

Larger Tumours at Presentation in Triple-Negative Breast Carcinoma of Young Women: A Single-Centre Pathological Analysis

Vibhuti Thukral¹, Biswasree Deb², Ankita Mehra², Anjali Sharma², Srishti Saini², Sunita Singh³

¹Senior Resident, Department of Pathology Department of Pathology, Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

²Junior Resident, Department of Pathology Department of Pathology, Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India.

³Professor and Head, Department of Pathology Department of Pathology, Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India

Abstract

Background: Triple-negative breast cancer (TNBC) is usually regarded as a disease of younger women, but its frequency and presentation at the two age extremes are rarely compared directly in Indian tertiary-care practice. **Material and Methods:** We retrospectively analysed 45 women with invasive breast carcinoma on mastectomy or breast-conserving surgery specimens with axillary dissection, diagnosed over 12 months at a single centre: 19 younger than 40 years and 26 aged 60 years or above. TNBC was defined as ER-negative, PR-negative and HER2-negative (HER2 1+ and 2+ counted as negative). Tumour size, nodal status, Nottingham grade, Ki-67 and the Nottingham Prognostic Index (NPI) were compared using Fisher's exact and Mann-Whitney U tests, with Hodges-Lehmann shift and confidence intervals as effect sizes. **Results:** TNBC occurred in 10/19 young (52.6%) and 12/26 older women (46.2%) ($p = 0.77$). Among TNBC cases, young women had much larger tumours (median 6.5 cm, IQR 4.6–9.3, versus 3.0 cm, IQR 2.9–3.6; $p = 0.0003$; Hodges-Lehmann difference 3.0 cm, 95% CI 1.3–7.0), and 6/10 exceeded 5 cm compared with 0/12 older women ($p = 0.003$). Nodal positivity (60.0% vs 41.7%), grade 3 (40.0% vs 33.3%) and Ki-67 $\geq 20\%$ (40.0% vs 33.3%) did not differ significantly. Median NPI was higher in young women (5.1 vs 4.6; $p = 0.048$), largely reflecting tumour size. The size difference persisted after excluding HER2 2+ cases ($p = 0.001$). **Conclusion:** In this small series, TNBC was equally frequent in young and elderly women, but young women presented with substantially larger primary tumours, without a clear difference in grade, proliferation or nodal burden. Earlier detection in women under 40 may matter more than any age-specific biology. Larger multicentre studies are needed.

Keywords: Triple-negative breast neoplasms, young adult, aged, tumour size, Nottingham Prognostic Index, lymph node metastasis, India.

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INTRODUCTION

Breast cancer in women under 40 years is relatively uncommon but is associated with more aggressive features and poorer outcomes than in older women.^[1–4] Younger patients more often have high-grade, hormone receptor-negative tumours, and these differences are attributed to distinct tumour biology rather than stage alone.^[2,3] In Asian populations, including India, a larger proportion of breast cancers arises in younger women than in Western series, which makes age-related differences clinically relevant to local practice.^[5]

TNBC, defined by absent oestrogen receptor (ER), progesterone receptor (PR) and HER2 expression, accounts for a minority of breast cancers overall but carries a high risk of early recurrence and lacks targeted endocrine therapy.^[6,7] It is frequently described as over-represented in young women.^[7,8] Older women are less often studied: they are under-represented in trials and their tumours are generally believed to be more indolent and receptor-positive, yet TNBC does occur in the elderly and is clinically important.^[9,10]

A direct comparison of the two age extremes, young (<40) against elderly (≥ 60), may clarify whether the TNBC phenotype differs by age beyond receptor status. We

therefore retrospectively analysed the triple-negative phenotype in these two age groups. We asked whether TNBC is more frequent in young women and whether tumour size, nodal burden, grade, proliferation and the Nottingham Prognostic Index (NPI) of TNBC differ between the two age groups.

MATERIALS AND METHODS

This was a retrospective, observational study carried out in the Department of Pathology, Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, over a 12-month period from September 2025 to August 2026. Data were collected retrospectively from archived histopathology reports and records. Women with a histopathological diagnosis of invasive breast carcinoma on a surgical specimen, either modified

Address for correspondence: Dr. Biswasree Deb,
Junior Resident, Department of Pathology Department of Pathology, Post Graduate
Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India
E-mail: debbiswasree@gmail.com

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radical mastectomy (MRM) or breast-conserving surgery with axillary lymph node dissection, were eligible if they were younger than 40 years or aged 60 years or above at diagnosis. Trucut (core needle) biopsies were excluded, as were women aged 40–59 years, who were left out by design to maximise the contrast between age extremes. All eligible cases during the study period were included. The final cohort comprised 45 women (19 young, 26 older). Because this was a retrospective study using anonymised records, ethical approval was not required and informed consent was not applicable.

Specimens were examined and reported according to standard protocols. Histological type was recorded, and tumours were graded by the Nottingham (Elston–Ellis) system¹¹. Tumour size was the maximum gross or microscopic dimension in centimetres. Lymph node status was recorded as positive nodes over nodes examined. Lymphovascular invasion (LVI) was recorded where present. ER and PR were assessed by immunohistochemistry and scored using the Allred system, which sums a proportion score (0–5) and an intensity score (0–3) to give a total of 0–8; a total score of 3 or more was considered positive¹². HER2 was scored 0 to 3+ according to ASCO/CAP guidelines¹³; scores of 0 and 1+ were negative and 3+ positive. Cases with a score of 2+ were reported as negative in the original reports, and in situ hybridisation was not performed; these were retained as negative in the present analysis. Ki-67 was reported as a percentage of positive tumour nuclei; where a range was reported, the midpoint was used, and values reported as “<x%” were assigned x/2. A cut-off of 20% defined high proliferation¹⁴. The NPI was calculated as $(0.2 \times \text{tumour size in cm}) + \text{nodal stage}$ (1 = no nodes, 2 = 1–3 nodes, 3 = ≥ 4 nodes) + grade, and classified as excellent (≤ 2.4), good

(2.41–3.4), moderate (3.41–5.4) or poor (>5.4)¹⁵. TNBC was defined as ER-negative, PR-negative and HER2-negative (HER2 scores of 0, 1+ and 2+ counted as negative); all other tumours were classed as non-triple-negative.

Continuous variables are presented as median with interquartile range (IQR) and compared with the Mann–Whitney U test, with the Hodges–Lehmann median difference and a 95% percentile bootstrap confidence interval (5,000 resamples) as the effect size. Categorical variables are presented as numbers and percentages and compared with Fisher’s exact test; risk differences are given with Newcombe 95% confidence intervals. All tests were two-sided with significance set at $p < 0.05$. Because of the small sample size and the number of comparisons, all subgroup findings should be regarded as exploratory and no correction for multiple testing was applied. To test the robustness of the main finding, a sensitivity analysis excluded TNBC cases with HER2 2+. Analyses were performed in Python 3 (SciPy).

RESULTS

The cohort included 19 women under 40 years and 26 women aged 60 years or above. All tumours were invasive carcinoma of no special type, except one tumour in the young group, which was a medullary carcinoma and also triple-negative. LVI was present in every node-positive case. Compared with older women, young women had larger tumours (median 4.5 vs 2.5 cm; $p = 0.0002$), a higher proportion of tumours larger than 5 cm (31.6% vs 3.8%; $p = 0.031$) and a higher median NPI (5.0 vs 3.7; $p = 0.002$) (Table 1). No grade 1 tumours occurred in the young group, whereas four older women (15.4%) had grade 1 tumours; the difference in grade 3 frequency (36.8% vs 15.4%) was not statistically significant. ER, PR and HER2 expression did not differ significantly between age groups.

Table 1: Clinicopathological characteristics of the whole cohort by age group

Parameter	Age <40 years (n = 19)	Age ≥ 60 years (n = 26)	p value
Tumour size, cm – median (IQR)	4.5 (3.8–6.5)	2.5 (2.5–3.4)	0.0002
Tumour size >5 cm – n (%)	6 (31.6)	1 (3.8)	0.031
Node-positive – n (%)	10 (52.6)	9 (34.6)	0.36
≥ 4 positive nodes – n (%)	7 (36.8)	4 (15.4)	0.16
Grade 1 / 2 / 3 – n	0 / 12 / 7	4 / 18 / 4	–
Grade 3 – n (%)	7 (36.8)	4 (15.4)	0.16
ER positive – n (%)	7 (36.8)	13 (50.0)	0.55
PR positive – n (%)	4 (21.1)	9 (34.6)	0.51
HER2 positive (3+) – n (%)	2 (10.5)	4 (15.4)	1.00
Triple-negative – n (%)	10 (52.6)	12 (46.2)	0.77
Ki-67, % – median (IQR)	12.5 (5.0–30.0)	10.0 (5.0–10.0)	0.07
NPI – median (IQR)	5.0 (4.5–6.0)	3.7 (3.5–4.6)	0.002
NPI poor prognostic group (>5.4) – n (%)	8 (42.1)	4 (15.4)	0.09

IQR, interquartile range; NPI, Nottingham Prognostic Index. Continuous variables compared by Mann–Whitney U test, categorical variables by Fisher’s exact test.

TNBC was found in 10 of 19 young women (52.6%, 95% CI 31.7–72.7) and 12 of 26 older women (46.2%, 95% CI 28.8–64.5); the difference was not significant (risk difference 6.5 percentage points, 95% CI –21.4 to 33.0; $p = 0.77$). ER negativity was likewise similar (63.2% vs 50.0%; $p = 0.55$). Three of the 22 triple-negative tumours were HER2 2+ (one young, two older).

Among triple-negative tumours, young women had

markedly larger tumours than older women (median 6.5 cm, IQR 4.6–9.3, versus 3.0 cm, IQR 2.9–3.6; $p = 0.0003$), a Hodges–Lehmann difference of 3.0 cm (95% CI 1.3–7.0) (Table 2, Figure 1A). Six of ten young women had tumours larger than 5 cm, compared with none of twelve older women ($p = 0.003$; Figure 1B). By contrast, nodal positivity (60.0% vs 41.7%; $p = 0.67$), involvement of four or more nodes (30.0% vs 25.0%; $p = 1.0$), grade 3 (40.0% vs 33.3%;

$p = 1.0$) and high Ki-67 ($\geq 20\%$: 40.0% vs 33.3%; $p = 1.0$) were similar. LVI was present in all node-positive tumours in both groups (6 of 10 and 5 of 12). The single medullary carcinoma occurred in a woman under 40; it was triple-negative, 4.5 cm in size, grade 2, with no nodal metastasis (0 of 10 nodes), and had a Ki-67 of 10%. The median NPI of triple-negative tumours was higher in

the young group (5.1 vs 4.6; $p = 0.048$), although the confidence interval of the difference included zero (-0.2 to 2.8), and the proportion in the poor prognostic group did not differ (40.0% vs 25.0%; $p = 0.65$). Because tumour size contributes directly to the NPI, this difference largely restates the size finding rather than representing an independent prognostic signal.

Table 2: Characteristics of triple-negative breast carcinoma by age group

Parameter	Age <40 years (n = 10)	Age ≥ 60 years (n = 12)	p value	Effect size / 95% CI
Tumour size, cm – median (IQR)	6.5 (4.6–9.3)	3.0 (2.9–3.6)	0.0003	HL difference 3.0 cm (1.3–7.0)
Tumour size >5 cm – n (%)	6 (60.0)	0 (0)	0.003	Risk difference 60% (22–83)
Node-positive – n (%)	6 (60.0)	5 (41.7)	0.67	18% (–21 to 51)
≥ 4 positive nodes – n (%)	3 (30.0)	3 (25.0)	1.00	5% (–29 to 39)
Grade 3 – n (%)	4 (40.0)	4 (33.3)	1.00	7% (–29 to 41)
Ki-67 $\geq 20\%$ – n (%)	4 (40.0)	4 (33.3)	1.00	7% (–29 to 41)
Ki-67, % – median (IQR)	13.8 (10.0–35.0)	10.0 (10.0–20.0)	0.34	–
NPI – median (IQR)	5.1 (4.9–6.7)	4.6 (3.7–5.0)	0.048	HL difference 1.1 (–0.2 to 2.8)
NPI poor prognostic group – n (%)	4 (40.0)	3 (25.0)	0.65	15% (–22 to 48)

HL, Hodges–Lehmann median difference (95% bootstrap CI). Risk differences (young minus older) are in percentage points with Newcombe 95% CI.

After excluding the three HER2 2+ cases, the size difference persisted (nine young vs ten older women; median 7.0 cm, IQR 4.5–10.0, versus 3.0 cm, IQR 3.0–3.9; $p = 0.001$). In non-triple-negative tumours the size gap was

smaller (median 3.5 vs 2.5 cm; $p = 0.039$). In this subgroup, grade 3 was seen in 3 of 9 young and 0 of 14 older women ($p = 0.047$), and no other comparison was significant. These secondary findings are exploratory.

Table 3: Prevalence of Microalbuminuria in the Study Population

Parameter	Number of Patients (n)	Percentage (%)
Patients with Microalbuminuria	32	53.30%
Patients without Microalbuminuria	28	46.70%
Total	60	100%

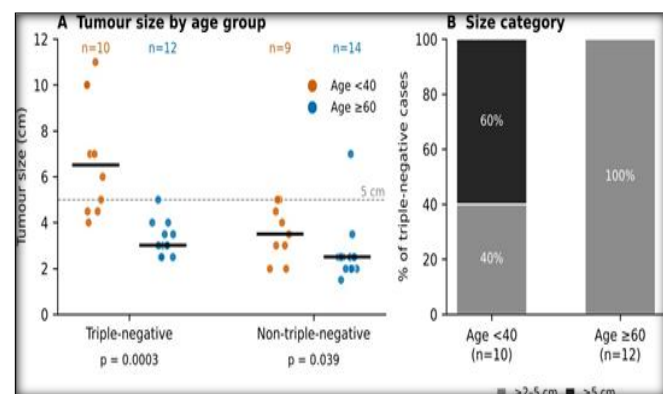


Figure 1: (A) Tumour size in individual cases by age group, in triple-negative and non-triple-negative tumours; horizontal bars are medians. (B) Proportion of triple-negative cases by size category. Triple-negative tumours in women under 40 were larger; none in women aged 60 and above exceeded 5 cm.

DISCUSSION

In this 12-month series, the triple-negative phenotype was about equally frequent in women under 40 (52.6%) and in women aged 60 and above (46.2%). The clear difference between the age groups was not in receptor profile, grade, proliferation or nodal burden among triple-negative tumours, but in tumour size: young women presented with tumours roughly twice as large, and more than half exceeded 5 cm, whereas none of the older women's triple-

negative tumours did.

The similar frequency of TNBC in the two groups differs from the usual teaching that TNBC predominates in the young.^[7,8] Two points temper this. First, the sample is small, so the confidence interval of the difference is wide (-21 to $+33$ percentage points), and a true difference in either direction cannot be excluded. Second, the overall proportion of TNBC here is much higher than the 15% or so usually cited for unselected populations⁶, and this probably reflects case mix at a tertiary pathology service, the small cohort, and our decision to count HER2 2+ cases as negative. Even so, the data support the view that TNBC is not a disease of the young only, and that older women with TNBC are a sizeable and sometimes neglected group.^[9,10]

The main finding, much larger triple-negative tumours in the young, can be explained in at least three ways. One is delayed detection: women under 40 fall outside population mammographic screening, have denser breasts that hinder both clinical and imaging detection, and may be less likely to attribute a lump to cancer, so tumours are presented late.^[1,4] A second is biology, namely faster growth in young women's tumours, but our data do not support that strongly, since grade and Ki-67 were not significantly different between triple-negative groups. A third possibility is that older women notice or present with smaller tumours, for example through greater health-service contact or screening, although we have no data on symptom duration or mode of detection. Whichever explanation applies, the practical message is the same: early

diagnosis in young women is where the gain lies. The fact that the size difference was smaller in non-triple-negative tumours may indicate that rapid growth of triple-negative disease amplifies any diagnostic delay, but this observation is exploratory and the numbers are too small for an interaction test to be reliable.

Nodal burden was not different between triple-negative groups (60.0% vs 41.7% node-positive; four or more nodes in 30.0% vs 25.0%). Triple-negative tumours metastasise preferentially by haematogenous routes, and nodal involvement is often less closely tied to tumour size than in receptor-positive disease.^[7] In our data nodal positivity did not track tumour size in the young group, which fits this idea, but we cannot confirm it from 22 cases. All node-positive tumours showed LVI, as expected, and LVI could not be analysed as an independent variable.

The higher median NPI in young women with TNBC (5.1 vs 4.6) is mostly a consequence of tumour size, which is one of the three NPI components.^[15] Both groups fell mostly in the moderate prognostic category. The NPI was therefore not a sensitive discriminator between age groups in TNBC beyond what size already shows, and the borderline p value (0.048) should not be over-interpreted.

One tumour in the young group was a medullary carcinoma, a histological subtype that is typically triple-negative and classically carries a better prognosis than other TNBCs. In our series it was node-negative, which fits that pattern. This single case does not affect the conclusions, and we did not exclude it, but it illustrates that the triple-negative group is heterogeneous.

The main limitation is the small sample (45 cases; 22 triple-negative) from a single centre over one year, so power is limited and confidence intervals are wide; only large differences such as tumour size could be detected. Subgroup and secondary analyses were exploratory and unadjusted for multiple testing. HER2+ cases were not confirmed by *in situ* hybridisation, so some tumours classed as triple-negative could be HER2-low or HER2-amplified, although the sensitivity analysis suggests this did not drive the result. Ki-67 was recorded as reported by different observers, and ranges were converted to midpoints. We had no information on symptom duration, mode of detection, treatment or outcome, so we cannot say whether larger size translated into worse survival. LVI was recorded only in relation to nodal status and not as a separate variable, and the 40–59 age group was deliberately omitted, which prevents a view of age as a continuum. The study is retrospective and hospital-based, and because only surgical specimens with axillary dissection were included (trucut biopsies were excluded), women who did not undergo surgery are not represented, which introduces selection bias.

CONCLUSION

In this small hospital-based series, triple-negative breast carcinoma was about equally common in women under 40 and women aged 60 and above, but women under 40 presented with markedly larger tumours, without a clear difference in

grade, Ki-67 or nodal burden. These findings suggest that late presentation, rather than distinct tumour biology, may underlie the poorer outlook often seen in young women, and they highlight the importance of earlier detection in women under 40. Larger, multicentre studies including the intermediate age group and outcome data are needed to confirm this.

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Conflicts of interest

There are no conflicts of interest.

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