



**A DEEP INSIGHT INTO INCIDENCE, PREVALENCE, COMPLETE  
EPIDEMIOLOGY, AND PREDICTIVE ASSOCIATIONS AMONG  
MULTIPLE FACTORS OF BREAST CANCER IN KARACHI, PAKISTAN:  
A CROSS-SECTIONAL SURVEY OF 2023**

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**ABSTRACT**

Breast cancer is recognized as a global issue affecting millions of women with a greater impact on their lives. Worldwide, breast cancer is among the most prevalent forms of the disease. Throughout their lives, 12% of American women will experience a breast cancer diagnosis, and in 2017, more than 250,000 new cases were reported to the medical community. This study was conducted in a cross-sectional approach retrospectively in a tertiary care hospital in Karachi, Pakistan, in which data of all types of cancer patients were gathered from 1<sup>st</sup> January 2023 – 31<sup>st</sup> December 2023 in a pre-designed/translated data collection form. Initial analysis was piloted in the form of descriptive statistics such as percentages and frequencies. Chi-square tests and Monte Carlo tests were used to analyze breast cancer occurrence and risk factor associations, considering p-value <0.05 as statistically significant. Following the analysis, an incidence of 11.51 and a prevalence of 13.36 were calculated for 2023. confirms the occurrence of breast cancer among middle-aged women (Mean age 48.67±12.14 years) at an advanced stage in Karachi, Pakistan. A highly statistically significant correlation was detected between hormonal status

and stage ( $p < 0.01$ ), type of breast cancer and stage ( $p < 0.01$ ), gender and habits ( $p < 0.01$ ), and ethnicity and habits ( $p < 0.01$ ), respectively. On the other hand, marital status was not correlated to the stage of breast cancer ( $p = 0.913$ ). No significant association was found between ethnicity and segregated hormone receptor status. These findings suggest the need for interventions such as awareness programs, lifestyle adoption, and breastfeeding /hormonal usage training programs to prevent diagnosis postponements, awareness, and prevention, thus reducing disease load. Also, the unavailability of data highlights the need for a centralized national cancer control body promoting the entry of updated data of these patients across the private and public sectors.

## INTRODUCTION

Breast cancer is recognized as a global issue affecting millions of women with a greater impact on their lives<sup>(1)</sup>. This form of cancer initiates in the breast tissue, more specifically affecting milk ducts and lobules present in the breast. It also affects males but is less prevalent than in females<sup>(2, 3)</sup>. Worldwide, breast cancer is among the most prevalent forms of the disease. Throughout their lives, 12% of American women will experience a breast cancer diagnosis, and in 2017, more than 250,000 new cases were reported to the medical community<sup>(4)</sup>. Following lung cancer, it is another main reason causing cancer-related deaths in women overall, but it is more prevalent among Black and Hispanic women<sup>(5, 6)</sup>. It results in a substantial impact on one's well-being and a potential loss of 14.8 million Disability Adjusted Life Years. Countries with a very high Human Development Index reported a breast cancer occurrence rate of 54.5 per 100,000 female population globally when compared with countries with low to moderate Human Development Index, confirming that the incidence of breast cancer is much greater in developed countries. It continued to have the greatest death rate among females and was the most common cause of cancer-related fatalities in women<sup>(7-10)</sup>.

Its incidence keeps rising regardless of decades of epidemiological, laboratory, and clinical investigations<sup>(11)</sup>. The consequences extend beyond one's physical well-being to include social interactions, emotional stability, and general quality of life. Facing a breast cancer diagnosis can be extremely upsetting for the sufferer and their family since it instills anxiety and uncertainty about the future<sup>(12)</sup>. There is a notable variation in incidence rates between low-income and high-income countries. In high-income countries, breast cancer incidence rates have been rising, attributed to factors such as aging populations and increased breast cancer screening and education. In contrast, rates in low-income countries have been rising more slowly, partly due to limited access to screening and diagnostic facilities. To support breast cancer detection at an early stage, the World Health Organization outlined 2 distinctive but correlated approaches: early detection, which refers to cancer with early symptoms, and screening, which refers to disease-free symptoms on objective in a healthy population<sup>(13)</sup>.

Conveying population-derived investigation is particularly difficult in a health system that is understaffed, highly fragmented, underequipped, and lacking the networks to promote the quality services required for testing, screening, and treatment, with

consequently most LMICs. Institutions lacking such of cancer screening program using imaging techniques to identify tumor features and identify tumors as clinical cases many valuable to physicians. These imaging modalities are mainly ultrasonography, mammography, computed tomography, positron emission computed tomography, magnetic resonance imaging, and single-photon emission computed tomography <sup>(14)</sup>. An ideal treatment strategy for breast cancer needs a coordinated, multidisciplinary team including surgical, medical, and radiation oncologists. Early-stage disease generally begins with surgery, while locally advanced breast cancers (LABCs) benefit from systemic therapy first to downstage the tumor, followed by surgery, radiotherapy, and postoperative systemic therapy. The involvement of primary care physicians is crucial from the outset, familiarizing them with the diagnostic and treatment basics (15).

## **METHODOLOGY**

### **Study scheme and participants**

A cross-sectional study in a retrospective manner was conducted in Jinnah Post Medical Centre, Karachi, Pakistan, in which data of all types of cancer patients were gathered from 1<sup>st</sup> January 2023 – 31<sup>st</sup> December 2023. This hospital was selected because of its major influx of cancer patients in Karachi, Pakistan.

### **Sample Size Calculation**

To estimate with 95% confidence and account for 10% potential loss/attrition, a sample size of 830 is needed for the estimated prevalence of 24.1% <sup>(16-18)</sup>. This will ensure an absolute precision of  $\pm 3\%$  margin of error. The expected 95% CI with this sample size is (21.1%, 27.1%). The Scalex SP calculator was used to determine this sample size <sup>(19)</sup>.

### **Inclusion Criteria**

- List of all cancer patients to identify the prevalence of breast cancer from 1<sup>st</sup> January 2023 – 31<sup>st</sup> December 2023.

Detailed data of all positive breast cancer patients receiving all types of treatment for breast cancer.

Patients in the age bracket 18 and above

All types of breast cancers.

All stages of breast cancer are from 0 to IV.

### **Exclusion Criteria**

Severe cognitive and verbal impairments.

Patients who refused to participate.

Patients who have multiple chronic diseases.

Patients who are not conscious to respond.

Patients who are mentally unstable/have psychiatric disorders.

### **Ethical Considerations and Participant's Consent**

Approval of the research protocol was granted by the local institution board of Jinnah University for Women in Karachi under the IERB number JUW/IERB/PHARM-ARA-007/2023. Before any patient data was collected, the study's goal was well communicated to them. Additionally, verbal consent was requested from each survey participant. All information was kept confidential in compliance with moral principles.

### **Data Collection and Questionnaires**

On a pre-designed and translated data-collecting form, data were pooled from a routine review of patients' profiles and their medication charts in each of the participating units. Complete questionnaires were coded by the registration number assigned by the hospital for record keeping. Patients and oncologists were contacted for any missing information. To ensure data authenticity and rectify bias, data collection was conducted by the main researcher herself. Data collected includes patients' registration number, name, age, menopausal status, gender, mother tongue, duration of symptom, type of case, marital status, occupation, co-morbidities, symptoms reported, side affected, habits, type of breast cancer, stage of breast cancer, hormone receptor status, and risk factors such as family history, breastfeeding history, use of

hormone replacement therapy and contraceptive history respectively. Data regarding hormone receptor status was included, specifying missing data, as it is considered an essential pillar in breast cancer evaluation.

#### Data coding and statistical investigations

Data was entered and coded using Microsoft Excel 2016. The SPSS version 21 (Student Package for Social Sciences version 21) was used for further analysis. Initial analysis was piloted in the form of descriptive statistics

such as percentages and frequencies. Chi-square tests and Monte Carlo tests were used to analyze breast cancer occurrence and risk factors, considering p-value <0.05 as statistically significant.

#### RESULTS

Based on our data collection from a single center, 6339 cancer cases were reported in 2023. Out of these, a total of 847 breast cancer cases were reported, of which 707 were new cases and 140 were old and reoccurrence cases.

**Table 1: Complete demographic picture of patients**

Characteristics	Number (N)	Percentages (%)
<b>Age Groups (Years)</b>		
18-30	48	5.7
31-40	215	25.4
41-50	230	27.2
51-60	212	25.0
61 and above	142	16.8
<b>Gender</b>		
Female	840	99.2
Male	7	.8
<b>Ethnicity</b>		
Urdu	468	55.3
Sindhi	143	16.9
Punjabi	69	8.1
Balochi	46	5.4
Pashto	50	5.9
Others	71	8.4
<b>Occupation</b>		
Employed	69	8.1
Unemployed	778	91.9
<b>Marital status</b>		
Married	777	91.7
Unmarried	46	5.4
Widow	23	2.7
Divorced	1	.1
<b>Menopausal status</b>		
Pre-menopausal	440	51.9
Post-menopausal	400	47.2
Not Applicable	7	.8

Co-morbidities		
No	468	55.3
Not available	71	8.4
Diabetes	49	5.8
Hypertension	136	16.1
Heart disease	10	1.2
Diabetes plus hypertension	59	7.0
Multiple comorbidities	26	3.1
Other comorbidities	28	3.3

**Table 1** elucidates a complete demographic depiction of the selected population, concluding that the mean age of breast cancer patients was  $48.67 \pm 12.14$  years, predominantly consisting of the female population, which is 99.2% with more than half being Urdu speaking (55.3%). The majority, i.e., 27.2% comes under the age slab

of 41-50 years, with 51.9% confirmed as premenopausal women. Over 90% were married and unemployed. More than half, i.e., 55.3% patients, did not report any kind of co-morbidity, with hypertension reported in 16.1% patients and hypertension along with diabetes in 7% patients, respectively.

**Table 2: Predictive risk factors for breast cancer development**

Risk Factors	Number of participants (N)	Percentages (%)
<b>Family History of Cancer</b>		
No	565	66.7
Yes	248	29.3
Not available	34	4.0
<b>Habits</b>		
No	678	80.0
Alcohol	1	.1
Smoking	9	1.1
tobacco	53	6.3
Others (betel leaf, betel nut, etc.)	106	12.5
<b>History of breastfeeding</b>		
No	393	46.4
Yes	242	28.6
Not available	205	24.2
Not applicable	7	.8
<b>History of contraceptive use</b>		
No	421	49.7
yes	214	25.3
Not available	205	24.2
Not applicable	7	.8
<b>Use of Hormone replacement therapy</b>		

No	420	49.6
Yes	215	25.4
Not available	205	24.2
Not applicable	7	.8

For risk factors evaluation, it was concluded that no family history was reported in more than half of patients, i.e., 66.7%, with a positive history in almost 29.3% patients. The majority 80% had no such addictions contributing to breast cancer development, with 12.5% using betel leaf /betel nut, 6.3% using tobacco, and 1.1% reporting smoking history. No breastfeeding history was reported by nearly half, 46.4% of patients, and no contraceptive use and hormonal therapy use was reported by 49.7% and 49.6% of patients.

Data for the use of Hormone replacement therapy, contraceptive use, and breastfeeding were not available in 24.2% patients, and did not apply to 0.8% patients representing male patients, respectively. **(Table 2)**

**Figure 1** shows the trend reflecting the positive contribution of breastfeeding at all ages, for developing breast cancer by showing the incidence of the majority of breast cancer cases in women who did not breast-feed (400 cases) than those who did (239 cases), regardless of their age.

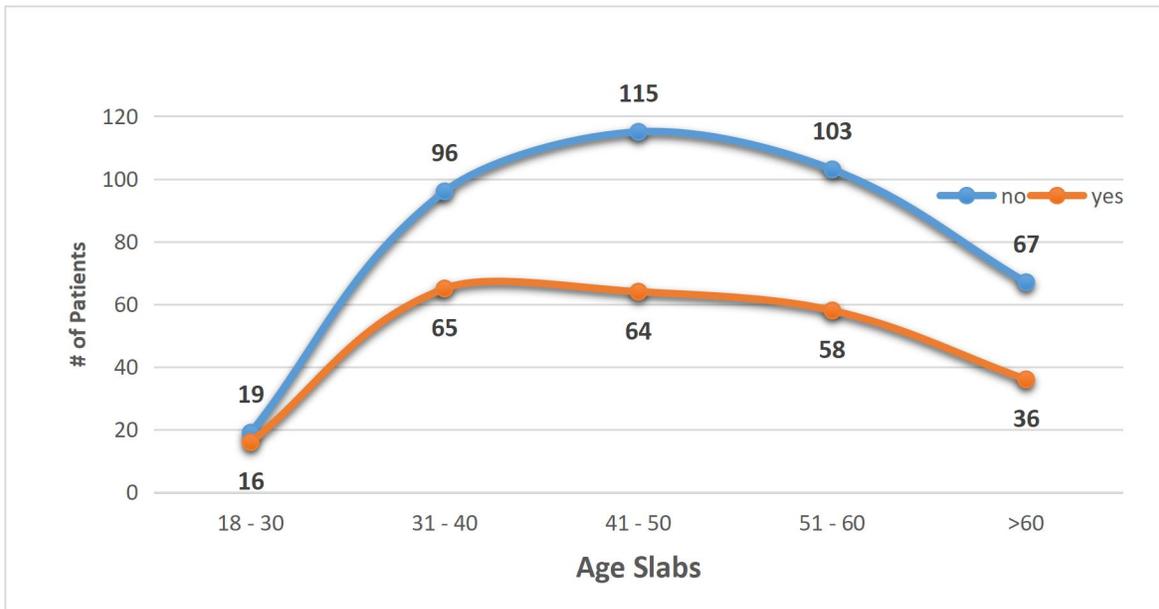
**Table 3: Disease overview of study participants**

	Number of participants (N)	Percentages (%)
<b>Type of Breast Cancer</b>		
Invasive ductal carcinoma	792	93.5
Invasive lobular carcinoma	24	2.8
Ductal carcinoma in situ	20	2.4
Others	11	1.2
<b>Stage of breast cancer</b>		
<b>0</b>	20	2.4
I	10	1.2
II	70	8.3
III	576	68.0
IV	171	20.2
<b>Symptoms</b>		
Not Available	37	4.4
Other symptoms	18	2.1
Multiple symptoms	166	19.6
Lump breast	357	42.1
Lump breast/axilla	12	1.4
Breast pain	44	5.2
Breast tenderness	69	8.1
Itching/ulceration	21	2.5
Pain in the axilla	6	.7
Lump and pain in the breast	106	12.5
Lump and pain in the axilla	6	.7
Lump in the axilla	5	.6

<b>Onset of Symptoms</b>		
<3	105	12.4
3-12	348	41.1
>12	186	22.0
NA	190	22.4
Reoccurrence	18	2.1
<b>Type of case</b>		
New	707	83.5
Old	122	14.4
Reoccurrence	18	2.1
<b>Side affected</b>		
Left	474	56.0
Right	361	42.6
Bilateral	12	1.4
<b>Hormone status</b>		
<b>ER status</b>		
Positive	444	52.4
Negative	194	22.9
Not available	209	24.7
<b>PR status</b>		
Positive	418	49.4
Negative	220	26.0
Not available	209	24.7
<b>HER 2 neu status</b>		
Positive	194	22.9
Negative	444	52.4
Not available	209	24.7

**Table 3** reflects breast cancer features and found that >90% patients were diagnosed with invasive ductal carcinoma, followed by invasive lobular carcinoma in 2.8% and ductal carcinoma in situ in 2.4% patients, respectively. More than half, i.e., 68% were diagnosed at stage III and 20.2% at stage IV, respectively. Breast lump was reported as the most common presenting symptom in 42.1% patients, and it was found that 22 % patients

reported their symptoms after a year. 83.5% cases were new, followed by 14.4% old and 2.1% recurrent cases. In >50% individuals, the left side was affected than the right side, which was 42.6% and 1.4% bilateral cases. Hormone receptor status reported 52.4% ER-positive, 49.4% PR-positive, and 52.4% HER2–negative. Data for 24.7% cases was not available.



**Figure 1: Breastfeeding history by Age slabs**

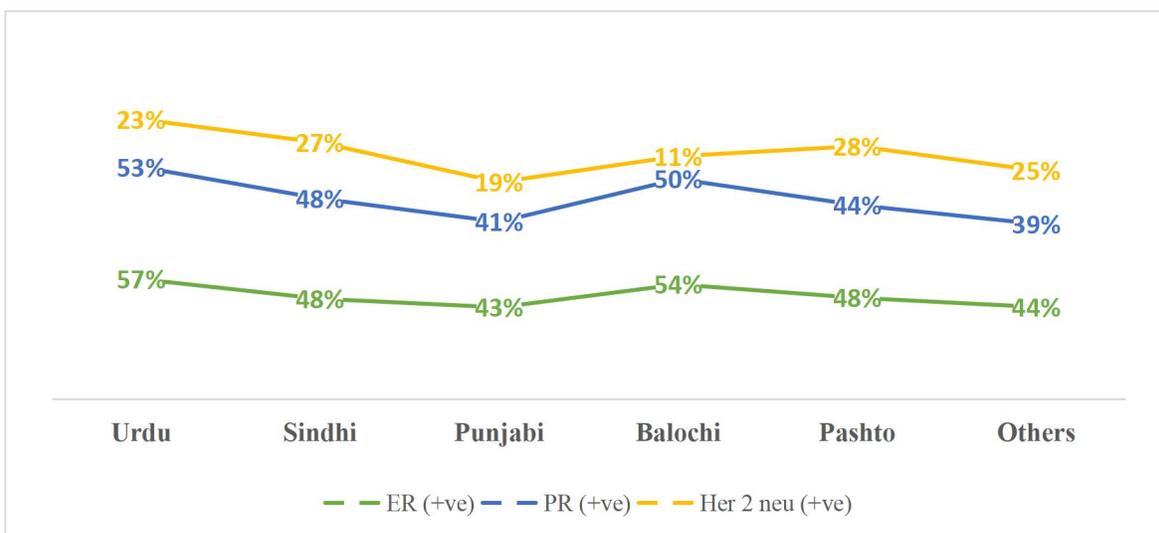
**Table 4: Associations among different Breast cancer factors**

S.No	Variable 1	Variable 2	p-value
1.	Breast cancer type	Breast cancer stage	<0.01*
2.	Marital status	Breast cancer stage	0.913
3.	Hormonal status	Breast cancer stage	<0.01*
4.	Ethnicities	Habits	<0.01*
5.	Gender	habits	<0.01*
6.	Ethnicities	Hormonal status (ER)	0.69
7.	Ethnicities	Hormonal status (PR)	0.16
8.	Ethnicities	Hormonal status (HER-2 neu)	0.59

P-value <0.05=statistically significant\*

**Table 4** shows that a highly statistically significant correlation was detected between hormonal status and stage ( $p < 0.01$ ), as well as between type of breast cancer and stage ( $p < 0.01$ ), indicating a positive contribution of hormonal receptor expression and tumor biology to disease advancement. Gender and habits ( $p < 0.01$ ) and ethnicity and habits ( $p < 0.01$ ) were significantly associated, indicating that sociocultural/behavioral factors may influence risk profiles. On the other hand, marital status was not correlated to the stage

of breast cancer ( $p = 0.913$ ). There was no significant association between ethnicity and segregated hormone receptor status. The ER positivity was highest in Urdu-speaking (56.8%), followed by Balochi (54.3%) and Pashto (48%) patients. The PR positivity was also elevated in the Urdu-speaking (53.2%) and Balochi (50%) people as well. HER2-positivity was more prevalent in Pashto patients (28%); however, the difference was not statistically significant among the ethnic groups. (**Figure 2**)



**Figure 2: Associations between Ethnicities and Hormonal Status**

## DISCUSSION

As it is a major mortality and morbidity contributor, its prevalence is higher in developed countries. However, lack of effective treatment strategies, screening methods, economic conditions, nutritional deficiencies, and lifestyle factors such as pan, gutka, fast food, and adulterated food all these factors have all contributed to increasing its prevalence in Pakistan, with 19 million new cases reported in 2020<sup>(20, 21)</sup>. In Pakistan, a report on breast cancer patterns and incidence from 1991-2021 lists breast cancer, prostate cancer, bone cancer, leukemias, and colorectal cancer as more frequently diagnosed cancers<sup>(18)</sup>. Compared to men, it is the most common cancer in females. <1 % of all diagnosed cases of breast cancer are reported in males, but it is anticipated to rise by 25% than in women and 40% (1975-2015), as confirmed by SEER data. An 18% mortality rate was predicted by the American Cancer Society in 2019, with an estimation of 2670 new breast cancer cases in males in the US<sup>(22)</sup>. Breast cancer is believed to make up 1/3<sup>rd</sup> of all cancers among the Karachi female population<sup>(23)</sup>, with a high incidence reported in Sindh, with around 1/3<sup>rd</sup> occurrence among

Sindhi females<sup>(24)</sup>. Based on our data collection from a single center, 6339 cancer cases were reported in 2023. Out of these, a total of 847 breast cancer cases were reported, of which 707 were new cases and 140 were old and reoccurrence cases. Considering these values, an incidence of 11.51 and a prevalence of 13.36 were calculated for 2023.

In developing countries, its prevalence has increased due to the increased use of tobacco, niswar, betel nut, etc.<sup>(25)</sup>. Metabolic risks are also believed to be the most attributable risk factors in augmenting its prevalence, following low physical activity, alcohol, smoking, and dietary lifestyles<sup>(26)</sup>. Pre-menopausal women make up more than half (2/3<sup>rd</sup>) of breast cancer cases. This may be due to several factors, with the more prominent one being the short-chain fatty acids-producing microbiome, making these women more susceptible to tumors and breast cancers. But this area is still not well-investigated<sup>(27)</sup>. Comorbidities such as Diabetes Mellitus can lead to more destructive forms of breast malignancy, leading to high mortality rates as they have inadequate options in treatments and late diagnosis<sup>(28)</sup>. Similarly, another very common comorbid condition causing breast

cancer is hypertension, which is also believed to augment the long-lasting risk of breast cancer. Additionally, one adverse effect of some anti-cancer treatments is also hypertension<sup>(29, 30)</sup>. Breast cancer incidence is believed to increase among all age groups, but its increased occurrence is observed in women below 50. Despite assuming a decline in fertility rates, it continues to increase in most districts<sup>(31)</sup>. In the US, one in every 196 women below 40 years is diagnosed with breast cancer. When compared to older women, women below 40 years of age are more diagnosed with breast cancer and also report poor survival rates<sup>(32)</sup>. A better prognosis has been reported in married individuals as compared to singles. Also, poor survival outcomes and advanced stage diagnosis were reported among single women than married ones<sup>(33)</sup>. This may be due to a lack of social and moral support. Therefore, from a public health angle, it is advised to give more attention to unmarried breast cancer patients to improve their health outcomes<sup>(34)</sup>. The presence of breast cancer in the family could be another reason that a patient shows up with breast cancer. Still, it is difficult to distinguish whether it's solely a family history, genetics, a specific lifestyle, or a blend of these factors that resulted in breast cancer<sup>(35)</sup>.

Previous investigations proved that breast cancer results from an increased alcohol uptake. Consumption of alcohol can also result in GI malignancies. The major reason for this is an alcohol can induce estrogen levels, leading to hormonal disruptions that may result in breast cancer. Smoking, on the other hand, whether active or passive, is another cause of breast cancer, which may be due to the presence of tobacco contents as they are actively transported into breast tissues, thus increasing the likelihood of causing disruptions in suppressor (p53) and oncogenes<sup>(36)</sup>.

Another important risk factor that can put a woman at breast cancer is the use of contraceptives, even in low doses, for long periods. Increased breastfeeding and pregnancy at an early age can prevent ER-negative and positive breast cancers<sup>(37)</sup>. Hormone replacement therapy can increase the possibility of breast cancer by 8% and only estrogens can increase the risk by 1% respectively (Women's Health Initiative)<sup>(35)</sup>. The majority of breast cancer cases, comprising almost 85% of cases, are Invasive ductal carcinoma and invasive lobular carcinoma, with the remaining 15% of other breast cancer types, including metastatic cancers<sup>(38)</sup>. The most common complaint the breast cancer patient shows up with is a breast lump<sup>(39, 40)</sup>. Among molecular types, luminal type-A cancer with ER-positive expressions comprises 60 % to 70% of all cases. These cancers are characterized by improved prognostic features, slow growth, low grade, narrow chemotherapy assistance, better response to hormonal therapy, improved survival rates, and fewer chances of relapses<sup>(41, 42)</sup>.

## CONCLUSION

This investigation confirms the occurrence of breast cancer among middle-aged women at an advanced stage in Karachi, Pakistan. These findings suggest the need for interventions such as awareness programs, lifestyle adoption, and breastfeeding /hormonal usage training programs to prevent diagnosis postponements, awareness, and prevention, thus reducing disease load. Also, the unavailability of data highlights the need for a centralized national cancer control body promoting the entry of updated data of these patients across the private and public sectors. This body should be responsible for providing cost-effective management options, quality of care, cancer prevention campaigns, and free-of-cost screening /diagnostic facilities, apart from managing data. Additionally, building research associations with developed

countries will result in deeper insights regarding updated and targeted therapies and techniques helpful in lowering the burden of this life-threatening illness.

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#### **Conflict of interest**

None

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