Association between sociodemographic factors and estrogen receptor-positive, progesterone receptor-positive breast cancer subtypes: A cross-sectional study

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Abstract

Background: The presence of risk factors have a high risk of developing breast cancer. Our study aimed to find an association between sociodemographic factors and the risk of estrogen receptor (ER)-positive, progesterone receptor (PR)-positive breast cancer among women. **Methods**: A cross-sectional study was conducted on 200 women with breast cancer. Association between sociodemographic factors and hormone receptor subtypes of breast cancer was found using the Chi-square test. Multiple logistic regression analysis was used to know the strong predictors of hormone receptor subtypes. **Results**: The mean age was 50.08 (10.67) years. Comorbidities had a statistically significant association with ER-positive subtype ($p = 0.007$). Body mass index had a statistically significant association with PR-positive subtype ($p = 0.042$). Comorbidities was found to be the strong independent predictor for ER-positive (OR 2.28; 95% CI: 1.28–4.05, $p = 0.01$) and PR-positive subtypes (OR 1.78; 95% CI: 1.01–3.13, $p = 0.03$). **Conclusion**: We conclude that in our study, body mass index was associated with PR-positive subtype, and comorbidities were associated with ER-positive subtype of breast cancer among the women. Comorbidities remained to be a strong independent predictor of ER-positive and PR-positive subtypes of breast cancer.

Keywords: body mass index, breast cancer, comorbidities, estrogen receptor, progesterone receptor

Introduction

As per the World Health Organization, breast cancer accounts for 14% of all cancers among Indian women and killing 627,000 globally. In India, the incidence rates are high in the early thirties and reach its pinnacle between 50 and 64 years.[1] The risk of breast cancer grows exponentially, with the presence of risk factors such as age, age at menopause, menopausal status, age at first delivery, family history, breastfeeding history, number and spacing of births, use of oral contraceptives, diet, and physical activity. Many research studies reported a significant association between sociodemographic risk factors such as physical activity,[2] family history,[3] breastfeeding,[4] and body mass index (BMI),[5,6] comorbidities.[7–9] Awareness about these risk factors and education on managing modifiable risk factors can help prevent breast cancer to some extent.

Modifiable risk factors such as BMI and physical activity decrease the worsening of cancer and improve the remission response to the treatment. These factors do not bother the patients much. Comorbidities, however, cannot be modified but can be managed. Indeed, BMI and physical activity will influence the severity of the comorbidities. Awareness about these sociodemographic

factors in patients may help them to use for the remission. Our study aimed to know the association between sociodemographic factors and hormone receptor subtypes, namely, estrogen receptor (ER)-positive and progesterone receptor (PR)-positive, of breast cancer.

Methods

We carried out a descriptive cross-sectional study on 200 breast cancer patients, attending the Department of Medical Oncology and having confirmed diagnosis and hormone receptor subtypes of breast cancer. The study duration was six months (01/08/2019 to 31/01/2020).

Institutional Ethical Committee approved our study (VIPT/IEC/68/2019). We performed the study according to the guidelines outline in the Declaration of Helsinki, 1964. Informed consent was obtained from patients who were willing to participate.

Patients with the following criteria were included in the study: confirmed diagnosis, first time and referral patients, with comorbidities, and complete diagnostic data on receptor subtypes. Patients with the following criteria were excluded: with HIV as comorbidity,

critically ill patients, recurrent breast cancer, and referral to surgery.

Simple random sampling technique was used to select the breast cancer patients. The estimated sample size was 197 (margin of error 5%, the confidence level 95%, population size 400, and response distribution 50%).

Breast cancer cells with ERs are called ER-positive (ER+) and vice versa. Breast cancer cells with PRs are PR-positive (PR+) and vice versa. Menopausal status was defined by criteria based on Breast Cancer Surveillance Consortium.[10] Postmenopausal status was defined as age ≥55 years or report of natural menopause or removal of both ovaries or current use of hormone therapy or 365 days since last menstrual period. Premenopausal status was defined as no stopping of menstrual periods or ongoing use of birth control hormones or <180 days since last menstrual period. BMI was categorized based on the Asian population indices.[11] Patients with BMI <18.5 kg/m^2 were categorized as underweight, with BMI between 18.5 and 22.9 kg/m^2 as normal, with BMI between 23.0 and 24.9 kg/m^2 as overweight, and with BMI ≥25 kg/m^2 as obese. Physical activity was defined as performing activities like running or jogging intensely for at least three days a week with a minimum of 20 minutes per session for intense work-up or a minimum of 30 minutes per session for moderate work-up like for elderly.[12]

The data collection was divided into three parts. The first part deals with collecting sociodemographic details like age, marital status, comorbidities, menopausal status, physical activity, family history, number of live births, age at first delivery, and breastfeeding history. The second part consists of collecting clinical details like type of cancer, tumor grade, tumor size, lymph node status, type of treatment, and receptor status of breast cancer. The third part deals with tabulation and analysis of the data.

Frequencies and percentages were calculated for qualitative data. Shapiro-Wilk test was applied on the quantitative data. Based on the normality assumptions, data were represented as mean and standard deviation or median and interquartile range, whichever is appropriate. Chi-square test was performed to find out any significant association between independent variables and receptor status. Multivariate logistic regression analysis was performed to predict the independent risk factor for the hormone receptor subtype of breast cancer. Odds ratio and 95% confidence intervals were used to show the results of the analysis. The level of significance was considered at $p < 0.05$. Jeffrey's Amazing Statistics Program (JASP, version 0.12.1) software was used for the statistical analysis of the data.

Results

Table 1 presents an overview of the sociodemographic characteristics of the patients. The mean (SD) age of breast cancer patients in our study was 50.38 (10.67) years. The age group 41–55 was high (43.5%) in frequency. The frequency of patients without comorbidities (55.5%), no family history of breast cancer (90.5%), no history of breastfeeding (85.5%), no physical activity (66.0%) was high. The table also shows the high frequency of number of live births ≤ 3 (83.5%) and obese patients (45.0%).

Table 2 outlines the clinical characteristics of breast cancer patients in our study. Our study's most observed pathologic type of breast cancer was the invasive ductal type (89.0%). The frequency of patients with tumor size between 2 and 5 cm (60.5%), stage II (67.5%), and grade II tumors (66.0%) were high. Patients with lymph node status, N$_2$ (31.5%), and receiving three modalities of treatment (42.0%) were found to be high in frequency. ER-positive breast cancer patients account for 54%. PR-positive breast cancer patients account for 46%.

Table 1. Sociodemographic characteristics of the patients

Name of the characteristics	Frequency (%)
Age (in years)	
25–40	50 (25.0)
41–55	87 (43.5)
55–70	59 (29.5)
70–85	4 (2.0)
Comorbidities	
Yes	89 (44.5)
No	111 (55.5)
Physical Activity	
Yes	68 (34.0)
No	132 (66.0)
Family History	
Yes	19 (9.5)
No	181 (90.5)
Menopausal Status	
Premenopausal	175 (87.5)
Postmenopausal	25 (12.5)
Breastfeeding history	
Yes	29 (14.5)
No	171 (85.5)
No. of live births	
≤3	167 (83.5)
≥3	33 (16.5)
Body Mass Index	
Underweight	15 (7.5)
Normal	66 (33.0)
Overweight	29 (14.5)
Obese	90 (45.0)
Age at first pregnancy	
<30	176 (88.0)
≥30	24 (12.0)

Table 3 outlines the statistically significant association between comorbidities and estrogen receptor subtype. Table 4 depicts a significant association between BMI and progesterone receptor subtype.

Table 2. Clinical characteristics of the patients

Name of the characteristic	Frequency (%)
Pathologic type	
Invasive ductal	178 (89.0)
Invasive lobular	7 (3.5)
Medullary	8 (4.0)
Papillary	7 (3.5)
Tumor size	
T_1 (<2 cm)	12 (6.0)
T_2 (2–5 cm)	121 (60.5)
T_3 (>5 cm)	67 (33.5)
Tumor staging	
Stage I	17 (8.5)
Stage II	135 (67.5)
Stage III	48 (24.0)
Tumor grade	
Grade I	13 (6.5)
Grade II	132 (66.0)
Grade III	55 (27.5)
Lymph node status	
N_0 (0)	45 (22.5)
N_1 (1–3)	56 (28.0)
N_2 (4–9)	63 (31.5)
N_3 (≥10)	36 (18.0)
Estrogen receptor subtype	
Positive	108 (54.0)
Negative	92 (46.0)
Progesterone receptor subtype	
Positive	92 (46.0)
Negative	108 (54.0)
Type of treatment	
CT + RT + ET	84 (42.0)
CT + RT	78 (39.0)
CT	32 (16.0)
Others	6 (3.0)

CT: Chemotherapy, RT: Radiotherapy, ET: Endocrine Therapy, Others: RT (3) and ET (3).

Table 5 shows that the odds ratio of ER-positive patients with comorbidities are 2.28 times (OR = 2.28; 95% CI: 1.28–4.05; p = 0.01) than that of patients with no comorbidities. The odds ratio of PR-positive patients with comorbidities are 1.78 times (OR = 1.78; 95% CI: 1.01–3.13; p = 0.03) than that of patients with no comorbidities. We observed comorbidities as an independent risk factor for hormone receptor-positive subtypes of breast cancer.

Table 3. Association of sociodemographic variables with the estrogen receptor subtype

Sociodemographic variables	Estrogen receptor subtype		Total	p
	Positive	Negative		
Age in years				
25–40	24	26	50	
41–55	48	39	87	0.774
55–70	34	25	59	
70–85	2	2	4	
Physical activity				
No	75	57	132	0.265
Yes	33	35	68	
Family history				
No	94	87	181	0.070
Yes	14	5	19	
Body mass index				
Underweight	10	5	15	
Normal	35	31	66	0.322
Overweight	19	10	29	
Obese	44	46	90	
Menopausal status				
Premenopause	97	78	175	0.283
Postmenopause	11	14	25	
Breastfeeding history				
No	93	78	171	0.790
Yes	15	14	29	
Comorbidities				
Yes	58	31	89	0.007*
No	50	61	111	
No. of live births				
≤3	92	75	167	0.617
≥3	16	17	33	
Age at first pregnancy				
≤25 years	94	76	170	0.382
25–35 years	14	16	30	

*$p < 0.05$

Table 4. Association of sociodemographic variables with the progesterone receptor subtype

Sociodemographic variables	Progesterone receptor subtype		Total	p
	Positive	Negative		
Age in years				
25–40	20	30	50	
41–55	39	48	87	0.611
55–70	31	28	59	
70–85	2	2	4	
Physical activity				
No	63	69	132	0.494
Yes	29	39	68	
Family history				
No	81	100	181	0.274
Yes	11	8	19	
Body mass index				
Underweight	9	6	15	
Normal	24	42	66	0.042*
Overweight	19	10	29	
Obese	40	50	90	
Menopausal status				
Premenopause	83	92	175	0.283
Postmenopause	9	16	25	
Breastfeeding history				
No	78	93	171	0.790
Yes	14	15	29	
Comorbidities				
Yes	48	41	89	0.061
No	44	67	111	
No. of live births				
≤3	81	86	167	0.159
≥3	11	22	33	
Age at first pregnancy				
≤25 years	77	93	170	0.633
25–35	15	15	30	

*$p < 0.05$

Table 5. Multiple logistic regression analysis of sociodemographic variables and hormone receptor subtypes of breast cancer

Name of the variables	Estrogen receptor subtype		Progesterone receptor subtype	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.08 (0.65–2.19)	0.32	0.89 (0.37–1.25)	0.14
Family history	2.32 (0.89–7.49)	0.05	1.39 (0.65–4.14)	0.69
Comorbidities	2.28 (1.28–4.05)	0.01*	1.78 (1.01–3.13)	0.03*
Body mass index	0.59 (0.54–1.82)	0.55	1.52 (0.92–3.18)	0.05
Physical activity	1.19 (0.77–2.51)	0.16	1.29 (0.60–2.21)	0.69
Menopausal status	1.85 (0.68–3.68)	0.19	1.68 (0.67–3.82)	0.19
Breastfeeding history	1.31 (0.50–2.44)	0.47	0.98 (0.40–1.97)	0.47
No. of live births	1.28 (0.61–2.75)	0.30	1.68 (0.85–4.12)	0.07
Age at first pregnancy	0.74 (0.34–1.50)	0.24	1.27 (0.55–2.26)	0.38

*$p < 0.05$; OR= Odds Ratio; CI =Confidence Interval.

Discussion

The age group 41–55 years was found to be of high risk for breast cancer. Studies from India reported varying age groups ranging from 40 to 60 years.[13–15] Age at different points in women's lives, such as menarche, first pregnancy, menopause, increases the risk of breast cancer. Family history score (FHS) is a new methodology that considers the expected numbers of the family cohort, cumulative person-years in the family cohort, and corresponding national annual, age-specific breast cancer incidence rates. A combination of FHS and age at diagnosis of breast cancers in relatives would be a good predictor of breast cancer risk.[3]

Invasive ductal carcinoma was the most common form of breast cancer in our study. Two studies reported similar results.[16,17] The Majority of tumors belonged to T2 (2–5 cm) category, stage II, and grade II in our study. Prior study[18] reported similar findings to tumor category and grade. Other studies reported stage IV[17] and stage III[16] as predominant type of tumors. Lymph node involvement was reported by previous study[19]; however, the study did not specify the number of lymph nodes involved. ER-positive patients (54%) and PR-negative patients were high in our study. Few studies reported similar results for ER-positive patients.[16,17,19]

Hormone receptor subtypes influence the outcome of breast cancer patients. For example, preceding study[19] reported significantly improved overall survival in ER-positive and PR-positive patients than in ER-negative and PR-negative patients. Another study[20] also reported a decreased incidence of local and distant recurrence in ER-positive and PR-positive patients than in ER-negative and PR-negative patients.

Breastfeeding for a minimum duration of 12 months shown to decrease a 4% reduction of breast cancer.[21] A case-control study also reported a decreased risk in premenopausal women with a long breastfeeding duration.[22] Breastfeeding was associated with hormone receptor subtype of breast cancer. Previous study[4] reported a significant inverse association between ER-negative breast cancer and breastfeeding. Even a shorter duration of breastfeeding (<6 months) may decrease ER-negative breast cancer.

Unlike age, family history, we can modify physical activity and body mass index to decrease the risk of breast cancer. Vigorous physical activity and being overweight or obese, between 18–30 years, decrease the risk of breast cancer.[2] Hypothesized mechanisms include physical activity that decreases body fat, estrogen, and androgen levels. It modifies acquired immune response and promotes the elimination of cancer cells.[23,24] Being overweight or obese throughout adulthood increases the risk of postmenopausal breast cancer.[2]

We observed a significant association between BMI and the PR subtype. High BMI is a risk factor for breast cancer. However, the risk of breast cancer varies based on menopausal status. BMI increase, along with parity and menopausal status, constitutes a risk factor for ER-positive breast cancer. Previous study[5] observed that parity and an increase in BMI affected the risk of ER subtypes of breast cancer. Nulliparous women and an increase in BMI (5.0–9.9 kg/m^2 or ≥10 kg/m^2) decreased the risks of ER-positive breast cancer. However, a change in BMI was not related to the risk of ER-positive breast cancer among parous women.

A meta-analysis on the effect of BMI on menopausal status concluded that BMI has no significant effect on the incidence of breast cancer during the premenopausal period.[22] Another study[6] also reported a relation between higher BMI at the time of diagnosis of breast cancer and a higher risk of recurrence and death, specifically in hormone receptor-positive disease. Although a significant association was reported with hormone receptor-negative breast cancer, hormone receptor-positive breast cancer showed a stronger association with BMI.[25] Hypothesized mechanisms that explain the association between high BMI and recurrence/metastasis include insulin, a steroid hormone, adipokine, and inflammatory pathways. They may promote breast cancer cell proliferation and tumor growth.[6,26]

In our study, comorbidities were significantly associated with ER subtype breast cancer. Multiple logistic regression analysis results also suggested comorbidity as a strong independent risk factor for ER-positive and PR-positive breast cancers. Comorbidities affect the survival outcomes of patients with breast cancer and hormone receptor subtypes. For example, previous study[7] observed that premenopausal women with diabetes had more often PR-negative breast cancer. Another study[8] also reported a similar association between premenopausal diabetic women and PR-negative breast cancer. However, other study[27] reported a significant association between premenopausal women and ER-negative breast cancer. Earlier study[9] reported increased odds of triple-negative (ER-/PR-/HER-) breast cancer was higher among diabetic women or who had used a diabetes medication for a long duration before cancer diagnosis compared with nondiabetic women.

There are many reasons of how comorbidities decrease the overall disease prognosis: reduces the likelihood of receiving guideline-recommended treatment,[28–31] elevates the risk of chemotherapy-induced adverse effects,[32,33] and lower quality of life.[34] Hypertension and obesity

increase the risk of heart failure with trastuzumab, and worse functional health.[35,36]

Our study observed an association between BMI and comorbidities with PR and ER subtypes. Comorbidities were a strong independent risk factor for both ER-positive and PR-positive breast cancers. There are a few limitations to our study. As the sample size was small, we cannot generalize our findings for the women with ER or PR subtype of breast cancer. Due to the small sample size, we could not find which comorbidity was associated with the hormone receptor subtypes.

Conclusion

We conclude in our study that BMI and comorbidities are associated with PR and ER subtypes, respectively. Comorbidity was found to be a strong independent risk factor for both ER-positive and PR-positive breast cancer patients in our study.

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Conflict of Interest Statement

The authors declare no conflicts of interest.

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