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Clinico-Epidemiological and Pathological Characteristics of Breast Cancer in Young Women (<40 Years).

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ABSTRACT

Background: Breast cancer in young women (BCYW) is showing an increasing trend in incidence among women of India and other Asian countries compared to western countries. **Methods:** A retrospective study was carried out on total 579 patients treated between January 2010 and December 2017 to evaluate the clinico-epidemiological and pathological characteristics in BCYW. Cases were divided into two groups i.e the younger (<40 years) and the older (≥40 years) age group. Data were analyzed by chi square test using IBM SPSS version 21 for windows. P value less than 0.05 was considered significant. **Results:** The breast cancer in younger women (<40 years) was found in 20.2% of cases and was found to have greater proportion of unmarried women (p=0.002), higher frequency of nulliparity (p=0.006), greater incidence of bilateral breast cancer (p=0.017), greater incidence of multifocal or multicentric tumour (p=0.033), higher grade tumours (p=0.007), advanced T stage (p=0.003), advanced N stage (p=0.012) and overall advanced TNM stage (p=0.011) at diagnosis, higher frequency of lymphovascular invasion (p=0.00013), higher frequency of estrogen and progesterone receptor negativity (p=0.0005 and 0.0001 respectively). HER-2 expression rate was not found different between the two groups, whereas its expression rate was found significantly lower among women of age >50 years at diagnosis (p=0.001). Higher frequency of triple negative breast cancer was found in the younger age group (33.3% vs. 19.3%, p=0.001). **Conclusions:** Advanced stage presentation of BCYW warrants inclusion of younger age women in breast cancer screening and encouraging for breast self-examination.

Keywords: Breast cancer, Clinico-epidemiology, Pathology, Young women.

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INTRODUCTION

Globally breast cancer is the commonest cancer (24.2%) among females with an estimated incidence of 2.1 million in the year 2018 and it is the commonest cause of cancer mortality in female (15%). Similarly it is the most common type of cancer and cancer specific mortality in females of India (15.46% and 12.11% respectively).[1] Worldwide, breast cancer presents as a disease of elderly women. Whereas in India and South Asian countries, the average age of diagnosis of breast cancer has shifted towards younger age. Breast cancers in Indian women are found a decade earlier than that of western countries, found commonly in younger premenopausal women in India.[2] Previous study has shown that breast cancer diagnosed at younger age has poorer outcome probably because of more aggressive tumour biology and late presentation.[3] Late presentation of breast cancer in young women could be due to heavy glandular breast tissue delaying the detection of any breast lump and lack of breast screening in women of younger age group. The objective of present study was to study the clinico-epidemiological and pathological characteristics in young women (<40 years of age) diagnosed with breast cancer and it's comparison with breast cancer of older age group (≥40 years).

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MATERIALS & METHODS

All newly diagnosed and histopathologically proven cases of primary breast cancer registered between January 2010 and December 2017 were included in the study population. Detailed information of different clinico-epidemiological and pathological parameters was retrieved from the individual patient file from the record section of the Department of Radiotherapy of the Regional Cancer Centre, Regional Institute of Medical Science, Imphal after taking permission from the concerned authority. Cases with incomplete data were excluded from the study. Data of all pathological parameters including

nodal staging were obtained. All hormone receptor status was tested using immunohistochemistry (IHC) except for those cases with equivocal result for HER-2 by IHC, which were confirmed by Fluorescent In-Situ Hybridization (FISH). Total number of patients was divided into two groups with patients diagnosed at <40 years of age were taken in the younger age group and those diagnosed at ≥40 years of age were taken in the older age group. Cancer staging was done using AJCC 8th (2017) edition. Statistical analysis of different clinico-epidemiological and pathological parameters was performed by chi square test using IBM SPSS statistical package version 21 for windows. P value less than 0.05 was considered significant.

RESULTS

Important clinico-epidemiological and pathological characteristics have been highlighted in the [Table 1] and table 2 respectively.

Clinico-epidemiological characteristics: A total of 579 newly diagnosed patients of breast cancer were recruited randomly in the study. Out of which 20.2% were diagnosed at <40 years of age. The overall mean age at diagnosis was 52 year (± 12.26, range of 22 - 87), it was 34.94 year (± 3.97) for younger age group and 55.87 year (± 9.8) for older age group. Younger age group had greater proportions of unmarried women (6% vs. 1.3%, p value 0.000), greater proportions of nulliparous women (7.7% vs. 1.5%, p value 0.006). The age of menarche and family history of breast cancer was not found significantly different between the two groups (p value 0.540 and 0.094 respectively). Most common presenting symptom in both the age group was painless breast lump, whereas greater proportion of patients in the younger age group presented with breast lump with nipple discharge (6% vs. 2.4%, p value 0.035). Disease at presentation was most common in left breast (upper outer quadrant) in both the group, whereas bilateral breast cancer was found significantly more in the younger age group (4.3% vs. 0.9%, p value 0.017). Multifocal or multicentric tumours were found more frequently in the younger age group (6% vs. 2.2%, p value 0.033). BIRADS 5 lesions were most common mammographic findings in both the age group (p value 0.138).

Pathological characteristics

Histopathological type most commonly found in both the age group was invasive ductal carcinoma (IDC). Greater proportions of younger women were found to have high grade tumours (76.1% vs. 60.2%, p value 0.007). Cases in younger age group were commonly diagnosed in advanced T stage (T3 and T4 disease collectively constituted 50.4% vs. 37.6% in older age group with p value 0.003), advanced N stage (N2 and N3 disease collectively constituted 40.2% vs. 27.1% in older age group with p value 0.012). The overall TNM stage at diagnosis was found to be significantly advanced in the younger age group (stage 3 and 4 disease collectively constituted 65.8% vs. 49.2% in older age group with p value 0.011), whereas metastasis rate at initial diagnosis was not found significantly different in both the age group (9.4% vs. 8% in younger and older age group respectively with p value 0.612). Young women with breast cancer were found to have significantly higher rate of positive lymphovascular invasion (56.4% vs. 36.6%, p value 0.00013). Nipple areolar complex (NAC) involvement was found more among young women and the difference was not significant (p value 0.060). The rate of perineural invasion (PNI) and extensive intraductal component (EIC) was not found different in both the age group (p value 0.343 and 0.852 respectively). Estrogen receptor and progesterone receptor expression rate was found significantly lesser among young women (29.9% vs. 47.6% with p value 0.0005 and 26.5% vs. 46.1% with p value 0.0001 respectively). The rate of HER-2 expression was not different between the two age groups (p value 0.074). When the older age group was divided into sub groups of 40-50 years and >50 years, we got significantly lesser rate of expression of HER-2 among women of >50 years as compared to women of 40-50 years or <40 years old (38.5% vs. 57.2% vs. 56.5% respectively with p value 0.001). The rate of triple negative breast cancer (TNBC) was found significantly higher in the younger age group (33.3% vs. 19.3% with p value 0.001). There was no difference in site of metastasis at diagnosis between the two age groups (p value 0.803).

Table 1: Clinico epidemiological characteristics.

Parameters	"Study group" Age < 40 years (N=117)	"Control group" Age ≥ 40 years (N=462)	P value
Age (in years)			
Mean	34.97 (± 3.97)	55.89 (± 9.8)	
Range	22-39	40-87	
Age of Menarche (in years)			
11	27 (23.1%)	96 (20.8%)	
12	59 (50.4%)	219 (47.4%)	
13	28 (23.9%)	128 (27.7%)	0.540
14	0	5 (1.1%)	
Unknown	3 (2.6%)	14 (3%)	
Marital status			

Married	109 (93.2%)	450 (97.4%)	
Unmarried	7 (6%)	6 (1.3%)	0.002
Unknown	1 (0.9%)	6 (1.3%)	
Parity			
Nulliparous	9 (7.7%)	7 (1.5%)	
Monoparous	51 (43.6%)	189 (40.9%)	0.006
Multiparous	56 (47.9%)	260 (56.3%)	
Unknown	1 (0.9%)	6 (1.3%)	
Family history			
Present	5 (4.3%)	8 (1.7%)	
Absent	109 (93.2%)	446 96.5%)	0.094
Unknown	3 (2.6%)	8 1.7%)	
Symptoms			
Painless lump	102 (87.2%)	433 (93.7%)	
Lump + discharge	7 (6%)	11 (2.4%)	
Pain	5 (4.3%)	8 (1.7%)	0.035
Retraction	0	6 (1.3%)	
Unknown	3 (2.6%)	4 (0.9%)	
Side			
Right	49 (41.9%)	226 (48.9%)	
Left	63 (53.8%)	232 (50.2%)	0.017
Bilateral	5 (4.3%)	4 (0.9%)	
Quadrant			
Upper outer	87 (74.4%)	359 (77.7%)	
Lower outer	4 (3.4%)	11 (2.4%)	
Lower inner	2 (1.7%)	7 (1.5%)	
Upper inner	11 (9.4%)	26 (5.6%)	0.509
Central	6 (5.1%)	24 (5.4%)	
All quadrants	4 (3.4%)	9 (1.9%)	
Unknown	3 (2.6%)	26 (5.6%)	
Multifocal or Multicentric disease			
Yes	7 (6%)	10 (2.2%)	0.033
No	105 (89.7%)	421 (91.1%)	
Unknown	5 (4.3%)	31 (6.7%)	
BIRADS			
3	1 (0.9%)	0	
4	28 (23.9%)	115 (24.9%)	
5	81 (69.2%)	315 (68.2%)	0.138
Unknown	7 (6%)	32 (6.9%)	

Table 2: Pathological characteristics.

Parameters	Age < 40 years (N=117)	Age ≥ 40 years (N=462)	P value
Histopathology			
DCIS	0	2 (0.4%)	
LCIS	0	8 (1.7%)	
IDC	103 (88%)	381 (82.5%)	
ILC	7 (6%)	17 (3.7%)	
Medullary	1 (0.9%)	11 (2.4%)	0.774
Mucinous	1 (0.9%)	7 (1.5%)	
Metaplastic	2 (1.7%)	5 (1.1%)	
Others	1 (0.9%)	6 (1.3%)	
Unknown	2 (1.7%)	25 (5.4%)	
Grade			
High	89 (76.1%)	278 (60.2%)	
Intermidiate	11 (9.4%)	67 (14.5%)	0.007
Low	15 (12.8%)	105 (22.7%)	
Unknown	2 (1.7%)	12 (2.6%)	
T stage			
T1	11 (9.4%)	56 (12.1%)	
T2	14 (12%)	225 (48.7%)	0.003
T3	50 (42.7%)	118 (25.5%)	
T4	9 (7.7%)	56 (12.1%)	
Unknown	3 (2.6%)	7 (1.5%)	
N stage			
N0	29 (24.8%)	162 (35.1%)	
N1	38 (32.5%)	168 (36.4%)	0.012
N2	27 (23.1%)	85 (18.4%)	
N3	20 (17.1%)	40 (8.7%)	
Unknown	3 (2.6%)	7 (1.5%)	
Metastasis			
Present	11 (9.4%)	37 (8%)	
Absent	104 (88.9%)	420 (90.9%)	0.612
Unknown	2 (1.7%)	5 (1.1%)	

TNM stage			
1	4 (3.4%)	34 (7.4%)	
2	34 (29.1%)	194 (42%)	0.011
3	66 (56.4%)	193 (41.8%)	
4	11 (9.4%)	34 (7.4%)	
Unknown	2 (1.7%)	7	
LVI			
Present	66 (56.4%)	169 (36.6%)	0.00013
Absent	50 (42.7%)	284 (61.5%)	
Unknown	1 (0.9%)	9 (1.9%)	
PNI			
Present	24 (20.5%)	78 (16.9%)	
Absent	64 (54.7%)	269 (58.2%)	0.343
Unknown	29 (24.8%)	115 (24.9%)	
NAC			
Yes	4 (3.4%)	5 (1.1%)	
No	82 (70.1%)	344 (74.5%)	0.060
Unknown	31 (26.5%)	113 (24.4%)	
EIC			
Present	8 (6.8%)	35 (7.6%)	0.852
Absent	77 (65.8%)	312 (67.5%)	
Unknown	32 (27.4%)	15 (3.2%)	
Estrogen receptor			
Positive	35 (29.9%)	220 (47.6%)	
Negative	80 (68.4%)	233 (50.4%)	0.0005
Unknown	2 (1.7%)	9 (1.9%)	
Progesterone receptor			
Positive	31(26.5%)	213(46.1%)	
Negative	84 (71.8%)	240(51.9%)	0.0001
Unknown	2 (1.7%)	9 (1.9%)	
HER 2			
Positive	65 (55.6%)	203 (43.9%)	
Negative	50 (42.7%)	249 (53.9%)	0.074
Unknown	2 (1.7%)	10 (2.2%)	
TNBC			
Yes	39 (33.3%)	89 (19.3%)	
No	76 (65%)	363 (78.6%)	0.001
Unknown	2 (1.7%)	10 (2.2%)	
Site of metastasis			
Bone	3 (2.6%)	9 (1.9%)	
Brain	2 (1.7%)	7 (1.5%)	0.803
Liver	2 (1.7%)	8 (1.7%)	
Lung	4 (3.4%)	8 (1.7%)	
Pleural fluid	0	3 (0.6%)	

DISCUSSION & CONCLUSION

Clinico-epidemiological characteristics: Breast cancer in young women (BCYW) has become a growing concern in India and Asian countries because of its rising trend and greater incidence, which is two folds higher than western countries.[4] Its burden has increased significantly in last few decades, particularly in the age group of 30-40 years (from 13.34% to 24.78% between 1970 to 2002).[5] Annual incidence of BCYW (<40 years) occurs in approximately 5-7.5% of the total breast cancer cases in Western Europe and USA.[6] Desmukh et al,[7] have reported its incidence in North India to be 14.8%. Whereas, our study has shown its incidence to be 20.2% in North East India. Positive family history of breast cancer is a strong risk factor for BCYW, which suggest the presence of familial cancer syndrome especially in women harboring germline mutation of BRCA1 gene.[8] BCYW are found to have poor survival outcome, but whether it is due to aggressive tumour biology or young age which itself is a poor prognostic factor is still not very clear. In our study, the proportion of unmarried women was more among younger age group, which was in concordance with Tehranian N et al.[9] In the present study, more proportion of cases in younger age group were nulliparous and there was no difference in age of menarche between the two age groups, which was contradictory to the finding of Tehranian N et al,[9] where they have found higher parity status and earlier age of menarche among younger women. Houssami N et al,[10] has shown the sensitivity of mammography to be significantly lesser among younger age group as compared to older age group particularly in detecting small sized lesions, whereas there was no significant difference in mammographic findings between the two group in our study, probably because of advanced tumour stage at presentation in most cases.

Pathological characteristics:

Most common histopathological type in both the group was invasive ductal carcinoma. Most of the BCYW constitute high grade tumours and was in concordance with previous studies.[7,11-17] In our study, BCYW were diagnosed commonly at advanced T and N stage and advanced overall stage

at diagnosis with most cases being diagnosed in stage 3, which was in concordance with previous study.[18] There was no significant difference between initial rate of metastasis during diagnosis. In our study, BCYW was associated with significantly higher rate of lymphovascular invasion (LVI), Similar finding was also found in other studies.[7,14,16,18] Our study showed the rate of estrogen receptor and progesterone receptor expression to be significantly lesser in the younger age group. This finding was in concordance with findings of other studies.[11,13,16,18,19] We did not find significant difference in HER-2 expression between the study and control group. This finding was in concordance with the findings of Sharma D et al.[18] Whereas, when older age group was divided into two sub groups i.e. 40-50 years and >50 years, we got significantly lesser rate of HER-2 expression in >50 years women (p value 0.001). In the present study, there was significantly higher rate of TNBC in younger age group, as seen similarly in previous studies.[8,19,21,22] Rosales AM et al,[22] in their study found hormone receptor (ER/PR) negativity and TNBC to be associated with higher rate of distant metastasis in BCYW. Previous studies have shown that adverse clinicopathological factors like advanced stage, high grade, LVI, PNI, hormone receptor negativity (ER/PR) are associated with poor survival outcome in BCYW.[7,11,17] Anders CK et al,[16] have suggested that apart from aggressive tumour biology, young age itself is an independent poor prognostic factor in breast cancer cases, Whereas Lee MK et al,[23] have shown that BCYW can have similar survival outcome as that of breast cancer in older women, if they are diagnosed in early stage and it needs more aggressive treatment. Majority cases of BCYW in our study were diagnosed in advanced stage probably because of lack of awareness of breast cancer incidence in young women and lack of breast cancer screening in this age group, late detection of breast lump because of dense breast tissue in younger age group, changing lifestyle of present day women.

Because of its increasing incidence trend, aggressive tumour behavior, late stage at presentation, breast cancer in young women has become a challenging task for oncologist in terms of early diagnosis and optimization of multimodality treatments. Therefore early breast screening programme, breast self examination, public awareness campaign on young age breast cancer should be encouraged for early detection of this disease. These women should be tested for BRCA 1/2 mutations to rule out hereditary breast cancer. Younger women with breast cancer require greater psychosocial support during and after treatment because of increased probability of emotional distress as compared to older breast cancer patients.

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