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Does triple negative breast cancer subtype carry poorer prognosis as compared to non-triple negative breast cancer lesion - A study from a tertiary hospital

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ABSTRACT

Background: The breast cancer (BC), in spite of tremendous advances has continue to remain an enigma. The major change in understanding of BC has taken place after understanding of molecular biology. **Aims and Objectives:** The objectives are as follows:(1) To categorize the incidence of triple negative BC (TNBC) in hospital based data. (2) To study the prognostic outcomes of TNBC. **Materials and Methods:** The study was an observational prospective for the period of 18th months, from February 2014 to August 2015, where total 146 cases were selected. The data regarding age, sex, tumor size, stage, grade, nodal status, Nottingham prognostic index (NPI), morphology was noted. All patients underwent immunohistochemistry (IHC) study, maintaining higher quality assurance in the same IHC laboratory. **Results**: Our study revealed that out of 146 patients, 71 patients are TNBC. The mean age of presentation was 54.06 years in TNBC group. About 69.0% patients presented with Grade III tumor and 74.6% patient presented with NPI ≥5.4 among TNBC. However, 56% patients presented with NPI ≥5.4 among NON TNBC. Most of the morphological variant was IDC (95.8%), 85.9% patients presented with only lymph nodes metastasis among TNBC. **Conclusion:** The study is tremendously significant from Indian perspective. It proofs that TNBC had the point of diagnosis, seems to be more aggressive. It suggests that Indian BC is likely to be younger at presentation as compared to its Western counterpart.

Key words: Breast cancer; Triple negative breast cancer; Immunohistochemistry; Nottingham prognostic index; Non triple negative breast cancer

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INTRODUCTION

The breast cancer (BC), in spite of tremendous advances, has continued to remain an enigma. The major change in understanding of BC has taken place after understanding of molecular biology. Through morphological characteristic, such as tumor size, nodal status, grade, and Nottingham prognostic index (NPI) continues to be pivotal, paradigm shift has gradually put molecular subtype as the central focus. Internationally triple negative BC (TNBC) has been looked on as a poor oncological type. Indian data on this issue scares. Moreover, it is argued that Indian BC is a decayed younger than its Western counterpart and is likely to be more basal in origin.

Aims and objectives

Aims

The aims of the study were to evaluate the clinico-pathological profile of TNBC and non-TNBC.

Objectives

The objectives of this study are as follows–

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1. To categorize the incidence of TNBC in hospital based data
2. To study the prognostic outcomes of TNBC.

MATERIALS AND METHODS

The study was conducted in the Department of surgery, SSKM Hospital and Comprehensive Breast Clinic Service at S. N. Pandit Hospital, Kolkata from February 2014 to August 2015. All the patients with diagnosis of TNBC and Non TNBC were included in the study. All the patients with diagnosis of other benign breast diseases and male BC were excluded from the study. The study was an observational prospective one, where total 146 cases were selected. The data regarding age, sex, tumor size, stage, grade, nodal status, NPI, morphology was noted. All patients underwent immunohistochemistry (IHC) study maintaining higher quality assurance in the same IHC laboratory (Figures 1-3).

Comparison was made focusing on (a) The incidences of TNBC versus non TNBC Lesions. (b) Association between age, sex, grade, stage, nodal status, NPI, morphological character of TNBC, and non-TNBC Lesions. Student's independent sample's t-test was applied to compare normally distributed numerical variables between groups; unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. The whole study was conducted within the available government facilities.

RESULTS

Our study revealed that out of 146 patients, 71 patients are TNBC. We have seen that 26% patients are Luminal A type, 6.8% patients are Luminal B type and 18.5% patients are human epidermal growth factor receptor 2 type (Table 1).

The mean age of presentation was 54.06 years in TNBC group, where in non-TNBC group, the mean age of presentation was 53.68 years (Table 2).

Among TNBC, proportion of postmenopausal patients (84.5%) was significantly higher than that of premenopausal patients (15.5%) (Table 3). The study showed all cases presented among TNBC from Stage II to Stage IV in which about 61 (89.7%) cases fall into the Stage III group (Table 3). This study also revealed, among TNBC, 9.9% patients presented with tumor size <2 cm, 32.4% patients presented with tumor size, 2.0–4.9 cm and 57.7% patients presented with tumor size >4.9 cm (Table 3). Our study

Table 1: Distribution of molecular subtype in patients

Group	Frequency (%)
Luminal A	38 (26.0)
Luminal B	10 (6.8)
HER	27 (18.5)
TNBC	71 (48.6)
Total	146 (100.0)

TNBC: Triple negative breast cancer, HER: Human epidermal growth factor

Table 2: Age distribution of triple negative breast cancer and nontriple negative breast cancer patients

Age (years)	Group (%)		
	Non-TNBC	TNBC	Total
≤30	4	1	5
Row	80.0	20.0	100.0
Column	5.3	1.4	3.4
31–40	33	14	47
Row	70.2	29.8	100.0
Column	44.0	19.7	32.2
41–50	24	38	62
Row	38.7	61.3	100.0
Column	32.0	53.5	42.5
51–60	13	13	26
Row	50.0	50.0	100.0
Column	17.3	18.3	17.8
>60	1	5	6
Row	16.7	83.3	100.0
Column	1.3	7.0	4.1
Total	75	71	146
Row	51.4	48.6	100.0
Column	100.0	100.0	100.0

TNBC: Triple negative breast cancer

Table 3: Distribution according to clinico-pathological parameters

Clinico-pathological parameters	TNBC, n (%)	Non-TNBC, n (%)	P
Menopausal status			
Premenopausal	11 (27.5)	29 (72.5)	<0.001*
Postmenopausal	60 (56.6)	46 (43.4)	
Stage			
I	0	3 (100.0)	<0.001*
II	2 (5.9)	32 (94.1)	
III	61 (62.2)	37 (37.8)	
IV	8 (72.7)	3 (27.3)	
Tumour size (cm)			
<2	7 (70.0)	3 (30.0)	0.0019
2–4.99	23 (33.3)	46 (66.7)	
≥5.00	41 (61.2)	26 (38.8)	
Nodal status			
0	2 (50.0)	2 (50.0)	<0.001*
1–3	5 (8.2)	56 (91.8)	
4–9	37 (72.5)	14 (27.5)	
>9	27 (90.0)	3 (10.0)	
Grade			
1	4 (33.3)	8 (66.7)	<0.001
2	18 (40.9)	26 (59.1)	
3	49 (54.4)	41 (45.6)	
NPI			
≤5.4	18 (35.3)	33 (64.7)	0.018*
>5.4	53 (55.8)	42 (44.2)	

TNBC: Triple negative breast cancer, NPI: Nottingham prognostic index

showed that only 2.8% cases presented without any lymph nodes metastasis, but 90.1% cases presented with ≥4 lymph nodes metastasis among TNBC. On the other hand, 74.7% cases presented with 1–3 lymph nodes positivity in non-TNBC group. We have found, about 69.0% patients presented with Grade III tumor and 74.6% patient presented with NPI ≥5.4. However, 56% of non-TNBC patients presented with NPI ≥5.4 (Table 3).

Table 4: Distribution according to histo-pathological examination

HPE	Group (%)		
	Non-TNBC	TNBC	Total
DCIS	2	0	2
Row	100.0	0.0	100.0
Column	2.7	0.0	1.4
IDC	70	68	138
Row	50.7	49.3	100.0
Column	93.3	95.8	94.5
LC	3	1	4
Row	75.0	25.0	100.0
Column	4.0	1.4	2.7
MC	0	2	2
Row	0.0	100.0	100.0
Column	0.0	2.8	1.4
Total	75	71	146
Row	51.4	48.6	100.0
Column	100.0	100.0	100.0

DCIS: Ductal carcinoma *in situ*, IDC: Invasive ductal carcinoma, TNBC: Triple negative breast cancer

Table 5: Distribution of metastasis of TNBC and non-TNBC patients

Metastasis	Group (%)		
	Non TNBC	TNBC	Total
Liver	1	1	2
Row	50.0	50.0	100.0
Column	1.3	1.4	1.4
Liver+bone	1	1	2
Row	50.0	50.0	100.0
Column	1.3	1.4	1.4
Liver+lung	1	2	3
Row	33.3	66.7	100.0
Column	1.3	2.8	2.1
Liver+lung+brain	1	2	3
Row	33.3	66.7	100.0
Column	1.3	2.8	2.1
LN	67	61	128
Row	52.3	47.7	100.0
Column	89.3	85.9	87.7
Lung	1	1	2
Row	50.0	50.0	100.0
Column	1.3	1.4	1.4
Lung+bone	1	1	2
Row	50.0	50.0	100.0
Column	1.3	1.4	1.4
No	2	2	4
Row	50.0	50.0	100.0
Column	2.7	2.8	2.7
Total	75	71	146
Row	51.4	48.6	100.0
Column	100.0	100.0	100.0

TNBC: Triple negative breast cancer

Among TNBC, most of the morphological variant was IDC (95.8%), whereas only 1.4% patient showed morphological variant of LC and in 2.8% cases were MC (Table 4).

We observed that among TNBC, 85.9% patients presented with only lymph nodes metastasis and 2.8% patients presented without any metastasis (Table 5).

DISCUSSION

TNBC are one of the most aggressive phenotype with discrete risk factors and ominous prognostic significance. Our study revealed, relatively high proportion of TNBC, which suggest that possibly most of our patients harbor higher incidences of basal carcinoma, which are likely to be more aggressive. The study showed 71 (48.6%) patients presented with TNBC. But Perou et al. and Carey et al.[1,2] study had showed that TNBC accounts for approximately 15–20% of newly diagnosed BC. In this study, the mean age of presentation was 54.06 years in TNBC group, whereas in Non TNBC group, it was 53.68 years. Thai study showed that the average age was 52 years.[3] Studies in Iran got lower results in which the mean age at diagnosis was 50±12 years and 47.9 years, meanwhile higher mean age of presentation (62.7 years) was found in Marshfield Clinic/St Joseph Hospital Wisconsin study,[4] reconfirms the fact BC in India and Asian population are a decade younger. The study revealed, among TNBC, all cases presented from Stage II to Stage IV in which about 89.7% cases fall into the Stage III group. Rahmani et al.[5] showed a total of 86 patients among 547 patients were included in TNBC group of which the stage of tumor was significantly higher. The study also could reveal that TNBC is likely to be more aggressive and present at relatively higher stage as compared to non TNBC lesions. We found that among TNBC, 57.7% patients presented with tumor size >4.9 cm. But among non TNBC group, 34.7% patient presented with tumor size >4.9 cm. Dogra et al. and Tawfik et al.[6,7] study showed that TNBC presented with high tumor size. Widodo et al.[8] and Hashmi et al. (2014)[9] studies also supported this result. The study showed that among TNBC, 90.1% cases presented ≥4 Lymph Nodes metastasis. In Tawfik et al.[9] study, it was seen that TNBC presents with high lymph nodes metastasis. Other studies also supported this result.[5,6,8,10] We found that about 69.0% patient presented with Grade III tumor. In Hashmi et al. (2014)[8] study, it has been found that 63.4% patients present with Grade III tumor among TNBC, But its counterpart NON TNBC patients presented with comparatively lower grade lesion.[11,12] In other studies, it is also seen that TNBC patients present with high grade tumor. The same is applicable for size and lymph

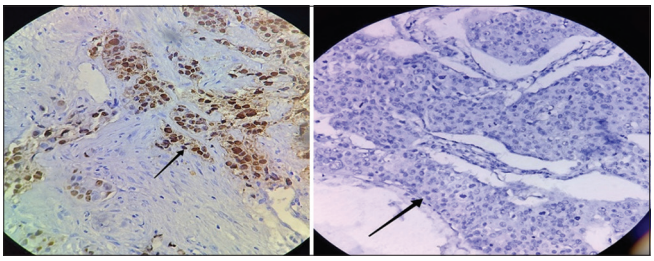

Figure 1: Estrogen receptor (ER) (+) and ER (-)

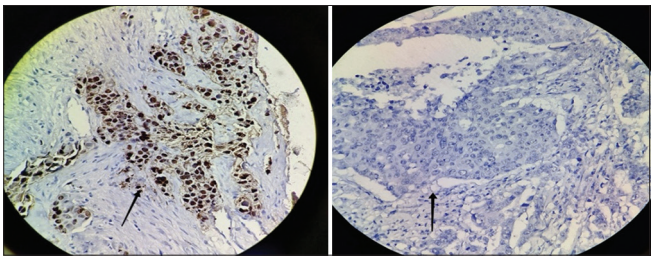

Figure 2: Progesterone receptor (PR) (+) and PR (-)

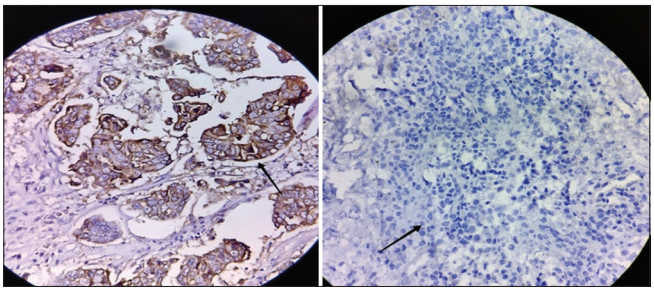

Figure 3: Human epidermal growth factor receptor 2 (HER-2) (+) and HER-2(-)

node status also. We have seen, 74.6% patients presented with NPI ≥5.4. But most of non TNBC patients presented with the lower NPI (<5.4). This is an ongoing study and is awaiting for the long term data of overall survival and disease free survival. Therefore, we have chosen NPI, as absolute criteria to predict the long-term outcome of the disease. This study also revealed that most of the TNBC falls in the morphological variant of IDC (95.8%). Pavani et al.[13] study showed among TNBC, 71.4% cases were IDC. But Hashmi et al. (2014)[9] study found 77.1% patients of TNBC having morphological variant of IDC. Rahmani et al.[5] study also showed that maximum number of patients (89.5%) among TNBC fall in the morphological variant of IDC. Again we found that among TNBC, 85.9% patients presented with only lymph nodes metastasis. The Thike et al. (2010)[14] study revealed lymph node metastasis present in 40% cases among TNBC. The Ghosn et al.[15] study showed 50.3% patients presented with lymph nodes metastasis and 25% cases presented with bone metastasis.

Limitations of the study

Small sample size. There was no long term follow up.

CONCLUSION

The study is tremendously significant from Indian perspective and reveals the fact that most of the patients in this subcontinent have a disease which originates from the basal layer and is therefore different from the molecular subtype of the West's. It further proofs that TNBC had the point of diagnosis, seems to be more aggressive as is evident from the data of tumor size, nodal status, stage, grade, NPI, etc. Finally, it suggests that Indian BC is likely to be younger at presentation as compared to its Western counterpart, however a population based study can only be able to emphasize this statement.

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Authors' Contributions:
SB - Data collection and prepared first draft of manuscript and final manuscript; **MMN -** Interpreted the results; reviewed the literature; **RKH -** Concept, coordination, review of literature and manuscript preparation; **AKD -** Concept and design of the study, Statistically analyzed and interpreted, preparation of manuscript and revision of the manuscript.

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