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Current Situation of Breast Cancer in Pakistan and the Dire Need of Early Diagnosis

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ABSTRACT

Globocan statistics underscore Pakistan's noticeable position in terms of the breast cancer burden, highlighting a concerning and escalating trajectory in its daily progression. Breast cancer stands as the most predominant and fatal malignancy in Pakistan, reporting 25,928 cases in the year 2020, accounting for 14% of all cancer diagnosis. The country is reported to have the maximum incidence and mortality rates in Asia, a dire result of the lack of national cancer registry. Late diagnosis, often determined by sociocultural factors, considerably contributes to the high mortality rate. Several risk factors, such as reproductive factors, age, dietary habits, further complicate the situation. Moreover, economic obstacles deter many from receiving the required treatment. The current review features the dire need for inclusive policies and improved affordability to battle breast cancer's escalating influence in Pakistan.

Keywords: Breast cancer, malignancy, mortality, Pakistan

1. INTRODUCTION

Worldwide, the number of breast cancer cases has seen a persistent increase and such cases remain a significant reason for mortality [1]. In 2020, approximately 2.3 million women were diagnosed with breast cancer, resulting in 685,000 associated mortalities. Breast cancer stands as the most predominant neoplastic growth, worldwide. In this regard, 7.8 million women were determined to have breast cancer disease toward the end of 2020 [2]. The risk of creating breast cancer has ascended in Pakistan, with one in every nine women with a lifetime chance to have this malignant growth [3]. Pakistan exhibits the highest mortality and incidence rates among all other Asian countries [4]. Furthermore, when contrasted with neighboring countries such as India or Iran, the rate of incidence was found to be 2.5 times higher in Pakistan [5, 6]. Pakistan faces a significant challenge in data quality for breast cancer records, primarily due to the lack

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of a national cancer registry. According to facility-based projections and studies, the estimation of new cases is between 34,000 and 90,000 cases, with 16,232 deaths [7].

2. CURRENT SITUATION OF BREAST CANCER IN PAKISTAN

2.1. Delayed Diagnosis of Breast Cancer as a Major Cause of Mortality

Among all the causative agents for breast cancer, delayed diagnosis is a major factor in increasing breast cancer mortality rate in Pakistan. Delay in seeking proper healthcare treatment is the reason that many cases of breast cancer have been reported at the last stages, resulting in mortality [8]. Based on previous reports, mortality in 1/3rd of women aged 50 or above can be prevented if the cancer is diagnosed in early stages. Patients diagnosed with breast cancer in its early stages have a higher chance of survival than patients diagnosed in later stages. The elevated prevalence of breast cancer may be attributed to certain factors, such as lack of knowledge, as well as social and financial constraints [9]. A noticeable causative factor of mortality among Pakistani women is the reluctance to seek medical help from male physicians, driven by the cultural taboo associated with exposing breasts, which is perceived as a sign of disrespect. A study conducted to evaluate the reasons behind delayed diagnosis demonstrated that approximately 40% of the women surveyed resorted to home remedies and alternative treatments in attempt to self-manage breast cancer, with the primary motivation being the avoidance of disclosing their breasts to male healthcare professionals. Additionally, 17% chose to ignore symptoms, while 10% were cognizant of their cancer but hesitated to seek treatment due to the cultural norms of associating breasts with secrecy and the imperative to conceal them at all costs [10]. The multiple reasons behind the delayed diagnosis of breast cancer are depicted in Figure 1 [11].

The likelihood of survival significantly diminishes when breast cancer is diagnosed at advanced stages. A recent study showed that about 46.26% of patients consulted doctors in Stage II, while 36.46% were in Stage III at the time they presented themselves. This is alarming as the cancer survival chances decrease if presented at later stages [12], as shown in Figure 2.

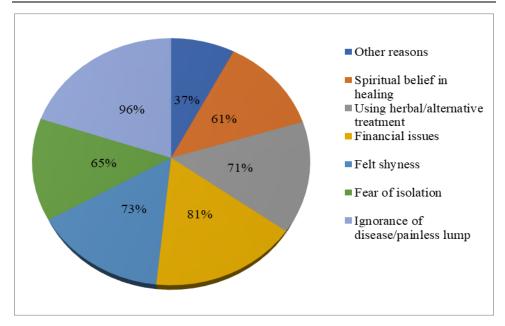


Figure 1. Percentage of Patients with Reasons for Delayed Diagnosis [11]

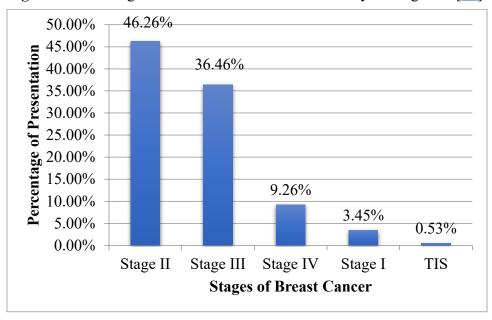


Figure 2. Stages of breast cancer at which patients presented themselves for medical assistance $[\underline{12}]$

2.2. Other Risk Factors for Increasing Breast Cancer Prevalence

Age is directly related to the incidence of breast cancer [13]. Women of age 40 years and above have been recorded to suffer from this cancer. Studies reported that women experiencing late menopause at age 55 or above are at the risk of breast cancer more than the ones who undergo menopause at 45 years of age [14]. Likewise, childbearing at an early age lessens the incidence of breast cancer. Delay in child bearing increases the risk of breast cancer by 3% per year. Also, increased number of pregnancies and breastfeeding are protective factors against breast cancer. A study reported that women with one child are 15% more likely to develop breast cancer than women with two children [15].

Melatonin hormone plays an important role in preventing cancer due to its anti-carcinogenic properties. However, reduced and disrupted sleep patterns reduce melatonin which may increase the chances for breast cancer. Reports indicated that more than 4% of breast cancer patients have the risk factor of night shifts and disrupted sleep patterns [16]. Similarly, smokers have a 20% more chance to suffer from breast cancer [17]. Additionally, physical barriers might also cause psychosocial stress as patients are reluctant to go through the demanding screening and treatment processes [18]. Only a few studies have examined the factors that contribute to cancer screening and treatment delays in Pakistan, such as lack of awareness [19], low socioeconomic status, accessibility and affordability of cancer treatments, and other risk factors (exposure to dangerous industrial chemicals) [20]. Vitamin D deficiency can cause the conversion of nonmetastatic cells to metastatic cells. Every one out of three women suffers from Vitamin D deficiency in Pakistan. Physical inactivity is directly related to breast cancer as it is associated with obesity which is the mother of all diseases. Females with increased BMI are at a much higher risk of developing breast cancer due to the increased amount of free estrogen produced as a result of elevated aromatase activity in adipose tissues [21]. Hence, physical inactivity is directly related to BMI, hormones, menstrual cycle, and immune system [22]. Women show a high rate of obesity than men (Figure 3). World obesity statistics show a national obesity risk of 6.5/10 in Pakistan.

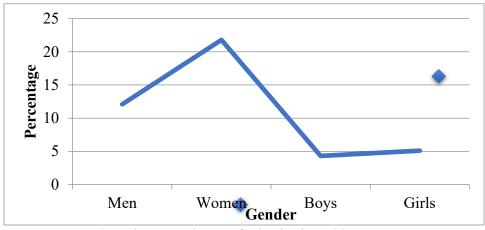


Figure 3. Gender-wise Prevalence of Obesity in Pakistan

Unhealthy dietary habits among the people of Pakistan represent a significant risk factor contributing to the burden of breast cancer. Research suggests that lifestyle modification can reduce the risk of breast cancer up to 40%. Among others, Pakistani diet is composed of fried items, fast foods, and trans fats [23]. The unhealthy diet patterns frequently used by the Pakistani population, which promote breast cancer and reduce immunity, include the consumption of processed meat, refined carbohydrates, white sugar, carbonated drinks, processed juices, excessive tea, tea whiteners, and caffeine (Table 1) [24]. For instance, barbecue produces heterocyclic amines and carcinogens can increase the risk of breast cancer [25].

Table 1. Unhealthy Foods Associated with Increased Risk of Breast Cancer in Pakistan

Sr. No.	Unhealthy Food	Sr. No.	Unhealthy Food
1	Fast food, fried food, oily food (halwa puri, samosas, pakoras)	8	Commercial mayonnaise
2	Processed meat	9	Margarine
3	Excessive tea, tea whiteners, caffeine	10	Products with fructose corn syrup and sorbitol
4	White and brown sugar	11	Doe
5	Carbonated drinks, processed juices	12	Supplements for cancer prevention
6	Barbecue	13	Fried fish / contaminated fish
7	Alcohol		

A study demonstrated that unmarried women are more likely to be associated with the risk of developing breast cancer as compared to married women [26]. Likewise, breastfeeding and pregnancy reduce the risk of breast cancer. Since pregnancy results in fewer menstrual cycles, the exposure to endogenous hormones is also reduced which reduces the risk of cancer [20]. Also, breastfeeding involves the maturation of breast cells. Matured and differentiated cells are less likely to develop cancer [27].

The effect of oral contraceptives on female hormones is complex. Although, studies show a positive relationship between the use of oral contraceptives and the incidence of breast cancer [28]. There are variable and complex reasons behind this finding. Possible reasons could be the enhancement of mitotic activity in breast cells due to estrogen and progesterone, while protective anovulation as estrogen is directly involved in the proliferation and differentiation of breast cells [29]. Table 2 indicates the list of factors associated with breast cancer incidence in Pakistan.

Table 2. Potential Factors Associated with Breast Cancer Incidence in Pakistan

1	Age	11	Hesitation for presentation
2	Environmental Factors	12	Socioeconomic status
3	Genetics	13	Late menopause
4	Family history	14	Late first pregnancy
5	Unhealthy food	15	Use of local low quality hair dyes
6	Physical inactivity	16	Use of low quality plastics for
		10	microwave
_ 7	Obesity	17	Vitamin D deficiency
8	Tobacco	18	Alcohol
9	Oral Contraceptives	19	Sleep routine and night shifts
10	Marital Status	20	Prolonged use of anti-hypertensive
		20	drugs

2.3. Hospitals and Research Centers

Currently, there are approximately 30 cancer hospitals (Figure 4) that effectively provide services to breast cancer patients including 11 hospitals in the Sindh province, 7 each in Khyber Pakhtunkhwa and Punjab, and 1 each in Gilgit, Baluchistan, and Baltistan. Unfortunately, there is no cancer hospital in Azad Kashmir [30]. Previous studies conducted among different

cities in Pakistan illustrated the statistical value of breast cancer among patients, resulting in a higher proportion in Lahore and a lower proportion in Gujrat, Faisalabad, Okara, and Sahiwal [31].

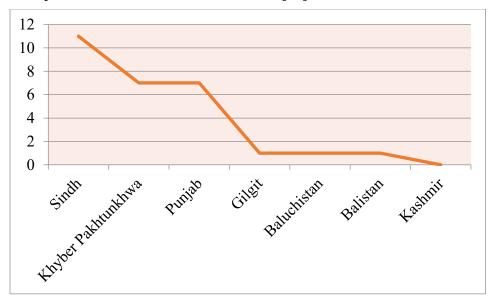


Figure 4. Number of Breast Cancer Hospitals in Pakistan [31]

There are several breast cancer research institutes functioning in Pakistan. Table 3 lists the top 20 research centers that conduct breast cancer research in Pakistan [32].

Table 3. Top 20 Breast Cancer Research Centers in Pakistan [32]

Rank	Name of Research institutes for breast cancer	City
1	Comsats University	Islamabad
2	Aga Khan University	Karachi
3	Quaid e Azam University	Islamabad
4	University of Karachi	Karachi
5	Govt. College University	Faisalabad
6	Shaukat Khanum Memorial Cancer Hospital & Research Center	Lahore
7	University of the Punjab	Lahore
8	Dow University of Health Sciences	Karachi
9	Bahauddin Zakariya University	Multan

Rank	Name of Research institutes for breast	City	
	cancer		
10	University of Lahore	Lahore	
11	University of Sargodha	Sargodha	
12	University of Agriculture	Faisalabad	
13	National University of Science &	Islamabad	
13	Technology		
14	Abdul Wali Khan University	Khyber-Pakhtunkhwa	
15	King Edward Medical University	Lahore	
16	Islamia University	Bahawalpur	
17	University of Veterinary & Animal	Lahore	
1 /	Sciences		
18	University of Health Sciences	Lahore	
19	University of Gujrat	Gujrat	
20	Armed Forces Institute of Pathology	Rawalpindi	

2.4. Breast Cancer Status in Different Cities of Punjab with BRCA1/BRCA2 Mutations

Among all the cities of Punjab, Lahore shows the highest rate of prevalence of breast cancer with 46% of women with *BRCA1/BRCA2* mutations [33], as shown in Figure 5.

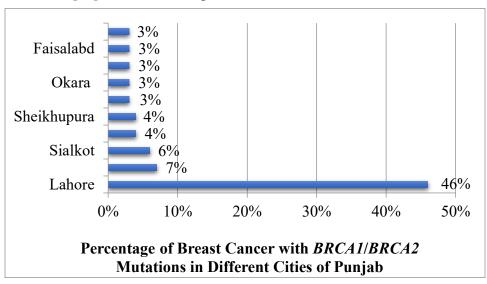


Figure 5. Status of Different Cities of Punjab with *BRCA1/BRCA2* Mutations [33]

2.5. Incidence and Mortality Rate of Breast Cancer in 2020

Based on the data provided by Globocan, Asia ranked first for the number of deaths due to breast cancer in 2020. The percentage of mortality was calculated as 50.5% in Asia, 20.7% in Europe, 12.5% in Africa, 8.5% in Latin America, 7.1% in North America, and 0.74% in Oceania, as shown in Figure 6.

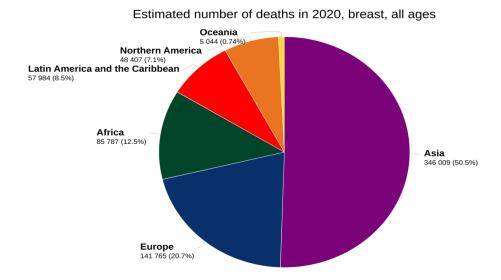
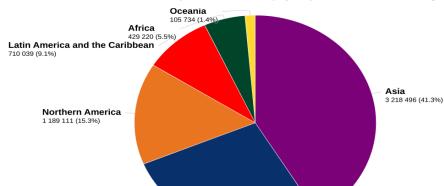


Figure 6. Estimated Deaths in 2020 in Different Continents Due to Breast Cancer [34]

Total: 684 996

According to the 2020 statistics of the World Health Organization (WHO), the estimated number of breast cancer prevalent cases for a 5-year period in Asia was 3,218,496 (41.3%), for Europe the number was 2,138,117 (27.4%), for North America the number was 1,189,111 (15.3%), for Latin America and the Caribbean the number was 710,039 (9.1%), for Africa the number was 429,220 (5.5%), and for Oceania the number was 105,734 (1.4%), as shown in Figure 7.



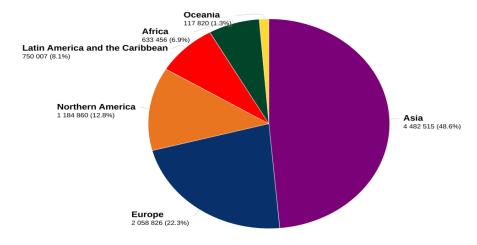
Estimated number of prevalent cases (5-year) in 2020, breast, all ages

Total: 7 790 717

Figure 7. Estimated Number of Prevalent Breast Cancer Cases in 5-year Period (2015-2020) in Various Continents

Europe 2 138 117 (27.4%)

Similarly, the estimated number of new breast cancer cases in Asia was reported to be 4,482,515, which is higher than other continents, as shown in Figure 8.



Total: 9 227 484

Figure 8. Estimated Number of New Breast Cancer Cases in 2020

Cancer reports of 2020 indicated the incidence of breast cancer to be the highest among all cancers in Pakistan, as shown in Figure 9.

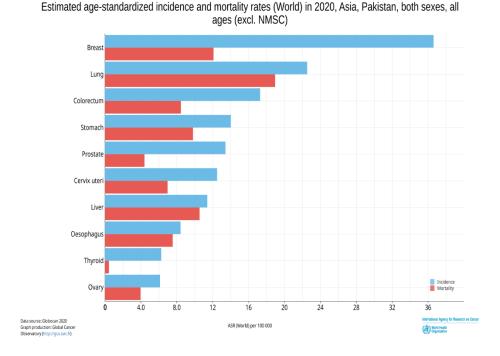


Figure 9. Prevalence of Different Cancers in Pakistan in 2020 with the Highest Incidence of Breast Cancer among All Cancers

2.6. Treatment of Breast Cancer in Pakistan

In low-income countries like Pakistan, it is often impossible for patients to afford breast cancer treatment. According to 2019 statistics, Pakistan is ranked 154th among 195 countries for expanding healthcare and it spends only a fixed 3.4% of GDP for health. On the open Budget Index on health, Pakistan scored poorly at 28/100. The minimum cost of breast cancer treatment is 3-4 hundred thousand PKR and it can go up to a million or more, depending on the stage of cancer. Although many research institutes and hospitals, such as Shaukat Khanum Cancer Hospital, Pink Ribbon Hospital, PAEC, Cancer Care Hospital, Bait-ul-Sakoon, and INMOL offer discounted treatments to low-income patients but the cost is so high that even the middle class cannot afford it. Figure 10 shows the comparison of total GDP spent on health among a few countries in 2019, while the current

treatment methodologies available in Pakistan and a list of novel strategies used worldwide are listed in Table 4.

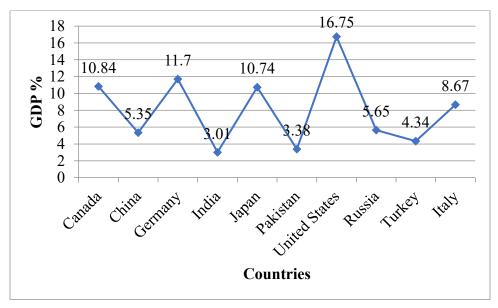


Figure 10. Country-wise Percentage of GDP Spent on Healthcare in 2019

Table 4. List of Breast Cancer Treatment Methods Used in Pakistan and Worldwide

Novel Treatments of Breast	Treatment of Breast Cancer in	
Cancer in the World	Pakistan	
	Surgery	
	 Lumpectomy 	
	 Mastectomy 	
Repurposing drugs	 Lymph node removal 	
	 Breast reconstruction 	
	 Prophylactic mastectomy 	
	 Prophylactic ovary removal 	
Metronomic therapy	Radiotherapy	
Antibody-Drug Conjugation	Chemotherapy	
Systems (ADCs)		
Nanoparticles and micelles	Targeted Therapy	
Targeting Breast Cancer Stem	Anti-Hormone Therapy	
Cells (BCSCs)		

2.7. Future of Breast Cancer in Pakistan (2020-2040)

The escalating burden of breast cancer and its rising trend over the past few decades remains an alarming concern for the future of healthcare in Pakistan. WHO estimated that the number of new cases in 2020 in Pakistan was 25928. This number is predicted to get doubled to 49008 in 2040, if the current situational factors such as lack of awareness, delayed diagnosis, and lack of latest treatment methods continue to prevail (Figure 11).

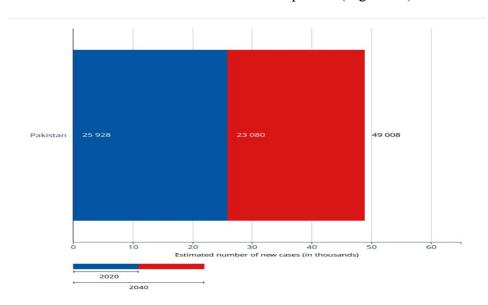


Figure 11. Estimated Number of New Cases of Breast Cancer from 2020 to 2040 in Pakistan ¹

Similarly, the estimated number of deaths in Pakistan due to breast cancer in 2020 was 13725, which is likely to become 26491 by 2040, considering the same situational factors prevail as of today (Figure 12 and Figure 13).

^{1 (}Globocan, 2020)

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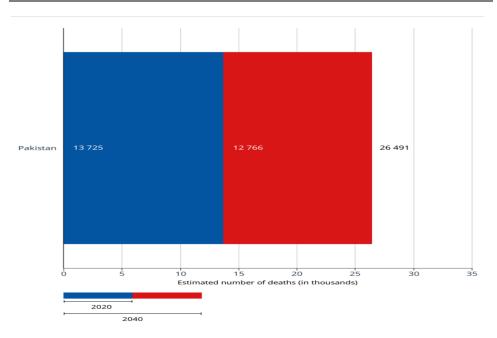


Figure 12. Estimated Number of Deaths from 2020 to 2040 Due to Breast Cancer in Pakistan ²

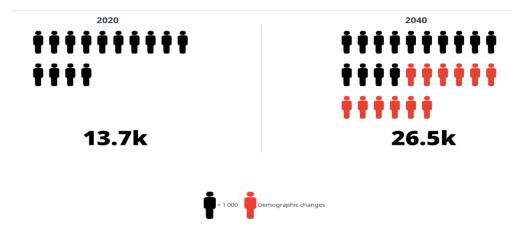


Figure 13. Estimated Number of Deaths from 2020 to 2040 Due to Breast Cancer in Pakistan³

Department of Knowledge and Research Support Services

²(Globocan, 2020)

³ (Globocan, 2020)

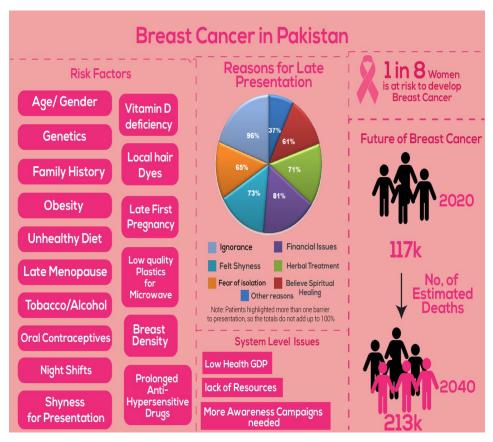


Figure 14. Graphic Representation of the Prevailing Breast Cancer Situation in Pakistan

3. CONCLUSION

According to Globocon observatory statistics, Pakistan ranks among the top countries with a substantial burden of breast cancer cases. The statistics underscore an alarming situation due to the upward trend of breast cancer cases in the country. Several risk factors contribute to this concerning situation including lack of awareness, hesitation of female patients toward male doctors, the prevailing social stigma surrouding the secreacy of breasts irrespective of life-threatning consequences, socioeconomic disparities, a small health budget, unhealthy diet patterns, reliance on homemade remedies for the cure, and spiritual superstitions. Multifactorial barriers in diagnosis including cultural pressure and low income have led to a late-stage presentation to doctors which is a leading cause of mortality. There is

a dire need to increase awareness among the local population of Pakistan regarding the early symptoms of breast cancer in order to avoid the disease burden. The lack of patient follow-up is the reason why accurate data cannot be calculated, as most of the women do not present for diagnosis and bear the pain to death. Currently, 30 cancer hospitals and 20 cancer research institutes provide services to patinets. Many awareness campaigns have been launched also. Still, a lot needs to be done to overcome this health hazard (Figure 14). Global statistics predict the doubling of the burden of this disease by year 2040 if the current conditions persist unchecked.

CONFLICT OF INTEREST

The authors of the manuscript have no financial or non-financial conflict of interest in the subject matter or materials discussed in this manuscript.

DATA AVALIABILITY STATEMENT

The data associated with this study will be provided by the corresponding author upon request.

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