histopathologically diagnosed with breast cancer and among which 989 patients included in analysis for the period of 2003 to 2010. 31 patients were excluded because of preliminary diagnosis, lack of patient's objective findings, diagnosis is not confirmed for any cancer, availability of incomplete data of patient like ethnic community, age, gender & belonging to geographic location and children ≤ 12 years. Majority of cases were received from state owned hospital at Karachi. The information is obtained from case sheets and patient's file available in medical record room of the hospital. The data collected include age, gender, ethnic group, occupation, cancer type, date of diagnosis and the pharmacotherapy/chemotherapy received. SPSS software applied to collected data to calculate occurrence of cancer in each ethnic group and mean age, standard deviation and standard error. The pharmacotherapy/chemotherapy was compared with the guidelines internationally recommended to treat breast cancer.

OBSERVATION AND RESULTS

Incidences: The findings of present study include Sindhis, Urdu Speaking, Balochs, Pukhtoons, Punjabis, Siraikis & Other Minorities female from January 2003 to December 2010 suffering from breast cancer, 1020 female patients attended the oncology wards out of which 989 were analysed & 31 (3%) were excluded from analysis due to incomplete information or loss of follow-up, among which 242 (25%) Sindhi female, 471 (48%) Urdu Speaking female, 56 (6%) Baloch female, 54 (5%) Pukhtoon female, 111 (11%) Punjabi female, 12 (1%) Siraiki female, 43 (4%) Minorities female (Pie Chart-I). Mean age of all females were 44.07 years with SE± 0.069 (Sindhi; 44.04, SE± 0.467, Urdu Speaking; 44.29, SE± 0.374, Baloch; 42.59, SE± 0.925, Pukhtoon; 43.12, SE± 0.979, Punjabi; 45.28, SE± 0.806, Siraiki; 44.45, SE± 2.397, Minorities; 43.80, SE± 1.067). The incidence rate among Urdu Speaking female is 17%, Sindhis 9%, Punjabis 4%, Balochs 2%, Pukhtoons 2%, Minorities female 2%. (Graph-I)

Screening of Breast Cancer: Pakistan, being a developing country, scarce resources, needed to develop strategies to reduce the burden of cancer in terms of financial and other losses. National Cancer Control Program (NCCP) should be implemented strictly and WHO, government and other health authorities including private sector NGOs should provide necessary resources to develop strategies for screening, prevention, diagnosis and treatment of breast cancer. Breast cancers can be minimized just by proper screening. The possible strategy, which has been implemented in very few hospitals of Karachi for prevention and early diagnosis of breast cancer is self and clinical examination of breast over age 20, mammography over age 40. The government, NGOs and private sector should design and implement effective awareness campaigns for general public for the age specific symptoms and screening and to emphasize that early diagnosis can not only reduce economic burden but also families emotions and painful treatment. The recommendation of American Cancer Society for early detection of breast cancer in average risk or asymptomatic people is mentioned in Table-I.[4]

Magnetic Resonance Imaging (MRI) also recommended in the cases where symptoms are available but mammogram is revealing false negative results. MRI can detect changes which are benign proliferative, fibroadenomas and any other minor or benign changes which are not detected in mammogram. The recommendation for MRI screening is for the patients include; family history of breast cancer, mutation in BRCA-1 and/or BRCA-2 genes, female with implant of breast, previous lumpectomy or history of biopsy surgery, metastases in axillary and unknown primary tumor, dense breast tissues.[5]

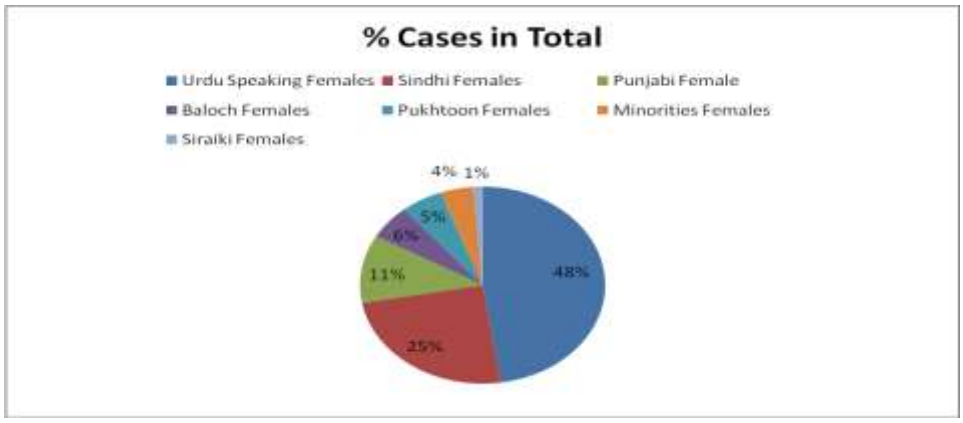
Pharmacotherapy/Chemotherapy: For the management of breast cancer there are many

treatments are available, some are recognized as standard and some are still under the evaluation. National Cancer Institute of USA generally recommend six different treatment options either use alone or sometime in the combination. These six treatments include; surgery (lumpectomy, partial mastectomy, total mastectomy, modified radical mastectomy), senile lymphnode biopsy then followed by surgery, radiation therapy, chemo or pharmacotherapy, hormone therapy, targeted therapy by monoclonal antibodies (Abs) or protein tyrosine kinase inhibitors. However our main focuss is on chemo/pharmacotherapy, hormone therapy and targeted therapy. If the disease is in the stage 2-4 then chemotherapy is imperative and is used for the period of 3-6 months in the combination. Most of the chemotherapeutic agents work by destroying the DNA of fast growing cells. The new approach is management of breast cancer by HER-2+ve case. 15-20% cases of breast cancer are HER-2 gene overexpression. The development of monoclonal antibody enhances the 5 years survival in HER-2+ve cases treatment significantly up to 95%.[6] Monoclonal antibodies are the antibodies made in the laboratory. These antibodies identify at molecular level changes in the tumor cells, once they find the molecule which is leading towards cancer, they start to kill them as well block their growth. These antibodies are given in the form of infusion and sometime in combination with anticancer drug, toxin or radioactive agent to detect the site of tumor. Herceptin is monoclonal Abs which acts by blocking the proliferative protein HRE2 and use in combination with chemo/pharmacotherapy. In the similar war protein tyrosine kinase inhibitor also blocks the HER2 protein as well as other proteins involve in the development of cancer. Hormone therapy involves the blockade of hormones particularly estrogen responsible for proliferation of cells. Tamoxifen is choice of medication for such type of action, however it may develop the risk of ovarian cancer and i.e. why pelvic exam once yearly require for women taken tamoxifen to rule out the development of ovarian cancer. Aromatase inhibitor is another class of drug use for the inhibition of estrogen by inhibiting the enzyme aromatase which is responsible for conversion of androgen to estrogen without the risk of ovarian cancer. Pharmaco/chemotherapy is the implications of drug which either kill the cancerous cells are stop their abnormal proliferation. The dosing of chemotherapy is based upon either body weight, body surface area (BSA), area under the time concentration curve (AUC), however, BSA is the most appropriate way as it represents accurate comparison of activity and toxicity and best can be correlated with cardiac output. Liver function as well as renal function should also be considered while evaluation the dose. Combination therapy is more effective than single drug therapy because to prevent resistance, biochemical enhancement of effects, protection of normal cells. When employing combination therapy, antitumor activity, difference in mechanism in action and minimization of overlapping toxicities should be evaluated. The chemotherapy observed in the breast cancer patients of hospitals of Karachi include combination of drugs FAC (Fluorouracil+Adriamycin+Cyclophosphamide), Paclitaxil or Taxol+Palmodronate, Docetaxil +Cisplatin, Gemcitabine+Cisplatin, FEC (Fluorouracil+Epirubicine+Cyclophosphamide), TAC (Taxol+Adriamycine+Cyclophosphamide), AC (Adriamycine+Cyclophosphamide). The combination of FAC and FEC was requiring precaution for the availability of normal CBC (Complete blood cell counts). The national cancer institute of USA recommends the following FDA approved combination of drugs for the treatment of breast cancer, these drugs includes AC, ACT, CAF, CM (Methotrexate) F, FEC. Another interesting finding is that Aspirin also reduces the risk of breast cancer.[7]

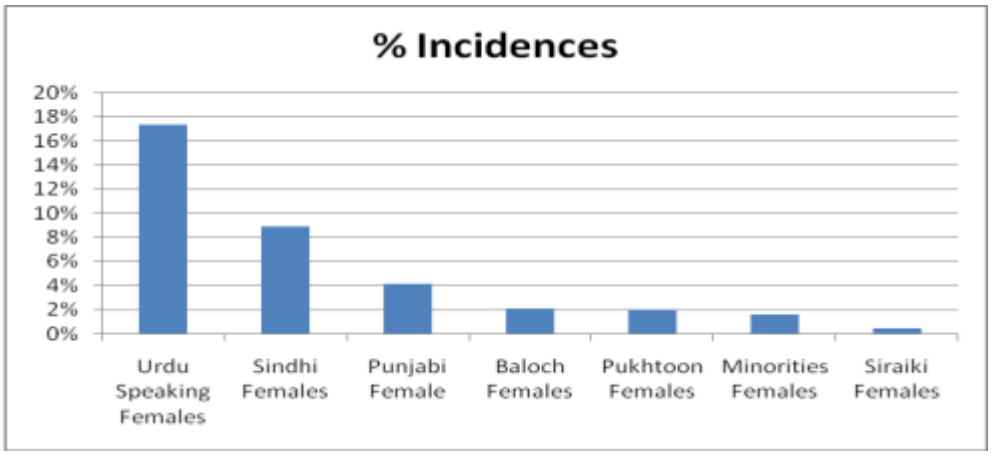
CONCLUSION AND DISCUSSION

Breast cancer is most prevalent among all ethnic groups of Karachi with the highest rate among urdu speaking female and accounts one third of cancer in females and it has been observed that incidence of breast cancer in Karachi is highest in Asia except Israel.[8] In another study of 46 patients, where analysis has done on the base of age groups, the most common age group was 40–49 years with 14 cases (30.4%), then 50-59 years with 12 cases (26.0%), followed by 30–39 years with 10 cases (21.73%), 60-69 years 07 cases (15.21%), 20–29 years 1 case (2.17%), 70–79 years 1 case (2.17%) and there was also one case (2.17%) of 80 years and above age group.[9] Breast cancer is also found to be the most common disease in the middle age group 40–59 years.[9-12], similar findings observed in the current study. Possible risk factors accounted for the development of breast cancer includes early menarche, late menopause, reproductive hormones, hormone replacement therapies, genetic factors (BRCA1 and BRCA2). Several studies conducted around the world include Malacia, Germany, USA and even India where breast cancer is detected at early stage because of better implementation of screening programs.[13-17] Although there are various types of regimens use for the chemotherapy of breast cancer, however combination of different type of drugs depends upon several factors include tumor

characteristicks, lymph node involvement, age of the patients, overall health condition of the patient, because after the age of 65 years the adverse effects increases in the patient.[18] The recommended adjuvant chemotherapy their cycles and frequency is mentioned in the table-II. Pakistan, being a developing country, scarce resources, needed to develop strategies to reduce the burden of cancer in terms of financial and other losses. National Cancer Control Program (NCCP) should be implemented strictly and WHO, government and other health authorities including private sector NGOs should provide necessary resources to develop strategies for screening, prevention, diagnosis and treatment of breast cancer. Pharmaceutical companies should invest in cancer research to come up with new cost effective medications which are not only safe but having compelling evidences of efficacy. The possible strategy for prevention and early diagnosis of breast cancer is self and clinical examination of breast over age 20, mammography over age 40. The government, NGOs and private sector should design and implement effective awareness campaigns for general public for the age specific symptoms and screening and to emphasize that early diagnosis can not only reduce economic burden but also families emotions and painful treatment.



Pie Chart-I (Proportions of cases in total diagnosed breast cancers)



Graph-I (Incidences of Breast cancer/Ethnic Group Female)

Table-I

Cancer Site	Population	Starting Age	Tests for Procedure
Breast	Women	20+	Self Breast Examination
		20+	Clinical Exam. Of Breast
		40+	Mammography

Table-II

Chemotherapy	Cycles & Frequency
CMF (Cyclophosphamide, Methotrexate, 5-fluorouracil)	4 weekly for 6 cycles
FAC or CAF (5-fluorouracil, Doxorubicine, Cyclophosphamide)	3 weekly for 6 cycles
AC or CA (Doxorubicine, Cyclphosphamide)	3 weekly for 4 cycles
AC-Taxol (Doxorubicine, Cyclphosphamide)	3 weekly for 4 cycles and followed by Paclitaxel 3 weeks for 4 cycles or weekly (at a smaller dose) for 12 weeks
TAC (Taxotere, Doxorubicine, Cyclophosphamide)	3 weekly for 6 cycles
FEC (5-flourouracil, Epirubicin, Cyclophosphamide)	3 weekly for 6 cycles
FECD (5-flourouracil, Epirubicin, Cyclophosphamide, Docetaxel)	FEC 3 weekly for 3 cycle and followed by Docetaxel 3 weekly for 3 cycles
TC (Taxotere, Cyclophosphamide)	3 weekly for 4 or 6 cycles

REFERENCES

1. American Cancer Society, global cancer facts and figures (2008). http://www.cancer.org/acs/groups/content/@epidemiologysurveilance
2. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, Mandelblatt JS, Yakovlev AY, Habbema JD, Feuer EJ. New England Journal of Medicine, 2005 Oct 27;353(17):1784-1792.
3. Bhurgri Y, Bhurgri A, Hasan SH, Usman A, Faridi N, Malik J, Khurshid M, Zaidi SM, Pervez S, Kayani N, Hashmi KZ, Bashir I, Isani Z, Sethna F, Ahsan H, Zaidi ZA, Naseeruddin S, Zaidi SA, Alam SM. J Pak Med Assoc. 2002 Jun; 52:244-246.
4. Smith RA, Cokkinides V, von Eschenbach AC, Levin B, Cohen C, Runowicz CD, Sener S, Saslow D, Eyre HJ. CA cancer J Clin, 2002 Jan-Feb;52(1):8-22.
5. Morrow M. *JAMA 2004.* **292** (22): 2779–2780
6. Jahanzeb M. Clin. Breast Cancer 2008. 8 (4): 324–33.
7. Holmes MD, Chen WY, Li L, Hertzmark E, Spiegelman D, Hankinson SE. Journal of Clinical Oncology. 2010 Mar 20;28 (9): 1467–1472.
8. Bhurgri Y, Pervez S, Usman A, Khan JA, Bhurgri A, Kasi Q, Kasi I, Rasool AG, Faridi N, Bhurgri H, Ajam A, Ajam A, Malik J, Hasan SH. J Pak Med Assoc. 2002 Dec; 52(12): 560-565.
9. Naeem M, Khan N, Aman Z, Nasir A, Samad A, Khattak A. J Ayub Med Coll Abbottabad 2008 Oct-Dec;20(4): 22-25.
10. Siddiqui M, Kayani N, Sulaiman S, Hussainy A, Shah S, Muzaffar S. J Pak Med Assoc 2000;50:174–177.
11. Siddiqui K, Rasool MI. J Coll Physicians Surg Pak 2001;11:497–500.
12. Baloch TA, Iqbal P. Med Channel 2006;12:47–48.
13. Kuraparthy S, Reddy KM, Yadagiri LA, Yutla M, Venkata PB, Kadainti SV. World J Surg Oncol 2007;5:56.
14. Klonoff-Cohen HS, Schaffroth LB, Edelstein SL, Molgaard C, Saltzstein SL. Ethn Health. 1998;3:189–198.
15. Yip CH; Taib NA; Mohamed I. Asian Pac J Cancer Prev. 2006;7:369–374.
16. Arndt V, Stürmer T, Stegmaier C, Ziegler H, Dhom G, Brenner H. J Clin Epidemiol 2001;54:719–727.
17. Oluwole SF, Ali AO, Adu A, Blane BP, Barlow B, Oropeza R. J Am Coll Surg 2003;196:180–188.
18. Von Minckwitz, G. Experts Opinion on Pharmacotherapy 2007; 8(4): 485–495.