

Ethnic Differences in the Expression of HER-2/neu Positive Breast Cancer Phenotype

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Breast cancer is a heterogeneous disease. Prognostic indicators include tumor size, tumor grade, lymph node status, hormone receptor, human epidermal growth factor receptor (HER-2/neu) expression and proliferation fraction assessed by ki-67. Breast cancer is the most common malignancy diagnosed among women in the world, with 2.2 million new cases diagnosed in 2020, which is 11.7% of all cancer cases [1]. **Fig. (1a&1b)** depict Globocan statistics for new cancer cases in 2020 in Pakistan for all ages and sexes and among females respectively [2].

Based on tumor biology, women respond in varied

fashions to treatment resulting in different outcomes. We know that other factors including underlying genetics result in different clinical behavior of these cancers requiring treatment other than traditional chemotherapy. Several targeted therapies are approved that can alter the biological behavior of these cancers. These may result in positive outcomes, in terms of both responses to therapy as well as improvement in survival [3]. **Fig. (2)** displays globally age-standardized incidence and mortality of top ten cancers. However, we do not have published data from Pakistan on survival outcomes in HER-2/neu-positive breast cancer.

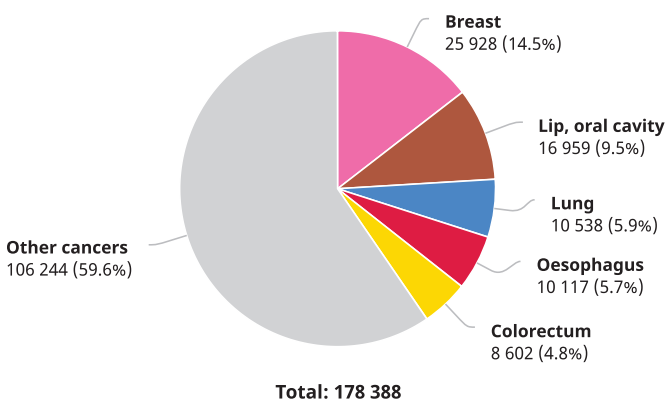


Fig. (1a): Globocan statistics for new cancer cases in 2020 in Pakistan among all ages and both sexes.

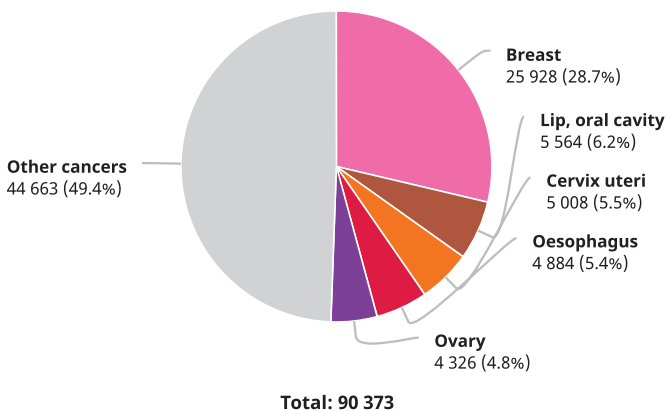


Fig. (1b): Globocan statistics for new cancer cases in 2020 in Pakistan among females.

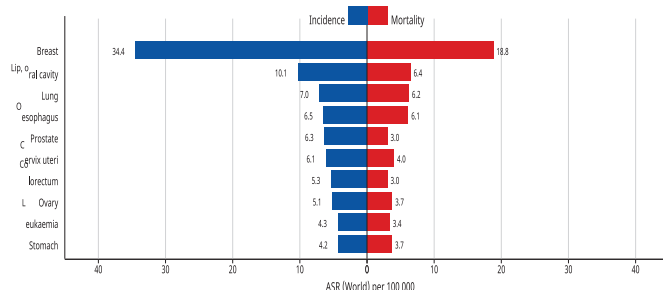


Fig. (2): Globally age-standardized incidence and mortality of top ten cancers.

The molecular sub-types of breast cancer are based on the expression of Estrogen/Progesterone receptors and the overexpression of the HER-2/neu. Conventionally the subtype groups are; Luminal A (ER+/PR+/HER-2/neu-, Ki-67<14%), Luminal B (B1: ER+/PR+/HER-2/neu, Ki-67>14% and B2: ER+/PR+/HER-2/neu+), HER-2 enriched (ER-/PR-/HER-2/neu+), Basal type (ER-/PR-/HER-2/neu-), also known as Triple negative breast cancer. The presence of the HER-2/neu molecular subtype may have clinical implications for women in terms of both treatment and prognosis. Some molecular subtypes reported in the literature are more common in certain ethnic groups and races. It is therefore important to identify these associations with HER-2/neu positive disease, especially as the financial cost of treatment for these patients is significantly greater compared to the HER-2/neu negative breast cancer.

Several studies have looked at the association between the subtypes of breast cancer in different race/ethnic subgroups. A study by Alison *et al.* looked at 40,936 women from California and calculated the absolute lifetime and age-specific probabilities of developing

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breast cancer subtypes. Their results showed that the luminal A and B breast cancer subtypes predominated across all racial/ethnic subgroups, with a lifetime lowest risk in Hispanic women and highest in white Caucasian women. HER-2/neu positive disease varied less by race and the lifetime risk of triple-negative breast cancer was highest in Black (African American) women [4].

Another study by Melina L. Telli *et al.* looked at the distribution of these subtypes in six different ethnic Asian groups in California. A total of 8,140 Asian women were studied. The distribution of HER-2/neu positive disease was found to be higher in Korean, Vietnamese, and Chinese women compared to non-Hispanic white women after adjusting for age, stage, grade, socioeconomic status, histology, year of diagnosis, nativity and hospital ownership status [4]. A study by Khan *et al.*, published in 2020 looked at the frequency of the different subtypes in different ethnic groups in Pakistan. They found a higher expression of ER/PR and HER-2/neu in the Pushtoon population compared to the other groups namely Urdu-speaking, Sindhi, Balochi and Punjabi [6].

The article that accompanies this editorial by Shumaila *et al.* "Ethnic differences in the expression of HER-2 positive breast cancer in different ethnic populations in Pakistan" shows that the Pushtoon population had a higher incidence of HER-2 positive breast tumors compared to other ethnic groups, namely Urdu speaking, Sindhi, Balochi and Punjabi. The results however, as reported in this study, were not statistically significant [7].

It is important that we keep studying the incidence of different subtypes in our population. According to the GLOBOCON 2020, 25,928 women were diagnosed with breast cancer, which is 28.7% of all cancer diagnosed in women. We have a younger population of breast cancer patients with high mortality [1]. Pakistan is a country with huge financial challenges. Treating breast cancer, especially HER-2/neu positive disease is expensive. This is a burden on patients and their families. It will be easier to ask for funding from the government as well as from the private sector and different non-governmental organizations if we can study and report data from women diagnosed with breast cancer in Pakistan.

In conclusion, it is important to conduct more research on breast cancer among various ethnicities living within our country. The prime focus of research may involve community-based research, quality diagnostic trials involving sequencing data and importantly converging the data from original research from various stakeholders to systematic reviews for meaningful interpretation of evidence. Furthermore, the research trial must also endeavor pharmacogenomic studies to refine therapy toward precision therapeutics for our breast cancer population. An attempt should also be made to develop consensus-based local search engines in line with the worldwide reputed "Catalogue of Somatic Mutations In Cancer" (COSMIC) [8]. It will be important to be a participant in this to be globally represented in the endeavors against this and other cancers. Last but not the least, governmental oversight of such cancers with high incidence rates is needed at the outset by adopting primary screening and measures so as to reduce adverse outcomes and reduce the cost of therapy.

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