

An Epidemiological study on Women Breast Cancer patients in the districts of Tamil Nadu in association with various risk factors causing Breast Cancer

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Abstract:

Background: Breast Cancer (BC) is the second leading cause of cancer deaths among women. The development of BC is a multi-step process involving multiple cell types, and its prevention remains challenging in the world. Studies have shown that the risk for BC is due to a combination of factors. The main factors that influence the risk of BC are being a woman and getting older. It is necessary to analyze the various risk factors of BC for early diagnosis and to provide other prevention mechanisms to the patients.

Materials and Methods: The current study focuses on the lifestyle risk factors associated with BC women in the districts of Tamil Nadu. Here, the lifestyle risk factors are mainly analyzed with the occupation details of the women. If the occupation of the woman is a farmer, then the pesticide exposure among women is analyzed. The study also analyses the other kinds of risk factors, such as aging, family history, menstrual history, etc. for BC. For analyzing several risk factors, firstly the data were collected. A total number of 227 BC cases were registered and gathered from the hospital-based cancer registries of the Erode and Coimbatore District. The cases were segregated by different risk factors using the SPSS Software. After segregation of data, the risks are analyzed with each collected data pattern and the questionnaire was presented for some of the factors.

Results: The results indicated that most farmers are affected by BC because of pesticide applications. It was resolved that the bulk of the patients in the collected cases were treated in locally advanced and metastatic stages. A multidisciplinary approach to BC, including awareness programs, preventive measures, screening programs for early detection, and accessibility of treatment facilities are critical for reducing both the incidence and death rate of BC in Indian women.

Key Words: Breast cancer (BC); Risk factors of breast cancer; Lifestyle; Environmental risk factors; Incidence; SPSS Software; Tamil Nadu.

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I. Introduction

The term cancer is a technical term that refers to uncontrolled cell growth in tissues, leading to malfunctioning of body organs in an extreme state of influence causing major suffering and even death [1]. More than thirteen thousand Indians die every day due to cancer, according to the National Cancer Registry Program of the India Council of Medical Research (ICMR) [2]. Additionally, in the past few decades, human has invested plenty of manpower, material resources, and financial resources to fight with cancer, but it produces very little effect [3]. BC is the most common cancer type among women in the world, and it is the fifth most common cause of death, according to the World Health Organization (WHO) [4]. BC causes the largest number of cancer-related deaths among women with malignancies [5]. BC is the most common cancer in women both in the developed and less developed world [6]. Types of BCs include: ductal, lobular, and invasive ductal, invasive lobular, phyllodes tumor, tubular carcinoma, mucinous carcinoma, and medullary cancer.

India has the maximum number of women dying of BC, and that number is huge (70,000!) [7]. Medical investigation on BC in the absence of proper methods for early detection is still a challenging one [8]. On the other hand, there is ample evidence that health and lifestyle behaviors may change across the lifespan and may simply be a part of aging [9]. The incidence of BC is related to age [10]. In the United States, one out of eight women has BC in their lifetime. The study shows that the average ages of women between 45 and 59 have more chance of cancer [11]. BC is the most commonly diagnosed non-skin cancer in women under the age of 40, comprising 30% of all cancer diagnoses in this group [12]. TNBC is reported to account for approximately 10%

of all invasive BCs in older women [13]. Recent studies suggest that environmental exposures, such as certain chemicals, diet, and social factors, during these critical stages of development, may increase the risk of BC later in life. Using both biomarkers of persistent, organochlorine pesticides elevates BC mortality while utilizing only one reduced BC mortality [14]. Pesticides are also believed to cause cancers in humans, e.g. glyphosate is associated with BC [15]. Then the women exposed to stress are at a higher risk of developing BC than the non-exposed ones. The common risk factors of BC in women are categorized in figure 1, It is known that 80-90% of human cancers may be caused by environmental and lifestyle factors, occupation, types of BC, chemical pesticide exposure, behavioral factors such as tobacco and betel nut usage, and alcohol consumption, Medical history, Menstrual History, Pregnancy history, Family history, Immunohistochemistry, and Histopathology. Early-stage BC can be treated with surgery or radiation, but the treatment of metastasis is more difficult and survival is reduced by about 25% [16]. Prevention, early detection, and treatment are vital to successful cancer control [17].

II. Materials and Methods

This study aimed to investigate the association between menstrual, environment, aging, family history, and lifestyle factors and BC in Tamil Nadu women. This study used a self-administrated questionnaire which was prepared on the basis of information collected from the different hospital managements consisting of many parts, such as general information, the personal dietary habit, tobacco and betel nut usage, types of BC, pesticide exposure, etc. In the questionnaire format, most options are Yes / No. This section includes the details about the data collection phase and how the data was statistically analyzed with the help of SPSS software. The current research methodology mainly focuses on five major risk factors for BC in women.

Data Collection

The data for the present study includes BC incidence, environmental risk factor and other details, which were collected from the females who had undergone medical treatment for BC at various oncology clinics in the districts of Tamil Nadu including Ariyalur, Coimbatore, Cuddalore, Dharmapuri, Dindigul, Erode, Kanyakumari, Karur, Krishnagiri, Madurai, Nammakkal, Perambalur, Salem, Thanjavur, Theni, Tirupur, Thiruvannamalai, Vellore, and Viruthunagar. A Total number of 227 BC cases were screened and the questionnaire was obtained with an informed concern form and the medical records were evaluated using stranded questionnaire with case reports. The patient's data are collected from the hospital management after getting necessary permissions from IHEC (Intuition Human Ethical Clearance).

The collected attributes from the hospital management include the details like age, education, marital status, district, occupation, and work area exposure like (pesticides), duration of work, food habits, types of BC for the women, chemical pesticide exposure, behavioral factors, such as the use of tobacco, betel, and alcohol consumption, medical history, menstrual history, abortion history, immuno-histochemistry, histopathology, breastfeeding, pregnancy history, and family history.

Statistical Analysis

Statistical analysis of the collected data was performed using the software, namely Statistical Package for the Social Sciences (SPSS). The SPSS analyzed the BC risk factors regards to residual pesticide exposure. A value of zero levels was assigned for results below the limit of exposure (BLE); the data were expressed as means \pm standard error. The *p* values less than 0.05 were considered to be statistically significant.

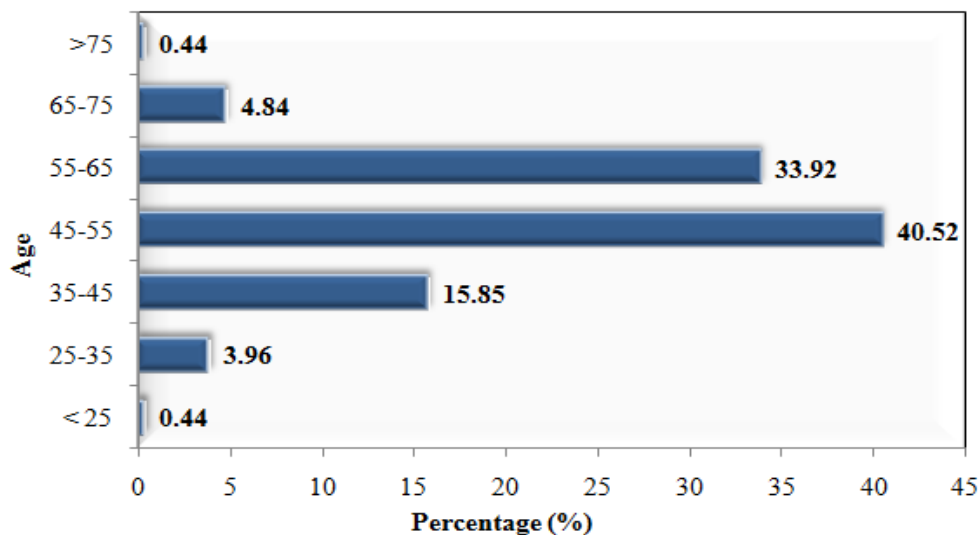
III. Results

This section discusses the results of the present research methodology with the analyzed reports. questionnaires were presented using the collected data of 227 BC cases; some of the risk factors associated with BC were discussed with them by yes or no questions. Table 1 shows the risk analysis of BC in women with general factors, such as age, marital status, education, occupation, and district. Here, the aging factor plays a vital role in increasing BC. The survey carried out by the Indian Council of Medical Research (ICMR) in the metropolitan cities from 1982 to 2005 showed that the incidence of BC was almost doubled. The analysis of the current study based on age group showed that the age group in the range of 45-55 reached the highest risk (40.52%) followed by age group in the range of 55-65 reached moderate risk (33.92%), and the age group between 35 to 45, 25-35, and <25 had the least amount of BC risks say 15.85%, 3.96%, and 0.44%.

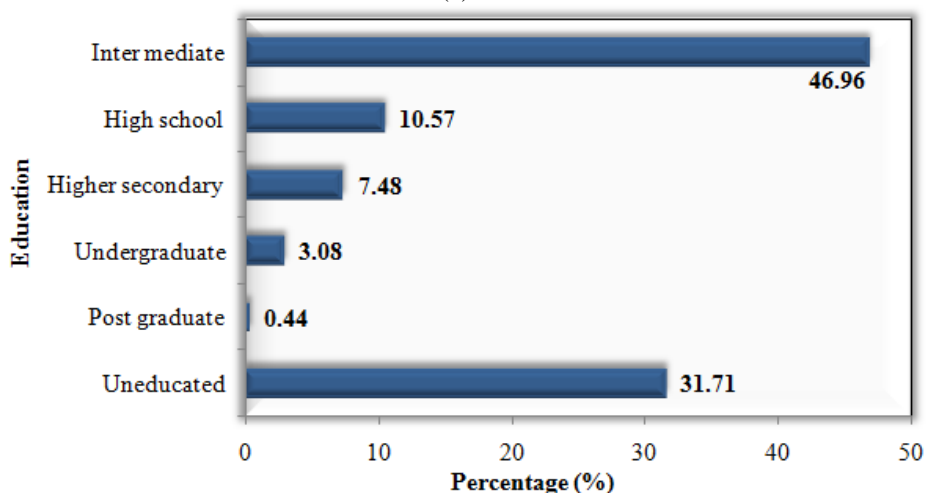
Table 1: Risk analysis of BC with general factors

General Information	Frequency (N=227)	Percentage (%)	
Age group (years)	Below 25	1	0.44
	25-35	9	3.96
	35-45	36	15.85
	45-55	92	40.52
	55-65	77	33.92
	65-75	11	4.84
	>75	1	0.44
Marital status	Married	223	98.23
	Unmarried	4	1.76
Education	Uneducated	72	31.71
	Postgraduate	1	0.44
	Undergraduate	7	3.08
	Higher secondary	17	7.48
	High school	24	10.57
	Intermediate	106	46.96
Occupation	Employed	189	83.25
	Unemployed	38	16.74
District wise District affected	Erode	71	31.27
	Coimbatore	36	15.85
	Salem	31	13.65
	Nammakkal	25	11.01
	Krishnagiri	13	5.72
	Dindugul	11	4.84
	Dharmapuri	10	4.40
	Karur	8	3.52
	Thirupur	9	3.96
	Viruthunagar	3	1.32
	Thiruvannamalai	1	0.44
	Ariyalur	2	0.88
	Thanjavur	1	0.44
	Perampalur	1	0.44
	Cuddalore	1	0.44
	Theni	1	0.44
	Kanyakumari	1	0.44
	Madurai	1	0.44
Vellore	1	0.44	

The education details of the collected data were also analyzed. The study shows that only a few cases came under PG (0.44%) and UG category (3.08%), the cases of the intermediate category (46.96%) were high when compared to others, and the uneducated found was 31.71%. The cases found in high school and higher secondary were 10.57% and 7.48%. The risk analysis of BC regarding age group and education is shown in figure 1.



(a)



(b)

Figure 1: Risk analysis of BC regarding age and education

When analyzing the risk factors in terms of marital status, married women had the highest amount of risk factor when compared to unmarried women. The analysis of the current study shows that out of 227, 223 (98.23%) were married women and only '4' were unmarried (1.76%). Likewise, the occupation-wise analysis was carried out, which shows that 83.25% of cases were employed and 16.74% were unemployed. The unemployed cases were mostly farmers. The analysis of both marital status and occupation were graphically shown in figure 2.

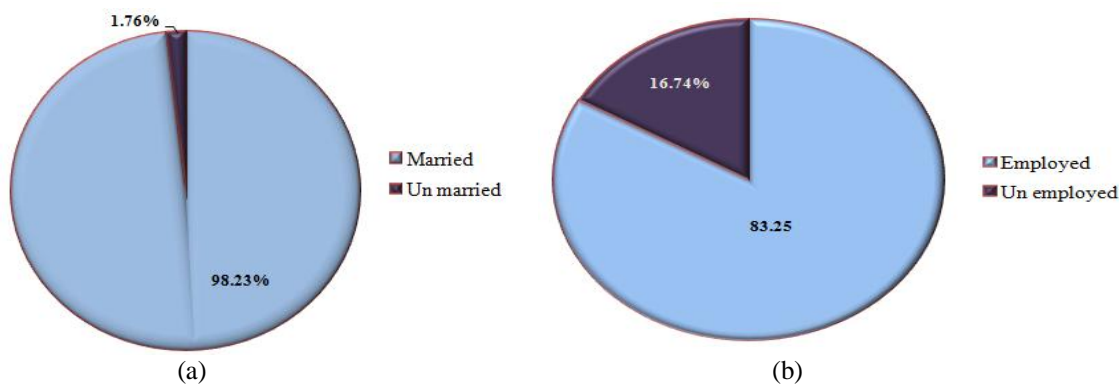


Figure 2: Risk analysis of BC regarding marital status and occupation

Table 1 also includes the detail about affected districts of the state of Tamil Nadu. The BC incidence in the Western region of Tamil Nadu was found to be varying from one area to another, with higher incidences in Coimbatore north and south talks. In the total number of 227 cases, Erode district had a high (31.27%) number of cases, Coimbatore (15.85%), Salem (13.65%), and Nammakkal (11.01) had average cases and other districts (Krishnagiri (5.72%), Dindigul (4.84%), Dharmapuri (4.40%), Karur (3.52%), Tirupur (9%), virudhunager (1.32%), then I (0.44), etc.) had a very few amount of cases.

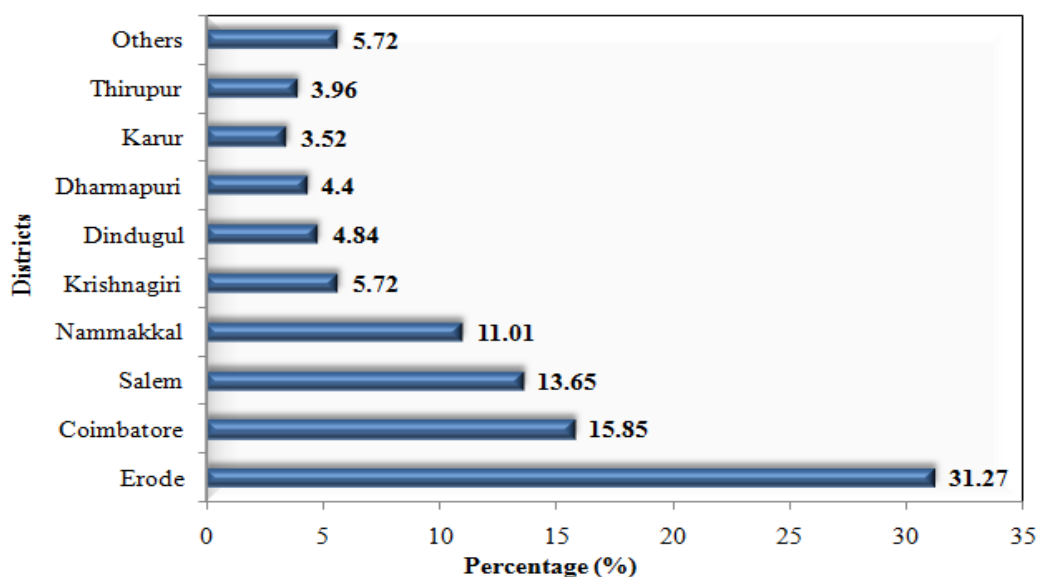


Figure 3: Risk analysis of BC regarding districts

Risk analysis of BC based on Occupation

Environmental compounds, their exposure, and occupation factors increase BC risks. Table 2 illustrates the risk factors of BC based on the occupation of the people. Table 2 gives the information about the occupation details of the people in the collected data. Table 2 shows that out of the 227 cases, 48.01% are farmers, 16.29% are unemployed, 7.04% are vegetable vendors, 2.64% are tailors, 3.08% are sweepers, and the remaining percentage of people comes under a different category of works, such as cotton mill workers, self-employed, textile workers, etc.

Table 2: Risk analysis of BC based on occupation

Occupation	Frequency (N=227)	Percentage (%)
Farmers	109	48.01
UN Employed	37	16.29
Vegetable Vendors	16	7.04
Spinning Mill workers	6	2.64
Tailor	7	3.08
Sweeper	7	3.08
Beady Company workers	5	2.20
Cotton Mill workers	5	2.20
Textile workers	5	2.20
Cement factory, chemical Industry, Fiber factory, Dye factory, former & cement factory, Lather & spinning mill, former& paper mill, Medical shop, Municipality, paper mill, self-employed (beady rolling), spinning and cement factory, steel industry, tea factory, Teachers and Thermal Industry workers.	3,2,3,3,2,3, 1,2,1,1,1,1,1, 1 and 3	1.32, 0.88, 1.32,1.32,0.88,1.32,0.44, 0.88, 0.44, 0.44, 0.44, 0.44,0.44, 0.44 and 1.32

Hire, table 2 clearly shows that the farmers are mostly affected by the BC when compared to other workers. So, the risk of having BC is high for farmers because of the usage of pesticides in their daily work. Other workers have a very less amount of risk for BC when compared with farmers. The collected data of BC cases were screened based on many other factors, such as food habits, tobacco usage, betel nut usage, early menarche, pesticide exposure of farmers, etc. which are presented as a questionnaire form in table 3.

Risk analysis of BC based on various factors

The risk of BC includes other kinds of factors also that include daily habits of people, family history, abortion history, histopathology, Immunohistochemistry, etc. Table 3 shows the risk factors associated with the

above-mentioned factors in the collected data (227 cases), which is shown in the questionnaire format. Out of 227, only 6 people (2.64%) were following a vegetarian diet and others (97.35%) were following both vegetarian and non-vegetarian diets. When analyzing the tobacco usage, only 25.99% of people were using tobacco and 74.008% of people were never taken tobacco in their life. Then, the betel nut usage of the data was analyzed, which shows that 48.89% of people used betel nut and 51.101% were not using the betel nut. The cases affected by early and late menarche were very few that were 3.96% and 3.08%, whereas the cases not affected by early and late menarche include 96.03% and 96.91%. Out of 227, 207 women gave breastfeeding after pregnancy and only 20 women did not breastfeed after pregnancy. The women having 1 abortion were 36.12%, 2 abortions were 4.84%, 3 abortions were 1.32, and the women having no abortions in their life were 57.709%. The family history of the BC affected cases was analyzed. This analysis includes the detail about whether the people in the family of BC cases were affected by any other tumor, such as cancer and other severe health issue or not. Table 3 shows that the risk of BC for women in terms of family history is low (26.43%) when compared to the risk of BC without family health history (73.56).

Table 3: Questionnaire of various factors associated with BC

Parameter	Frequency (N=227)	Percentage (%)	
Food habits	Vegetarian	6	2.64
	Veg and Non-Veg	221	97.35
	Non-Veg	0	0
Tobacco usage	Yes	59	25.99
	No	168	74.008
Betel nut usage	Yes	111	48.89
	No	116	51.101
Pesticide exposure	P_1	15	6.60
	P_2	82	36.12
	P_3	1	0.44
	P_4	5	2.20
	P_5	28	12.33
	P_6	11	4.84
	P_7	30	13.21
	P_8	55	24.22
Early menarche	Yes	9	3.96
	No	218	96.03
Late menarche	Yes	7	3.08
	No	220	96.91
Breast feeding	Given	207	91.18
	Not given	20	8.81
Pregnancy risk	1 abortion	82	36.12
	2 abortions	11	4.84
	3 abortions	3	1.32
	No abortion	131	57.709
Family affected	Affected	60	26.43
	Not affected	167	73.56
Immunohistochemistry	Her 2 New Positive	6	2.64
	Negative	1	0.44
	No	220	96.91
Histopathology	ER and PR Positive (239,211)	10	4.405
	Negative	1	0.44
	No	216	95.15

Her2/new is an oncogene whose protein product may function as a growth factor and may also be involved in promoting cellular differentiation, adhesion, and mortality. Amplification of Her2/ New is seen in almost all cases of intraductal carcinoma and about 20-30% of invasive ductal carcinoma. This over-expression can transform human breast epithelium. Biomarkers to predict recurrence or interventions to decrease the recurrence in HR-positive BC are needed for use in conjunction with adjuvant hormonal therapy. The Immunohistochemistry tested among 227 cases were 7, on that, '6' cases attained positive results, 1 attained negative results, and 220 cases were not tested with Immunohistochemistry.

Likewise, the histopathology of the data was analyzed which had 10 positive cases, 1 negative case, and 216 not tested cases. Progesterone Receptor (PR) is an ER regulated gene product with many of the same prognostic implications as ER in BC. Estrogens have long been recognized as being important for stimulating the growth of a large proportion of BC. The main factor associated with the BC risk among farmers is pesticide exposure. All over the world, 10.1 billion pounds of pesticides are used annually. Here, the pesticide exposure among the farmers and other cases are coming under 8 different classes $P_1, P_2, P_3, P_4, P_5, P_6, P_7$ and P_8 , which are defined as follows P_1 - Working before '8' hours of pesticide sprayed forms P_2 - Living nearby farm areas of pesticide application P_3 - Pesticides spraying women P_4 - Stored pesticides in their home P_5 - Consuming more amounts of pesticides applied vegetables P_6 - Washing work clothes worn during pesticides spraying P_7 - Farmers working with bare hands in pesticides applied forms P_8 - Without pesticides exposures Among all, the risk was 24.22% for without pesticide exposures (P_8), whereas the risk factor obtained by P_2 was higher (36.12%) when compared to other pesticide classes. That means, people living near the farm areas of pesticide applications had the highest risk of having BC. The risks of other classes such as P_1, P_3, P_4, P_5, P_6 , and P_7 attained the percentage of 6.6, 0.44, 2.2, 12.33, 4.84, and 13.21. Hereafter P_2 P_6 attained the highest amount of risk for BC. From the analysis, it is clear that the risk is high for farmers because of the pesticide application, which is analytically shown in figure 4.

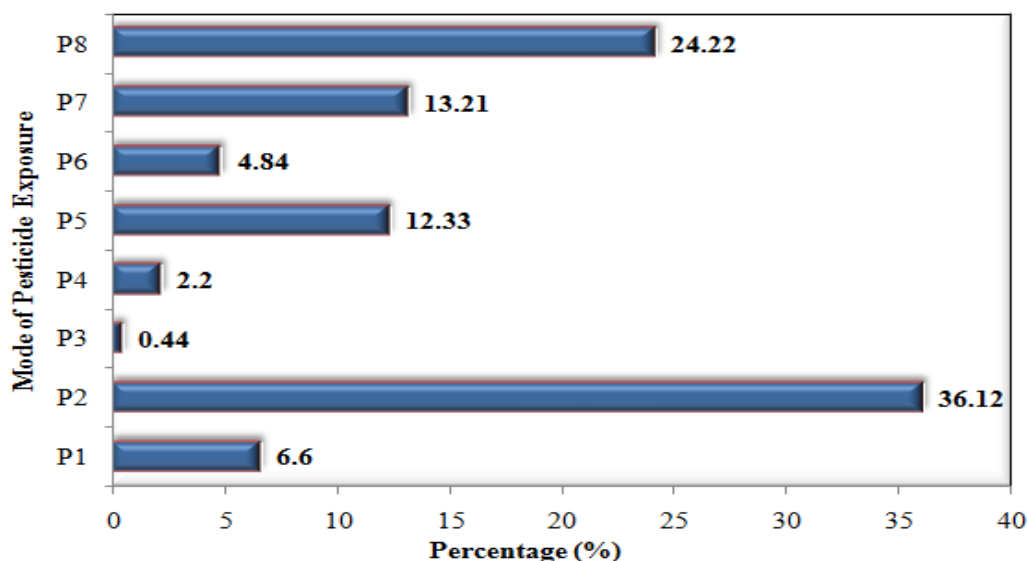


Figure 4: Risk analysis of BC regarding pesticide exposure

Analysis of tobacco and betel nut usage

To study the influence of behavioral factors, such as tobacco chewing and betel leaf consumption, data consisting of complete information regarding the consumption of tobacco and betel leaves were segregated. This section analyzes the tobacco and betel nut usage among educated and uneducated women, which is shown in table 4. The table only shows the percentage of tobacco and betel nut usage among BC people >10 years. Out of 155 educated women, 9 (3.96%) used tobacco and 26 (11.45%) used betel nut. In a total of 72 uneducated women, 70 (31%) used both tobacco and betel nut. It is clearly shown that the usage of tobacco and betel nut was high on uneducated people. It is necessary to make the awareness about the dangers of using both tobacco and betel nut to both educated and uneducated people because the educated people in the current study include the people from the medium of 3rd standard.

Table 4: Tobacco and betel nut usage

Education	Tobacco usage	Percentage	Betel Nut Usage	Percentage (%)
Educated	9	3.96	26	11.45
Uneducated	70	31.00	70	31.00

Analysis of types of BC

This section gives a detailed analysis of the types of BC faced by the women in Tamil Nadu. Out of 227, 96 (42.29%) had type 1, 48 (21.14%) had type 2, 35 (15.41%) had type 3, and 20 (9%) had type 4. Type 1, Type 2, Type 3, and Type 4 indicates the Infiltrating Ductal Carcinoma, Ductal Carcinoma, Invasive Ductal Carcinoma, and Metastatic Adenocarcinoma BCs. From the analysis, it is stated that the people were mostly affected by type 1 and type 2 cancers, and people affected by type 3 and type 4 cancers were minimum when compared to the cases of type 1 and 2. The diagrammatic representation of BC types in the women of Tamilnadu is shown in figure 7,

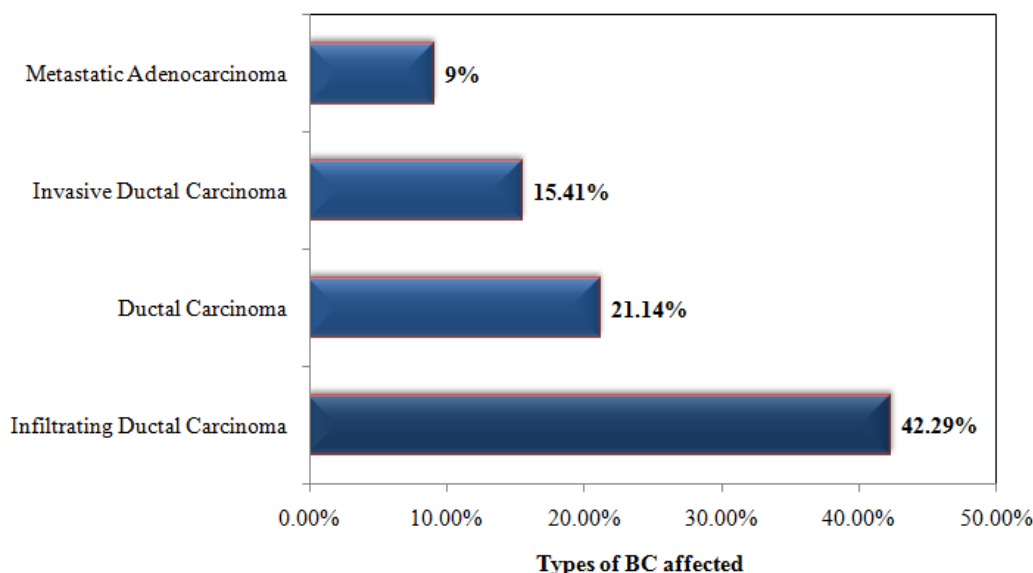


Figure 5: Analysis of affected BC types in women

Dominant side and Abortion history

This section shows the report of the dominant sides affected by the BC women, and the abortion history of the BC women, which are shown in figure 6. Figure 6 (a) shows that out of 227, 142 (62.55%) women were affected by the left side of BC, 80 (35.24%) were affected by the right side of BC, and the remaining (5-2.2%) were affected by both sides of BC. From figure 8 (b), it is stated that the women's had one abortion in their life was 37% and had more than one abortion was 6.6%, which includes (2, 3, and 4 abortions).

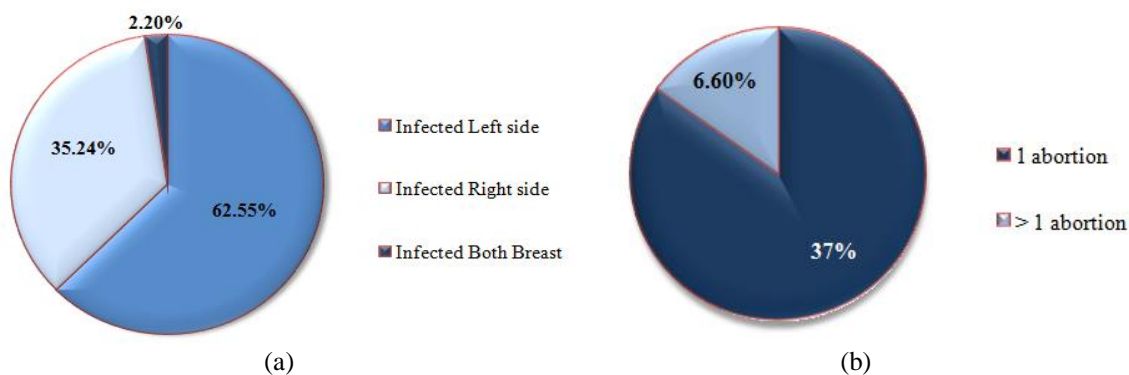


Figure 6: Analysis of dominant side and abortion history

Risk factors associated with Breastfeeding

Breastfeeding (BF) lowers the risk of developing BC, particularly if they have children when they are younger. The longer period of breastfeeding reduces the risk of having BC. The previous studies reported that the lifetime duration of BF was inversely associated with BC risk among premenopausal women and no such protective effect was demonstrated in the post-menopausal women [23]. Another case-control study conducted at a government medical college in Nagpur demonstrates that lack of or less duration of breastfeeding was

associated with the risk of BC [24]. This section presents the analysis of the risk factor associated with the breastfeeding history of the BC women from the collected data, which is shown in table 5.

Table 5: Breastfeeding history

Duration of BF	Number of cases (227)	Percentage (%)
BF given for 10 months (for 1 st child)	2	0.88
BF given for 9 months (for 1 st child)	1	0.44
BF for <6 months	86	38.00
BF gave for 1year	37	16.29
BF given for 2 years (for each child)	1	0.44
BF gave for >1year	69	30.39
BF not given	32	14.09

From the table, it is observed that the BC cases were higher in women who gave feeding to their babies less than 6 months (38%) and >1 year (30.39%). The average amount of BC cases was found in two categories: feeding for 1 year (16.29%) and feeding not given (14.09%). It is also clear that a very less amount of BC cases was found when BF was given for 9 months (0.44%) and 10 months (0.88%). Here, the women who gave BF >1 year had more BC cases because of their occupation. The BF>1 year, mostly came under the occupation category of farmers. They were mostly affected by pesticide exposure. When comparing the overall analysis, it is observed that a lesser amount of cancer cases was founded under this BF category. The report of BF history for the collected data is graphically plotted in figure 9,

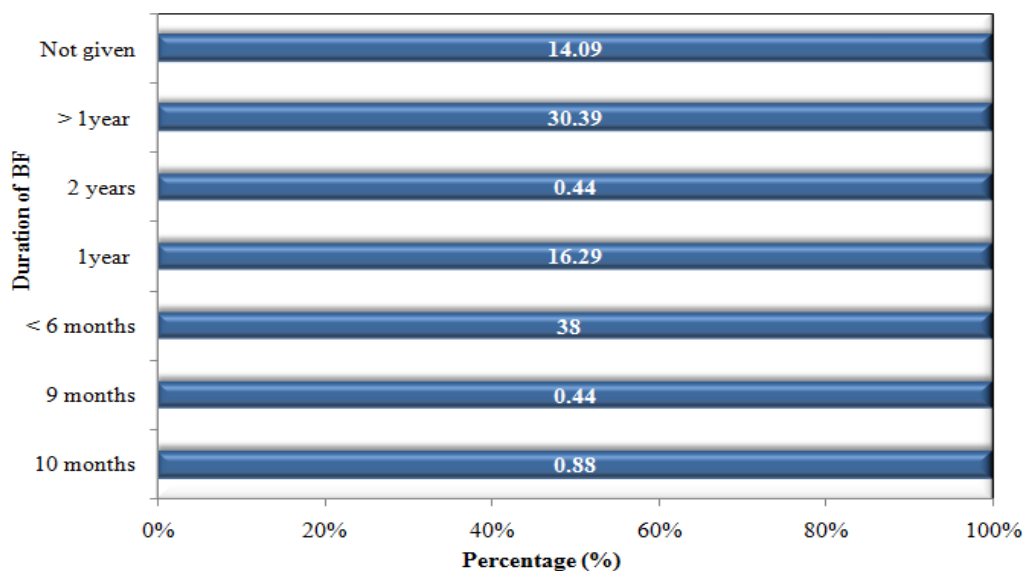


Figure 7: Analysis of BF history

The risk factor of BC based on Menstrual History

Statistically, it has been reported that women who got their periods early (before age 12) or went through menopause late (after age 55) have an increased risk for BC. This section gives a detailed analysis of the menstrual history of the women in the collected cases. Out of 227, only 36 (15.85%) cases attained menopause, which includes both primenopause (1-0.44%) and menopause (35-15.41%), 2 (0.88%) had post-menopause, 2 (0.88%) had the problem removal of ovaries (0.88%), and 187 (82.37%) participants did not face above problems. This analysis indicated that the risk factor of BC is low regarding menstrual history. The menstrual history analysis of the 227 participants is shown in figure 8.

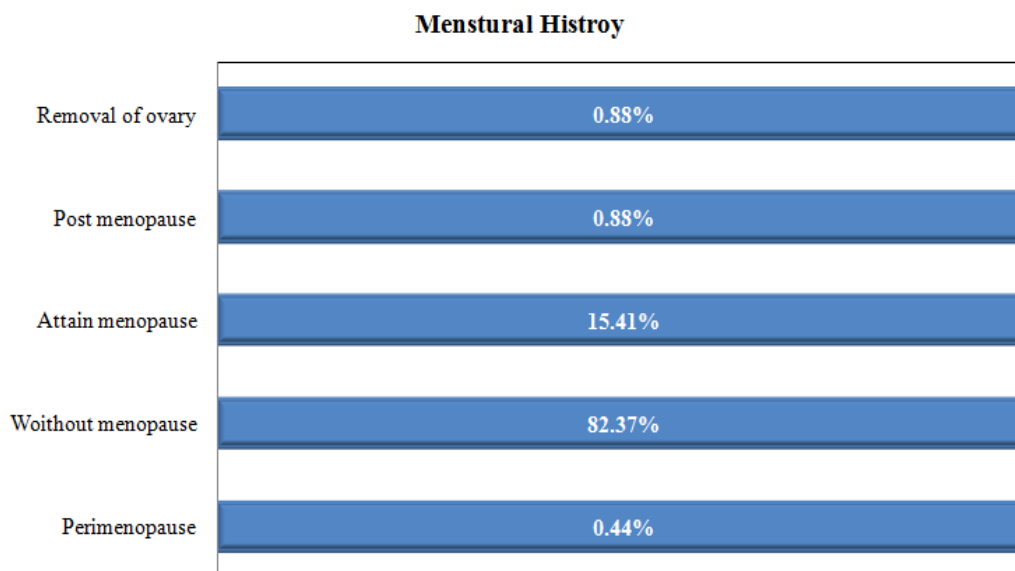


Figure 8: Menstrual history analysis

IV. Discussion

Lack of organized BC screening program, the paucity of diagnostic aids, and general indifference toward the health of females in the predominantly patriarchal Indian Society are also the drawbacks leading to increased BC incidence. The current study focuses on the analysis of various risk factors associated with BC in the state of Tamil Nadu. The results show that women are highly affected by BC due to aging and pesticide exposure. The study indicated that out of 227 cases, 109 were farmers, 36% of the participants lived in nearby fields of pesticide application, 58% of the participants worked more than 10 years in agricultural areas. The highest possibility of BC affected age group is 45-55 followed by 55-65. Only a limited amount of cases were found under the risks of tobacco, breastfeeding, and other factors. Among 227 participants, 96 participants (42%) were affected by Infiltrating Ductal Carcinoma, 48 participants (21%) were affected by Ductal Carcinoma, 35 participants (15%) were affected by Invasive Ductal Carcinoma, and 20 participants (9%) were affected by Metastatic adenocarcinoma. Only a few participants (26%) had a family history of BC. The main limitation of the study is the lack of information on individual risk factors for BC, such as pesticide exposure and occupational risk. It is reported that the individual risk factors correlate with the ambient soil pollution levels. Although measurements of pesticide exposures at certain selected locations may be used, they can result in misclassification of exposure because individuals may behave differently from the general population. Therefore, the current study is a preliminary attempt to assess the age-based response to environmental carcinogens. It was observed that a multi-disciplinary approach will be required to investigate the risk factors associated with BC along with traditional practices.

V. Conclusion

Through this, the study provides a directive to target treatment, preventive and awareness measures in terms of exposures, lifestyle, and behavior aspects. A multidisciplinary approach to BC, including awareness programs, preventive measures, screening programs for early detection, and availability of treatment facilities are vital for reducing both incidence and mortality of BC in Indian women. Although elucidating biological pathways is important, an association between environmental contaminants and cancers needs to be well established in terms of medical sciences. Such medical examinations and correlated results will provide an important contribution to the debate on reducing exposure to air, soil, and drinking water pollution.

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