

An institutional review of tumour biology of breast cancer in young Nepalese women

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Abstract

Introduction: Breast cancers in less than 40 years of age group usually present with aggressive biology and has poor prognosis. The aim of this study was to see clinic-pathological and hormone receptors of breast cancers in young women and compare with less than 40 year age group.

Methods: Prospective analysis of 97 breast cancer in patients less than 40 years out of total 373 patients (26%) over a period of 8 years (2007 Jan to 2014 Dec) was carried out at the Department of Surgery, Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

Result: Among the young women diagnosed with breast cancer, the mean age was 34.5±6.2 years. Mean tumour size was larger in younger women (5±2.5 vs 4.5±2.4 cm). Locally advanced disease was higher in younger patients (55% vs 47%). Lymphatic and vascular invasions were higher (63% vs 35% and 40% vs 25%). Grade II and III tumours was higher (56% vs 25%). ER, PR and HER2 positivity was detected in 46.9%, 48.9% and 28.9% respectively. Significant lower ER or PR expression (34.5% vs 54%) was seen in younger women, p=.002. Triple negative tumours (ER -ve, PR -ve and HER2 -ve) was proportionately higher in younger patients (23% vs 13.7%, p=.043).

Conclusion: Young Nepali women presents one quarter of all female breast cancers, more frequently locally advanced with aggressive tumour biology like ER/PR negative and triple negative breast cancers.

Keywords: Breast cancer; ER; HER2 neu; PR.

Introduction

Breast cancer is the most common cancer in women comprising 23% of all the cancer in women and is the leading cause of cancer death in women, with an estimated 1.15 million new cases per year¹. Breast cancer is a heterogeneous group of tumour with variable morphology, behaviour, response to therapy, and molecular profile. Tumour with similar clinic-pathological presentations have different behaviours. Young women develop more aggressive subtypes of breast cancer². Young age remains an independent risk factor for poor survival in breast cancer. Breast cancer incidence rate in young is low compared to elder population but it has unique biological features that are not observed in elder population³. Young breast cancer represents 5-7% of all breast cancer in developed

world whereas same incidence rate in developing countries is around 25%⁴. Young patients tend to have more ER-negative, higher grade, and have increased, Ki-67, and p53 with same HER 2 neu expression⁵. Diagnostic delay often occurs in young patient resulting advanced disease in initial presentation because of younger women themselves unaware of breast cancer and by physicians who are less suspicious of this disease in young patients⁶.

This study has been undertaken to look into incidence and tumour biology of breast cancer represented by the expression of hormone receptor status in young patient age less than 40 years and compare with older population in the same time frame.

Methods

This was a prospective study conducted in the Department of Surgery in Tribhuvan University Teaching Hospital, Maharajgunj Kathmandu Nepal from January 2007 to December 2013. Consecutive breast cancer patients who were operated in the institute were included in the study. Early Breast cancer patients were taken for upfront surgery either Modified Radical Mastectomy or Breast Conserving Surgery if qualified. (Figure 1) Locally advanced breast cancer patients were considered for neo-adjuvant chemotherapy and subsequently taken for surgery. Various parameters like demography, clinical history, tumour characteristics, treatment, histopathology and immunohistochemistry for hormone receptor: ER, PR, HER2 neu status were analysed. These parameters were analysed and compared between two age groups age less than 40 years considered as young breast cancer patients and that more than 40 years age group were considered as elder breast cancer patients. Clinic-pathological characteristics and tumour biology as expressed by hormone receptor status were analysed among these two groups.

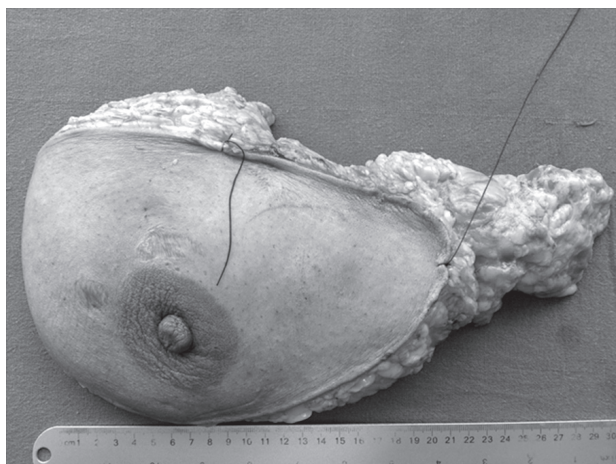


Figure 1: Modified Radical Mastectomy Specimen

The categorical data was analysed using Chi square/ Fisher exact test wherever applicable. The ordinal data like tumour grading was analysed by applying Chi square linear trend test. The student's t test was applied to compare continuous data in two groups. Computer software (SPSS/PC 20 version) was used to analyse the data. All the p- values less than 0.05 was considered as statistically significant.

Results

Comparative analysis of patient demography, tumour characteristics and tumour biology were done between age

less than 40 years and age more than 40 years. Total number breast cancer patients were 373 among them 97 (26%) were from less than 40 years age whereas 276 (74%) were from more than 40 years age group. Earliest age presenting with breast cancer is 22 years. Mean age at presentation in less than 40 years age group is 34.5±6.2 years and that in more than 40 years age group is 54.1±9.9 years. Higher percentage of breast cancer was from age less than 40 years from Tibeto-Burman descent compared to urban residents. (Table 1)

Table.1: Comparison of patient and tumour characteristics

Study groups	< 40 years patients	≥40 years patients	p- value
Number	97 (26%)	276 (74%)	
Mean age (years)	34.5±6.2	54.1±9.9	
Tibeto-Burman	56 (58.2%)	135(49.2%)	0.045
Urban Residents	42 (56.7%)	131(47.4%)	0.051
Mean menarche age(years)	13.5±1.5	14.2±1.5	0.001
Mean symptom duration(months)	7.6±6.5	6.5±5.7	0.004
Breast conserving surgery	27 (25.1%)	29(8.7%)	0.001
Neoadjuvant chemotherapy	54(55.1%)	126(47.1%)	0.001
Mean tumor diameter(cm)	5±2.5	4.5±2.4	0.005
Axillary lymph node positivity	71 (73%)	163(59%)	0.02
Locally advanced breast cancer	53(55.1%)	130(47.1%)	0.049
Ductal carcinoma variant	93(93.1%)	237 (86%)	0.4
Histological grade II or III	54(55.9%)	68 (24.5%)	0.002
Lymphatic invasion	61 (63.2%)	94(34.3%)	0.010
Vascular Invasion	38 (39.8%)	70 (25.4%)	0.020

Mean tumour diameter was statistically significantly higher in age less than 40 years 5 ± 2.5 cm compared to 4.5 ± 2.4 cm in age more than 40 years. In age less than 40 years age group 73%, 71 patients out of 97 patients had palpable axillary lymph nodes compared to 59%, 163 out of 276 among age more than 40 years age group. In more than 40 years age group more percentage of patients 55% (53 out of 97) presented as locally advanced breast cancer compared to 47% (130 out of 276) in more than 40 years age group.

Ninety percentage of breast cancer were of ductal carcinoma variants. Comparing histological grade between two groups Grade II and III tumours were higher in age less than 40 years group presenting as 55.9% (54 out of 97) compared to 24.5% (68 out of 276) in age more than 40 years age group. Lymphatic invasions were as much as 63.2% (61 out of 97) in age less than 40 years age group compared to 34.3% (94 out of 276) in age more than 40 years age group. Vascular invasions were also higher in age less than 40 years 39.8% (38 out of 97) versus 25.4% (70 out of 276) in age more than 40 years group.

On Immunohistochemistry analysis overall ER positivity rate 46.9% (175 out of 373), PR positivity rate 48.9% (182 out of 276) and HER2neu positivity 28.9% (108 out of 373). We studied hormone receptor status between two groups and compared the tumour biology. ER and/or PR positivity were less among less than 40 years age group 34.5% (33 out of 97) compared to 54% (149 out of 276) in age more than 40 years age group. (Table 2) There was not any statistical significant difference in HER 2neu positivity between two groups 26.4% in age less than 40 years versus 29.8% in age more than 40 years group. There was statistically significant difference in triple negative breast cancer in age less than 40 years compared to more than 40 years age group. In age less than 40 years age group 23% (22 out of 97) were triple negative breast cancer compared to 13.7% (38 out of 276) in age more than 40 years age group (p value 0.043).

Table 2: Comparison of ER PR HER 2 neu expression between two groups

Study groups	< 40 years patients	≥40 years patients	p-value
ER &/or PR positivity	33 /97 (34.5%)	149/276 (54%)	0.002
HER2 positivity	26/97 (26.4%)	82/276 (29.8%)	0.595
Triple negative tumors	27/97 (23%)	38/276 (13.7%)	0.043

Discussion

Young breast cancer presents with different tumour morphology and tumour biology compared to older patients. Young breast cancer patients usually present late and present with aggressive cancer and with adverse tumour biology compared to older breast cancer⁷. Incidence of young breast cancer is low in developed country corresponding to around 5-7% whereas incidence in Asian countries is high 25% being diagnosed at less than 40 years⁸. Young breast cancer comprises of 26% of total breast cancer patients in our study. Younger patients presented late mean duration of symptoms 7.6 ± 6.5 months versus 6.5 ± 5.7 in more than 40 years age group which was significant statistically. The diagnostic delay in young patients is usually due to patients themselves, as they are often less concerned about and aware of breast cancer, and by physicians, who have less suspicion of this disease in younger women⁹. Palpable lymph nodes present in axillae breast cancer represent aggressive and likely to have systemic disease compared to non-palpable axillary lymph nodes¹⁰. Young breast cancer patients had axillary lymph nodes palpable in 73% of the patients compared to 59% in breast cancer patients in age more than 40 years age group. Young breast cancer patients were more of locally advanced breast cancer 55% compared to 47.1% in age more than 40 years patient. Tumour size and lympho-vascular invasion is independent indicator of node negative breast cancer. Lympho-vascular invasion is a measure of metastatic potential that becomes severe when the tumour size is large¹¹. Ductal carcinoma of breast was major variant of breast cancer in this study accounting for 93.1%. Higher pathological grade of tumour, grade II and III was present in young breast cancer patients. Young breast cancer patients present with significant high percentage of lymphatic and vascular emboli in their pathological specimen compared to old breast cancer patients. Young breast cancer patients presents with aggressive histopathology indicator.

ER receptor pathway plays a critical role in the pathophysiology of human breast cancer. ER receptor is a well-established predictive and prognostic factor in breast cancer patients¹². PR is surrogate marker for ER. Overexpression of PR indicates that ER receptor pathway is intact even if ER is reported as negative. ER positive patients usually benefit from targeted hormonal therapy in adjuvant or palliative setting. ER positive tumours have usual association with older age, favourable nuclear histology and low proliferative index¹³. Lack of ER receptor has been consistently associated with poorer prognosis¹⁴. In this study, ER positivity is less in age less than 40 years age group 34.5% compared to 54% ER positivity in older age

group patients which had significant p value. HER2 neu another proliferative marker in breast cancer is associated with poor disease free survival rate in lymph node positive cancer patients¹⁵. However, this study showed no difference in expression of HER2neu receptor between young breast cancer patients and old breast cancer patients.

Triple negative breast cancer (TNBC) associated with distinct clinical and pathologic characteristics such as diagnosis at younger age and with higher grade¹⁶. Lack of established receptors reduces the therapeutic options and remains a challenge to treat by targeted therapy¹⁷. Patients with BRCA1 mutation tend to have ER, PR and HER 2 neu receptors negative and presents with higher grade¹⁸. In this study, there is statistically significant high percentage of triple negative breast cancer in less than 40 years age group compared to more than 40 years age group patients. Breast tumour biology is more aggressive and is associated with an unfavourable prognosis in younger women¹⁹. In this study, young breast cancer patients was found to have adverse tumour biology with more patients with TNBC, more patients with ER negative tumour, more of lymph node positivity and with higher grade compared to old breast cancer patients.

Conclusion

Young Nepalese women present one quarter of all female breast cancers, more frequently locally advanced with aggressive tumour biology like ER/PR negative and triple negative breast cancers.

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