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EPIDEMIOLOGICAL CHARACTERISTICS AND RISK FACTORS OF BREAST CANCER IN WOMEN DIAGNOSED AT PUBLIC HOSPITALS IN QUETTA, BALOCHISTAN, PAKISTAN

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Abstract
Breast cancer remains a major global health challenge and a leading cause of cancer-related death among women. The purpose of this research was to examine the epidemiological characteristics and associated risk factors of breast cancer in women patients from Quetta region, Balochistan. The study was conducted in the Center for Nuclear Medicine and Radiotherapy (CENAR) Hospital, and Bolan Medical Complex Hospital, Quetta. In this study, 386 female patients of different age groups were enrolled from January 2021 to December 2022. Data was collected on a structured questionnaire, along with laboratory reports and histopathology findings. Breast cancer was observed to affect the younger age groups than the older age groups and mostly the married patients (61%). Affected breast cancer patients's ethnicities were (21.76%) Pashtoon, (12.43%) Baloch, (6.99 %) Hazara, (26.16 %) Punjabi and (2.59 %) Sindhi. Only 49 had a family history of the disease and breastfeeding their children were observed in (62.95%) patients. Breast cancer on the left breast was the most common. Most affected patients (37%) belong to poor class and only 27 % patients had some knowledge and awareness about breast cancer. The NOS type of breast cancer was the most prevalent than other types. Most patient were in grade 0 followed by grade 1. Similarly, most patients were in stage 0 and 1. Common breast cancer symptoms were include; lump on breast, variation in breast size, swilling, redness and rashes on breast. It was concluded that breast cancer affecting the people of all ethnicities and age groups. Public hospitals are the primary cancer health care units in Balochistan. There is very lack of knowledge and awareness of about the breast cancer disease and its early signs and symptoms.

Key Words: Breast cancer, Balochistan, epidemiology, ethnicity, risk factors, women patients

INTRODUCTION
Breast cancer is a disease characterized by malignant or cancerous cells growing in breast tissue, and it is among the most diagnosed cancers worldwide. Breast cancer remains a major global health challenge and a leading cause of cancer-related death among women (Bray et al., 2018). Breast cancer is one of the most common forms of cancer worldwide. According to the World Health Organization (WHO), breast cancer has overtaken lung cancer as the most prevalent cancer, accounting for nearly 12% of all new cancer cases globally as of 2020. In 2020 alone, over 2.3

million women were diagnosed with breast cancer, and 685,000 lives were lost (Organization, 2020).

The primary risk factors associated with breast cancer include female gender, aging, certain genetic mutations (like BRCA1 and BRCA2), family history of breast cancer, and certain reproductive factors, such as early menstruation or late menopause (Daly & Olopade, 2015). Additionally, genetics plays a significant role in breast cancer prevalence. Around 5-10% of breast cancers are thought to be hereditary, caused by abnormal genes passed from parent to child. The most common cause of hereditary breast cancer is an inherited mutation in the BRCA1 or BRCA2 genes (Kuchenbaecker et al., 2017; Siegel, Miller, Fuchs, & Jemal, 2021). Environmental factors also contribute to breast cancer prevalence. Exposure to ionizing radiation is a well-established risk factor, and higher doses correlate with higher risk (Preston et al., 2002; Siegel et al., 2021).

A significant proportion of breast cancer cases are detectable by mammography before symptoms develop, which is crucial for early intervention and improved prognosis (Nelson et al., 2016). Treatment strategies typically involve a combination of surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapies, often contingent on the specific characteristics of the cancer (Siegel, Miller, & Jemal, 2019).

Incidence rates are increasing in nearly every region globally, indicating that breast cancer is a significant and growing health problem (Sung et al., 2021). Moreover, breast cancer impacts not only women but men too, though at far lower rates. The American Cancer Society reported in 2020 that about 1 in 833 men in the United States are at risk of developing breast cancer in their lifetime (Street, 2019).

Incidents of breast cancer in Pakistan are the highest, out of nine one woman is always at risk during her lifespan (Sohail & Alam, 2007). Even worse in Pakistan, there is no awareness and late diagnosis and lack of proper services, the mortality rate goes high (Begum, 2018). It is most significant for recovery that cases of breast cancer be detected as early as possible, whereas if delayed in diagnosis the survival rate is always lesser (Viale, 2020).

Shaukat Khanum Memorial Cancer Hospital & Research Center Pakistan has statistically analyzed the data of breast cancer during 2018 (January to December) collected from all provinces, including Balochistan, out of 1270 patients 1259 were females which were survived breast cancer (Yousaf A, et al. 2019). The prevalence of breast cancer varies based on age, with the risk of developing the disease increasing as a woman grows older. According to the American Cancer Society, the median age at diagnosis for women in the U.S. is 62 years (Viale, 2020). This study aims to examine the prevalence of breast cancer patients age-wise, grade-wise, ethnic-wise distribution, Socioeconomic, stage, and grade-wise in both male and female patients.

Material and Methods

Study design and risk factors

A cross sectional study was conducted at the two public sector hospitals; Center for Nuclear Medicine and Radiotherapy (CENAR) and Bolan Medical Complex Hospital, Quetta from January 2021 to December 2022. Overall 386 female enrolled in the study that were histo-pathologically positive for breast cancer. Non-modifiable and modifiable risk factors were studied (Ho et al., 2020). The non-modifiable risk factors that were evaluated include age at diagnosis, ethnicity, history of breast cancer in family and reproductive factors (breast feeding). The modifiable risk factors comprise socio-demographic aspects like marital status, awareness about breast cancer and economic status.

Histopathology

Breast cancer was confirmed by histopathological examination of biopsies. Cancer type (invasive or non-invasive), it's grade and stage were determined by histology (Asafudullah, Badruddoza, & Nur, 2022).

Data collection

The data was collected through in-person interview based on structured questionnaire from the breast cancer patients (Saeed et al., 2019). The data primarily covered risk factors of breast cancer: (i) non-modifiable risk factors which include; age at diagnosis, ethnicity, history of breast cancer in family, site of lesion and reproductive factors (breast feeding) and (ii) modifiable risk factors such as marital status, awareness about breast cancer and economic status. For the purpose of a detailed analysis of cancer prevalence among various ethnic groups that exist in Pakistan, especially in Quetta, Balochistan divisions like Pushtun, Baloch, Hazara, Sindhi, Punjabi and others were made. These groups were based on the home province and native language of the patient. Another group titled 'others' was designated for minor ethnicities that didn't fit into any of these sub-groups which included Afghan, Muhajir (Urdu speaking) and Hindko etc. Socio-economic status was determined by relating the information on income and occupation of self / husband or parents. Those who had some regular official source of income with an income of rupee twenty thousands or below were coded as 'lower class', those who had income between twenty to sixty thousands were considered 'middle class' and otherwise coded as 'upper class'. Regarding age patients were distributed into five groups as; < 27, 28–37, 38–47, 48-57 and above 58.Information collected is then entered into questionnaires. An identification key, including each patient's name, residence, age, date of visit to the hospital was used for linkage. Cases were interviewed once.

A written informed consent form was filled in by all persons who contributed to the current study. The study was approved by the local ethical committee University of Balochistan, Quetta, Pakistan.

Data Analysis

Data was managed and analyzed using SPSS. Descriptive analysis for non-modifiable and modifiable risk factors and for grade and stage of different types of breast cancer was performed. Results were reported as numbers with percentages for all quantitative variables. Chi square along with unconditional logistic regression analyses used to generate odds ratios (OR) and 95% confidence intervals (CI) for the association between risk factors and breast cancer. . OR univariate and multivariate logistic regression analyses conducted to identify the risk factors. A p-value of 0.05 was considered as significant.

Results

Table 01 shows a summary of descriptive analysis of 386 breast cancer patients. It was examined that all the age groups were affected by breast cancer. Results exhibited that the second age group (23.66%) and the third (23.21%) were more affected as compared to other age groups. The old age group above 58 years (6.87%) was also suffered by breast cancer. Out of 386 female breast cancer patients, 84 (21.76%) were Pashtoon, 48 (12.43%) were Baloch, 27 (6.99 %) were Hazara, 101 (26.16 %) were Punjabi only 10 (2.59 %) were from Sindhi community. Only 49 female patients had a family history of breast cancer. Breast cancer located on the left side is the most prevalent cancer as compared to the right side. Breastfeeding their children were observed in 243 (62.95%) patients.

Table 2 demonstrates the descriptive analysis of non-modifaible breast cancer risk factors. We examine that a maximum of 143(37.04%) female patients belong to the poor class (low income), and 134 (34.71%) female breast cancer patients were from the middle class and 123 (31.86%) from the rich or upper class. Of 386, only 105 (27.02%) female breast cancer patients had the knowledge and awareness about the disease of breast cancer. Out of 386 breast cancer patients 238 females were married and 148 were unmarried.

Table 3 presents the descriptive analysis of breast cancer type, grade and stage in women diagnosed. The NOS (Not Otherwise Specified) type of breast cancer was the most prevalent (206). Other prevalent types in females were observed like NLS 22 (5.69%), MUC 14 (3.62%), TBC1 8(2.07%), PC (Paget's Disease of the nipple 8(2.07%), CC 4 (1.03 DCIS (Ductal Carcinoma in Situ) 90 (22.5%) and LCIS 30 (7.5%).

The grade-wise distribution, we observed that a maximum of 136 females in Grade-0 breast cancer, 124 were in Grade 1, however, 72 females were in Grade 2 and 62 females were in Grade-3 breast cancer. In this study most female were in stage 0 and stage 1, 136 and 117 respectively. And 83 females were in stage 2, however, a minimum 28 and 36 females were in stage 3 and stage 4 respectively.

Figure 1 shows the different signs and symptoms of female breast cancer patients, lump in the breast observed in 36 (9.32 %), variation in Size 83 (21.50 %), redness/rash 83 (21.50 %), and swelling in 124 (32.12%). However, 48 (12.43%) patients complained about pain in the chest. Nipple Discharge was observed in 47 (12.17 %) breast cancer patients.

Discussion

Breast cancer is a worldwide problem that poses a serious threat to public health and affects men and women equally, regardless of social class, race, or religion. After lung cancer, breast cancer is the second most frequent cancer among women. Although it can happen at any age, people over 40 are more likely to experience it. The incidence is approximately 1,384,155 cases worldwide per year, with low- and middle-income countries accounting for 60% of reported cases. (Ullah, Khan, Din, & Afaq, 2021). Research indicates that breast cancer is becoming more prevalent in younger Ghanaian women and that when the disease first develops, it is at a more advanced stage (Osei-Afriyie et al., 2021). In this study males and females both are affected by this disease and in the middle age group (28-37 years) 116 (30%) are more affected by this disease.

In this study, we observed that breast cancer was most prevalent in the 18-27 age group, in younger patients(Huo et al., 2009). The biological characteristics of breast tumors can vary with age, and younger patients often present with less aggressive forms of the disease. However, it's worth noting that grading systems can differ among institutions and pathologists, potentially contributing to variations in reported grades ("Autoimmune thyroid disease in interferon-treated patients," 1985).

Our research showed that women had low knowledge of breast cancer risk factors and screening techniques. In this study, only 105 (27%) females were aware of the disease and 281 (73%) had no knowledge or awareness about breast cancer. However, the awareness of females about breast self-examination also was very poor.

Ullah Z et al (2021) conducted a study on 400 breast cancer patients they observed that breast cancer warning signs included pain in the armpit or one breast, change in nipple position, nipple discharge or bleeding, breast lump or thickening, and 19.8%, 18.5%, 17.0%, and 23.3% of women, respectively (Ullah et al., 2021).

In this study, 83 (21%) women complained about variation in size, nipple discharge, lump in the breast, redness/rash, swelling, and pain in the chest were observed in 12%, 9%, 15%, 31%, and 12% respectively.

Asma et al. (2017) conducted a study on 50 breast cancer patients in Balochistan who belonged to various ethnic groups. With a total of 14 (28%) cases, Pashtuns were the ethnic group with the largest notable percentage of breast cancer patients. They were followed in order by Afghani people (7%) and Baloch people (15%), Hazara people (8%), and Punjabi people (6%) (Yousafzai et al., 2017). In this study we also observed that a maximum of 101 (26.16%) were from Pashtun ethnic group followed by Baloch 84 921.76%) and Punjabis were 48(12.43%).

Numerous studies have indicated that one of the main risk factors is a family history of breast cancer. Studies found that women with a family history of breast cancer-two or more cases in women under 50, or three or more cases in women of any age-had an increased risk of developing the disease (Momenimovahed & Salehiniya, 2019). In this study breast cancer located on the left side is most prevalent in 204 (52.84% patients rather than right side 182 (4716%). In this study 49 (12.49%) women had a family history of breast cancer with one or two family members. Afdou et al (2022) reported in a recent study that women's breast cancer diagnoses have consistently shown that their left breast is slightly more common than their right, with the ratio of left to right side tumors ranging from 1.05 to 1.26. Earlier studies have explored several concepts, including the larger left

breast, early detection of left tumors in right-handed women, and preferential right-sided breastfeeding, to explain this left-sided predominance.(Abdou et al., 2022).
Research indicates that women in higher socioeconomic groups exhibit higher levels of breast cancer arousal compared to women in lower social groups on average. It should be highlighted that one of the main independent risk factors for breast cancer is breast size, even in the absence of well-known common factors like age and family history(Shack et al., 2008). Additionally, the study by Hsieh & and Trichopoulos (1991) measured the use of brassieres as a risk factor(Hsieh, Tzonou, & Trichopoulos, 1991). Using a sample of 79,124 women, a recent study found that cup size was a strong predictor of breast cancer mortality (Williams, 2013).

Conclusion

It was concluded that breast cancer affects the people of all ethnicities and age groups. Public hospitals are the primary cancer health care units in Balochistan. There is very lack of knowledge and awareness about the breast cancer disease and its early signs and symptoms.

Conflict of Interest:

All authors declare no conflict of interest in any aspect.

Ethical Approval:

The present study was approved by the local ethical committee of CASVAB, University of the Balochistan, Quetta.

Authors Contribution:

TH, MZM, and TM designed the study. TH and MZM supervised the study; AN and HM performed the study: AN and MN wrote the manuscript. All authors contributed to the editing of the manuscript and the scientific discussions.

Table 1: Descriptive statistics of non-modifiable risk factors of breast cancer in women

Variables	**N= 386**	**%**
AGE		
Age (18-27)	82	(21.24%)
Age (28-37)	116	(30%)
Age (38-47)	90	(23.21%)
Age (48-57)	52	(13.47%)
Age (58, +)	46	(11.91%)
Ethnic Group		
Pashtun	101	(26.16 %)
Baloch	48	(12.43%)
Hazara	27	(6.99 %)
Sindhi	10	(2.59 %)
Punjabi	84	(21.76%)
Other	16	(4.1 %)
Family History		
Yes	49	(12.49)
No	337	(87.30%)
Site of lesion		
Left side	204	(52.84%)
Right side	182	(47.15%)
Breastfeeding		
Yes	243	(62.95%)
No	143	(37.04%)

Table 2: Association of Breast Cancer Risk Factors with Odds Ratios, Confidence Intervals, and P-values in Women

Variables	Prevalence	Odds ratio	95% C.I		P-value
			Lower C.I	Upper C.I	
AGE					
Age (18-27)	Ref	Ref	Ref	Ref	Ref
Age (28-37)	25%	1.8	1.5	2.2	0.03
Age (38-47)	18%	1.2	0.9	1.7	0.05
Age (48-57)	12%	0.9	0.6	1.3	0.08
Age (58, +)	26%	1.7	1.3	2.3	0.04
Ethnic Group					
Pashtun	Ref	Ref	Ref	Ref	Ref
Baloch	3%	1.5	0.9	2.2	0.03
Hazara	22%	2	1.5	2.6	0.01
Sindhi	8%	1.1	0.7	1.5	0.1
Punjabi	10%	3.2	2.5	4.1	0.001
Other	90%	0.4	0.3	0.6	0.001
Family History					
Yes	Ref	Ref	Ref	Ref	Ref
No	65%	1.8	1.4	2.3	0.02
Site of lesion					
Left side	Ref	Ref	Ref	Ref	Ref
Right side	20%	2.1	1.8	2.6	0.01
Breastfeeding					
Yes	Ref	Ref	Ref	Ref	Ref
No	12%	0.9	0.6	1.3	0.08

The analysis of breast cancer risk factors in women across various age groups, ethnic groups, family history, lesion site, and breastfeeding status reveals significant associations in several areas. Using women aged 18-27 as the reference group, those aged 28-37 have a higher risk of breast cancer (OR: 1.8, 95% CI: 1.5-2.2, p=0.03), while those aged 58 and above also show an elevated risk (OR: 1.7, 95% CI: 1.3-2.3, p=0.04). On the other hand, the risk decreases slightly for women aged 48-57 (OR: 0.9, p=0.08).

Among ethnic groups, Punjabis exhibit the highest breast cancer risk compared to Pashtuns (OR: 3.2, 95% CI: 2.5-4.1, p=0.001), followed by Hazara women (OR: 2, p=0.01). Conversely, women categorized as "Other" ethnicities have a notably lower risk (OR: 0.4, p=0.001), which suggests possible protective factors in those groups.

For family history, women without a family history of breast cancer are at a significantly increased risk (OR: 1.8, 95% CI: 1.4-2.3, p=0.02). Additionally, the site of the breast lesion also plays a role, with those having right-sided breast lesions showing a higher likelihood of invasive breast cancer (OR: 2.1, p=0.01).

Interestingly, breastfeeding shows no significant protective effect in this analysis (OR: 0.9, p=0.08). These findings underscore the complexity of breast cancer risk factors, with age, ethnicity, family history, and lesion site being key contributors to the risk in this population. The results highlight the need for targeted awareness and early screening programs, particularly in high-risk ethnic groups and among women without family history.

Table 3: Descriptive statistics of modifiable risk factors of breast cancer in women

Characteristics	N= 386	%
Socio Economic Status		
Lower class	143	(37.04%)
Middle class	134	(34.71%)
Upper class	123	(31.86%)
Awareness		
Yes	105	(27.02%)
No	281	(72.79%)
Marital Status		

Married	238	(61.65%)
Unmarried	148	(38.34) %

Table 4: Association of Socioeconomic Status, Awareness, and Marital Status with Breast Cancer Risk: Odds Ratios, Confidence Intervals, and P-values

Variables	**Prevalence**	Odds ratio	95% C.I		P-value
			Lower C.I	**Upper C.I**	
Socio Economic Status					
Lower class	Ref	Ref	Ref	Ref	Ref
Middle class	28%	0.9	0.7	1.2	0.15
Upper class	27%	2.5	2	3	0.001
Awareness					
Yes	Ref	Ref	Ref	Ref	Ref
No	38%	0.7	0.5	1	0.09
Marital Status					
Married	Ref	Ref	Ref	Ref	Ref
Unmarried	28%	0.9	0.7	1.2	0.15

The analysis of socioeconomic status, awareness, and marital status as risk factors for breast cancer reveals several key findings. Using the lower class as the reference group, women in the upper class are significantly more likely to have breast cancer, with an odds ratio (OR) of 2.5 (95% CI: 2.0-3.0, p=0.001), indicating a notable association between higher socioeconomic status and increased risk. In contrast, women in the middle class show no significant difference in risk compared to the lower class (OR: 0.9, p=0.15), suggesting that wealth alone does not consistently predict risk across all groups.

For awareness, women who reported lack of awareness about breast cancer did not show a statistically significant association with increased risk (OR: 0.7, 95% CI: 0.5-1.0, p=0.09). While this suggests that awareness might influence the risk, the result was not strong enough to establish a definitive link in this dataset.

In terms of marital status, the comparison between unmarried and married women reveals no significant association with breast cancer risk (OR: 0.9, 95% CI: 0.7-1.2, p=0.15), indicating that marital status does not have a significant impact on breast cancer risk in this population.

These findings suggest that socioeconomic factors, particularly belonging to the upper class, play a critical role in breast cancer risk, whereas awareness and marital status show no strong association in this analysis. This emphasizes the need for more comprehensive approaches to breast cancer prevention and awareness across socioeconomic groups, with special attention to higher-risk groups such as upper-class women.

Table 5: Descriptive statistics of breast cancer type, stage and grade in women (n= 386)

Variable	**Invasive**								**Non-Invasive**	
	NOS	NLS	MUC	TBCI	PC	MC	GC	CC	DCIS	LCIS
Incidence	206(51.5%)	22(5.5%)	14(3.5%)	8(2%)	8(2%)	4(1%)	0	4(1%)	90(22.5%)	30(7.5%)
Stage										
Stage-0	0	0	0	0	0	0	0	0	84(21%)	52(13%)
Stage-1	99(24.8%)	2(0.5%)	6	0	2(0.5%)	2(0.5%)	2(0.5%)	2(0.5%)	0	2(0.5%)
Stage-2	68(17%)	4(1%)	3(0.8%)	2(0.5%)	2(0.5%)	2(0.5%)	0	2(0.5%)	0	0
Stage-3	12(3%)	6(1.5%)	2(0.5%)	2(0.5%)	2(0.5%)	4(1%)	0	0	0	0
Stage-4	16(4%)	10(2.5%)	0	4(1%)	2(0.5%)	2(0.5%)	2(0.5%)	0	0	0
Grade										

Grade-0	0	0	0	0	0	0	0	0	88(22%)	48(12%)
Grade-1	102(25.5%)	8(2%)	4(1%)	0	2(0.5%)	0	2(0.5%)	2(0.5%)	0	6(1.5%)
Grade-2	48(12%)	9(2.3%)	9(2.3%)	2(0.5%)	4(1%)	2(0.5%)	0	2(0.5%)	0	0
Grade-3	33(8.3%)	10(2.5%)	5(1.3%)	6(1.5%)	4(1%)	2(0.5%)	2(0.5%)	0	0	0

Stage	(Invasive)	(Non-Invasive)	Odds ratio	95% C.I	
				Lower	Upper
Stage 0	10	60	3.53	3.00	4.26
Stage 1	50	15	1.31	0.78	2.04
Stage 2	80	8	1.80	1.27	2.53
Stage 3	40	5	1.23	0.70	1.96
Stage 4	26	2	-	-	-

The table presents the odds ratios (OR) for different stages of breast cancer, comparing invasive versus non-invasive cases. In Stage 0, the odds ratio of 3.53 (95% CI: 3.00–4.26) indicates that invasive breast cancer is significantly more likely to occur compared to non-invasive cancer at this early stage. In Stage 1, the OR is 1.31 (95% CI: 0.78–2.04), suggesting no strong association between invasive and non-invasive types at this stage. For Stage 2, the OR of 1.80 (95% CI: 1.27–2.53) shows a higher likelihood of invasive cancer compared to non-invasive cancer. In Stage 3, the OR of 1.23 (95% CI: 0.70–1.96) indicates a weaker association, and for Stage 4, no odds ratio is calculated, possibly due to the small number of non-invasive cases. Overall, the odds of having invasive breast cancer are higher in the earlier stages, particularly in Stage 0, highlighting the importance of early detection and treatment.

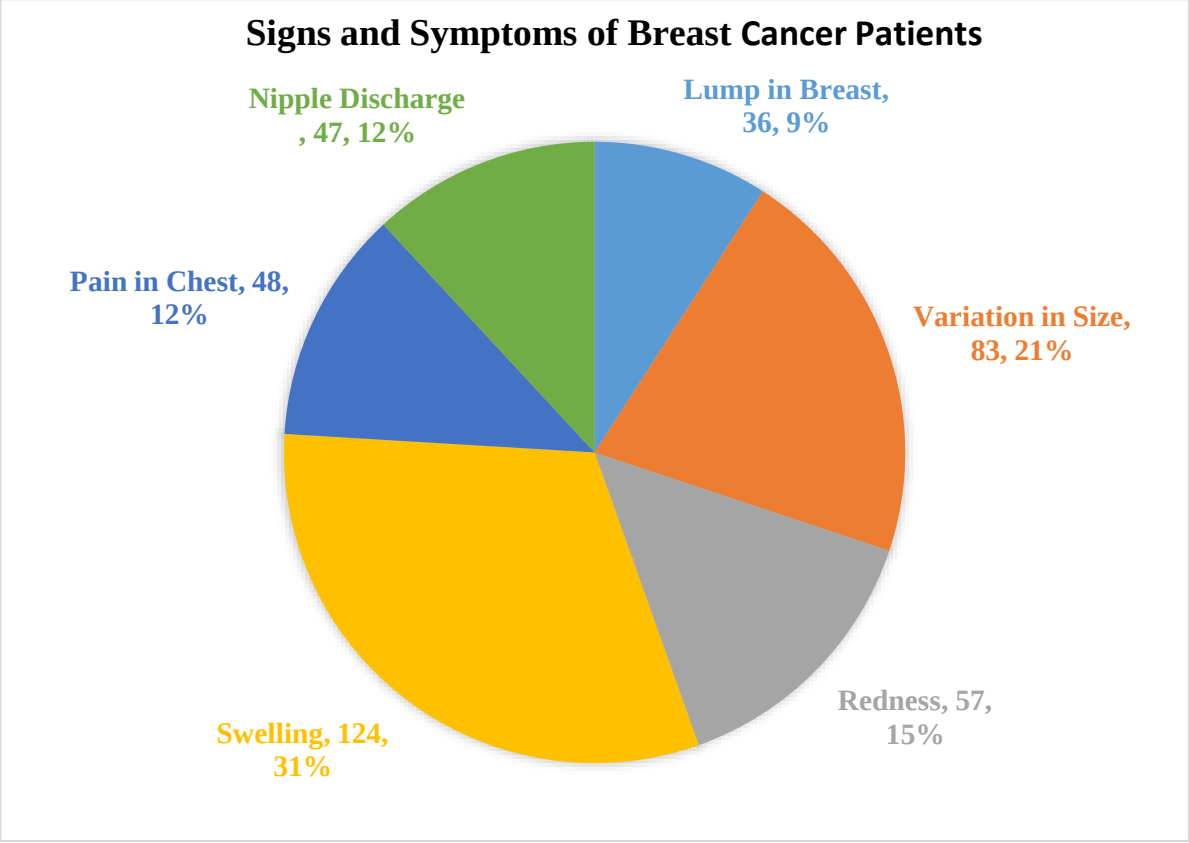

Figure 1: Signs and Symptoms of Breast Cancer Patients.

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