ORIGINAL ARTICLE

RELATION OF RADIOGRAPHIC BI-RADS (4 AND 5) SCORE AND TRIPLE NEGATIVITY IN PATIENTS WITH BREAST CANCER

Farah Afzal[1], Iffat Ara[1], Azmat Ali[2]✉, Ayesha Jabeen[3], Sadia Tahir[4], Sadaf Aziz[5]

[1]Sheikh Khalifa Bin Zayed Al Nahyan Hospital, CMH, Muzaffarabad-AJK

[2]Ayub Medical College, Abbottabad-Pakistan, [3]Armed Forces Institute of Radiology and Imaging, Rawalpindi-Pakistan

[4]PAF Hospital Rafiqui, [5]CMH Lahore Medical College, Lahore-Pakistan

Background: Breast cancer is a disease entity whereby abnormal growth of breast cells leads to tumour formation. Triple assessment including clinical examination, radiological imaging and histopathology is done to diagnose breast tumours. On radiological imaging, BIRADS (Breast imaging, reporting and data system) 5 lesions have the highest likelihood of malignancy followed by BIRADS 4c and then BIRADS 4b. On histopathology, triple negativity indicates tumours that don't have oestrogen or progesterone receptors and don't synthesize significant amount of protein HER2. Such tumours have faster growth rate and are more likely to metastasize and recur. **Methods:** This cross-sectional study was done at department of radiology, SKBZH CMH Muzaffarabad from Nov 2023 to March 2024. This study enrolled 100 patients who had BIRADS 4(4b or 4c) or 5 on radiological imaging and were later diagnosed as having breast cancer confirmed by histopathology through consecutive sampling. Radiological and histopathological reports were compared to determine the relationship between triple-negative tumors and radiographic BI-RADS 4 and 5 scores in patients diagnosed with breast cancer **Results:** The mean age of the patients was 48.45±14.663 years. A significant association of triple negative tumours and radiological grading (BIRADS 4 and 5) with *p*-values 0.00 were found. A significant association of triple negativity with histological grade of tumour, lymph node (LN) metastasis and tumour necrosis, with *p*-value 0.008, 0.016 and 0.001 respectively were found. No significant association of size of tumour with radiological grading and triple negative status were found. **Conclusion:** Although morphologically less malignant features are labelled as BIRADS 4, but when BIRADS 4 lesions are found positive for malignancy, they have more chances of being triple negative on histopathology compared to BIRADS 5 lesions and thus are more aggressive.

Keywords: Breast cancer; BIRAD 4 and 5; Triple Negativity; Mammography

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INTRODUCTION

Breast cancer, though present in both men and women, is the most prevalent form of cancer among women worldwide.[1] While majority of breast tumours are non-cancerous and can be effectively treated conservatively or through surgery[2] a quarter of them are malignant. This lethal illness caused the deaths of 8 million individuals in 2008, and it is estimated that this number will increase to 11 million by 2030.[3] Based on treatment options, one of the types of breast cancer is "triple negative" cancer as finalized at 12th International Breast Cancer Conference.[4]

Triple-negative breast cancer predominantly occurs in younger individuals and possesses characteristics such as elevated histological grades, increased recurrence rates, limited response to chemotherapy, and decreased survival rates.[5] This type of breast cancer lacks the expression of the progesterone receptor, oestrogen receptor, and HER2.[6] The aggressiveness of triple-negative breast cancer is notable due to the diverse molecular makeup of tumour cells.[7] The prevalence of triple-negative breast cancer varies between 6.7% and 27.9% across different countries, with India reporting the highest rates followed by Indonesia, Algeria, and Pakistan.[8]

Mammography and breast ultrasonography are considered as first line diagnostic modalities to detect breast cancer at an early stage.[9] An annual mammography screening can identify small breast tumours without any lymph node involvement that might not be palpable. Magnetic resonance imaging (MRI) can help detect additional breast tumours that were missed by both mammography and ultrasound screening, especially in patients with BRCA positive status or those with metastatic axillary lymphadenopathy of unknown origin. To standardize the reporting terminology in mammographic results, the American College of Radiology (ACR) has developed a tool called the "Breast Imaging

Reporting and Data System (BIRADS)". This system categorizes the findings based on edition one of BIRADS-Ultrasonography and edition four of BIRADS-Mammography, with the categories being as follows: BI-RADS 0: Incomplete, BI-RADS 1: Normal, BI-RADS 2: Typically benign, BI-RADS 3: Probably benign, BI-RADS 4: Suspicious abnormality, BI-RADS 5: Highly suggestive of malignancy, BI-RADS 6: Histologically proven malignancy.[10]

The objective of the study is that it will demonstrate the relationship between BIRADS scoring and triple negativity status as well as tumour size, grade of tumour, margins of tumour, lymph node metastasis and tumour necrosis. It would also provide baseline data for future researchers aiming to target the population of Pakistan and the Azad Kashmir region.

MATERIAL AND METHODS

This cross-sectional study was conducted at the Department of Radiology, Shaikh Khalifa Bin Zayed Combined Military Hospital Muzaffarabad., from November 2023 to March 2024, with prior approval from the Institutional Review Board (IRB), vide reference number DME-1145. The sample size was estimated as 100 cases using a 5% level of significance, 80% study power, with an expected correlation coefficient of r = 0.41 between BI-RADS and triple negativity among breast lesions. [11]

All patients who fulfilled the inclusion criteria were enrolled until required sample size was achieved using consecutive sampling. All the patients who reported for mammography in radiology department and who underwent mammography, ultrasound evaluation, and subsequent biopsy with histopathological confirmation during the same study period were enrolled. Inclusion in the study required patients having BIRAD 4 or 5 lesion and had complete imaging, histopathological, immunochemical and clinical and demoghraphic information record available at the time of enrolment. Written informed consent was obtained from the patient at the time of enrolment and data confidentiality was ensured

Initially, mammography was performed using a Philips mammography machine (Model No. 1125314). Two standard views—mediolateral oblique (MLO) and craniocaudal (CC)—were taken. Additional views were obtained if required in cases of diagnostic dilemma. In all patients, ultrasound correlation was performed using a Xario Doppler machine (Model No. 200G) by a consultant radiologist with at least 5 years of experience. For ultrasound, the radial technique was used with a double sweep. Based on mammography and sono-mammography, any mass present was identified. The number, size, vascularity, and margins of the mass were recorded, and BI-RADS scoring was done accordingly. The axillae were scanned for any abnormal lymph nodes, and abnormalities were documented and scored.

In cases of BI-RADS 4 or 5 lesions, patients were advised to undergo biopsy. Biopsies were performed under ultrasound guidance using the same machine by a consultant radiologist with at least 5 years of experience. A Tru-Cut needle (16-gauge) was used under local anesthesia, and three or more samples were taken and preserved in formalin. Fine-needle aspiration cytology (FNAC) of lymph nodes showing increased short-axis diameter (SAD), increased cortical thickness, or decreased length-to-transverse width (LT) ratio was performed in the same sitting. In cases of multiple suspicious lymph nodes, the node with the largest cortical thickness was sampled. Half of the FNAC samples were air-dried, and half were wet-fixed with alcohol.

Radiological and histopathological reports were compared to determine the relationship between triple-negative tumors and radiographic BI-RADS 4 and 5 scores in patients diagnosed with breast cancer. Lymph node (LN) metastasis, tumor grade on histopathology, tumor margins, and necrosis were also recorded. All procedures and results were finalized under the supervision of a classified radiologist with a minimum of 5 years of experience.

Data were analyzed using SPSS version 23. Mean, standard deviation, and median values were calculated for continuous variables. Frequency and percentage were calculated for categorical variables. An independent t-test was used to assess the association between age and radiological categories. The Chi-square test was used to evaluate associations between triple-negative (TN) status, tumor size, grades, tumor margins, necrosis, and lymph node metastasis in patients with BI-RADS 4 and 5 breast lesions. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 100 patients with breast cancer were included in this study. The mean age of the patients was 48.45±14.6 years. Table I shows that significantly younger patients had BIRADs 4 score compared to BI-RADS 5 score.

Table 2 shows the comparison of different morphological and histopathological factors between patients with BIRADS4 and BIRADS 5 score. Out of the total, 59 lesions were reported as BIRADS 4 score and 41 patients as BIRADS 5. Nine out of 41 patients with BIRADS 5 lesions were diagnosed with triple negative breast carcinoma, whereas among 59 patients having BIRAD 4 lesions 42 patients were

diagnosed as TN breast carcinoma on histopathology and the figures were statistically significant (p=<0.0001). Rest of the patients had tumours that were not triple negative (NTN). Tumour size was not significantly different between BIRADS 4 and 5.

The mean age of the patients with triple negativity were 47.27±16.074 and the patients with non- triple negativity were 53.93±14.729 as shown in table 4.

In table 4 there is comparison between morphological and pathological features and prognostic factors of groups with triple negative carcinomas (TN) and without triple negative carcinomas (NTN). Out of the total 100 patients, 51 patients were TN and 49 patients were NTN. Metastatic lymph nodes were found less commonly in TN tumours (p=0.016). There was no significant difference in tumour size between groups (p=0.745). The morphological features of the tumour were also evaluated in which 38 out of 51 TN tumours were well defined instead of being ill defined and indistinct, while 8 out of 49 non-TN had well defined margin (<0.0001).

Table-1: Association between Age and Radiological Grading

	Radiological Grading	Mean±SD	*p*-value
Age	BIRADS-4	47.47±15.89	0.019
	BIRADS-5	54.93±14.53	0.017

Table-2 Comparison of histopathological features between groups of BIRADS 4 and BIRADS 5

		BIRADS-4	BIRADS-5	Total	*p*-value
Triple Negative Status	Triple negative tumour	42 (82.4%)	9 (17.6%)	51 (51.0%)	<0.0001
	Non-triple negative tumour	17 (34.7%)	32 (65.3%)	49 (49.0%)	
Total		59 (59.0%)	41 (41.0%)	100 (100%)	
Size	<2 cm	36 (60.0%)	24 (40.0%)	60 (60%)	0.655
	2-5 cm	22 (59.5%)	15 (40.5%)	37 (37.0%)	
	>5 cm	1 (33.3%)	2 (66.7%)	3 (3.0%)	
Total		59 (59.0%)	41 (41.0%)	100 (100%)	
Lymph node Metastasis	Positive	2 (10.5%)	17 (89.5%)	19 (19.0%)	<0.0001
	Negative	57 (70.4%)	24 (29.6%)	81 (81.0%)	
Total		59 (59.0%)	41 (41.0%)	100 (100%)	

Table-3: Association between age and triple negative status

	Triple Negative Status	Mean±SD	*p*-value
Age	TN	47.27±16.074	0.034
	NTN	53.93±14.729	0.034

Table-4: Comparison of Histopathological and Morphological features between groups of TN and NTN

		TN (triple negative tumour)	NTN (Non-triple negative tumour)	Total	*p*-value
Tumour size	<2 cm	32 (53.3%)	28 (46.7%)	60 (60.0%)	0.745
	2-5 cm	18 (48.6%)	19 (51.4%)	37 (37.0%)	
	>5 cm	1 (33.3%)	2 (66.7%)	3 (3.0%)	
Total		51 (51.0%)	49 (49.0%)	100 (100%)	
Grade	1	7 (63.3%)	4 (36.4%)	11 (11.0%)	0.008
	2	10 (29.4%)	24 (70.6%)	34 (34.0%)	
	3	34 (61.8%)	21 (38.3%)	55 (55.0%)	
Total		51 (51.0%)	49 (49.0)	100 (100%)	
LN (lymph node) Metastasis	Positive	5 (26.3%)	14 (73.7%)	19 (19.0%)	0.016
	Negative	46 (56.8%)	35 (43.2%)	81 (81.0%)	
Total		51 (51.0%)	49 (49.0%)	100 (100%)	
Margin	Well- defined	38 (82.6%)	8 (17.4%)	46 (46.0%)	<0.0001
	Infiltrative	13 (24.1%)	41 (75.9%)	54 (54.0%)	
Total		51 (51.0%)	49 (49.0%)	100 (100%)	
Necrosis	Positive	37 (90.2%)	4 (9.8%)	41 (41.0%)	<0.0001
	Negative	14 (23.7%)	45 (76.3%)	59 (59.0%)	
Total		51 (51.0%)	49 (49.0%)	100 (100%)	

DISCUSSION

Breast ultrasound (US) is a vital imaging technique used to identify or diagnose breast abnormalities.[12] It is commonly employed to differentiate benign from malignant lesions.[13] The American College of Radiology (ACR) introduced standardized diagnostic guidelines for ultrasound regarding breast lesions in

2003, known as the BIRADS® atlas (first edition of ACR BIRADS US), further updated and presented as Second edition in 2013 after a period of ten years. The second edition of ACR BI-RADS US is based on sonographic features for assigning breast lesions to an appropriate category.[14] There are a total of seven categories. However, determining the BIRADS category based on radiological features relies primarily on the interpretation of the radiologist.[15] Furthermore, most of the microscopic features, like texture characteristics, might not be discernible through radiological interpretation.[14] Triple-negative breast cancer, named due to the absence of progesterone receptor, oestrogen receptor, and HER2 expression, represents a more aggressive form of breast cancer with faster growth rate, increased chances of metastases and recurrence.[16]

Our study results revealed that the mean age of the patients having BIRADS 4 was 47.47±15.89 month and the mean age of the patients having BIRADS 5 was 54.93±14.53 month. Similar results were found by Hu et al. in which mean age of the patients having BIRADS 4 was 41.0±10.0 month and the mean age of the patients having BIRADS 5 was 50.3±11.5 months.[17]

In this study, triple negative tumours were encountered more in patients with BIRADS 4 breast lesions. Similar results were found by the Oktay *et al*,[18] who concluded that the patients with BIRADS 4 have more percentage of TN than the patients having BIRADS 5. A significant correlation was found between triple negative tumours and BI-RADS 4 and 5 in our study as well.

Triple negative tumours of breast are a distinct type of invasive ductal carcinomas that exhibit different immunophenotypic characteristics. These tumours have a poor prognosis and currently lack targeted therapy options. It is highly probable for individuals with triple negative tumours to have a BRCA mutation.[19] Additionally, patients with triple negative tumours experience significantly higher rates of local or regional recurrence.[20]

Our research showed that triple-negative (TN) tumours tend to occur in younger individuals compared to non-triple negative (NTN) tumours, a finding that aligns with previous studies. The grades of the tumour as well as the rate at which cells proliferate are widely recognized as crucial indicators when assessing the prognosis of breast cancer. Our results support the existing literature by demonstrating that TN tumours exhibit a high mitotic rate and histological grade, suggesting an aggressive form of cancer. These outcomes reinforce previous reports which indicate that TN breast cancer is associated with a reduced overall survival rate. Furthermore, TN tumours are notorious for high risk of distant and locoregional recurrence. Consequently, it becomes vital to consider the specific subtype of the disease when formulating management and treatment strategies for individuals diagnosed with breast cancer. In terms of the physical characteristics of TN tumours, we observed a higher prevalence of necrosis, consistent with the findings reported in existing literature. These attributes may potentially prove useful in identifying and diagnosing TN breast cancer.[21]

The study we conducted had some limitations as it was centered in a single location and had a small sample size. Therefore, it is important to conduct a further study with a larger sample size to obtain more accurate results.

CONCLUSIONS

Although morphologically less malignant features are labelled as BIRADS 4, but when BIRADS 4 lesions are found positive for malignancy, they have more chances of being triple negative on histopathology compared to BIRADS 5 lesions and thus are more aggressive.

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AUTHORS' CONTRIBUTION

FA: Conceptualization of study design, write-up, data analysis and interpretation. IA: Literature search, data analysis. AA: Proof reading. AJ: Data collection, write-up. ST, SA: Literature search.

REFERENCES

1. Iacoviello L, Bonaccio M, de Gaetano G, Donati MB. Epidemiology of breast cancer, a paradigm of the "common soil" hypothesis. Semin Cancer Biol 2021;72:4–10.
2. Riis M. Modern surgical treatment of breast cancer. Ann Med Surg (Lond) 2020;56:95–107.
3. Sleeman KE, Gomes B, de Brito M, Shamieh O, Harding R. The burden of serious health-related suffering among cancer decedents: global projections study to 2060. Palliat Med 2021;35(1):231–5.
4. Medina MA, Oza G, Sharma A, Arriaga LG, Hernández Hernández JM, Rotello VM, *et al*. Triple-negative breast cancer: a review of conventional and advanced therapeutic strategies. Int J Environ Res Public Health 2020;17(6):2078.
5. Howard FM, Olopade OI. Epidemiology of triple-negative breast cancer: a review. Cancer J 2021;27(1):8–16.
6. Bando Y, Kobayashi T, Miyakami Y, Sumida S, Kakimoto T, Saijo Y, *et al*. Triple-negative breast cancer and basal-like subtype: pathology and targeted therapy. J Med Invest 2021;68(3–4):213–9.
7. Ensenyat-Mendez M, Llinàs-Arias P, Orozco JI, Íñiguez-Muñoz S, Salomon MP, Sesé B, *et al*. Current triple-negative breast cancer subtypes: dissecting the most aggressive form of breast cancer. Front Oncol 2021;11:681476.
8. Thakur KK, Bordoloi D, Kunnumakkara AB. Alarming burden of triple-negative breast cancer in India. Clin Breast Cancer 2018;18(3):e393–9.
9. Aristokli N, Polycarpou I, Themistocleous SC, Sophocleous D, Mamais I. Comparison of the diagnostic performance of

MRI, ultrasound and mammography for detection of breast cancer based on tumour type, breast density and patient's history: a review. Radiography 2022;28(3):848–56.
10. Arian A, Dinas K, Pratilas GC, Alipour S. The breast imaging-reporting and data system (BI-RADS) made easy. Iran J Radiol 2022;19(1):e121155.
11. Aziz S, Mohamad MA, Zin RR. Histopathological correlation of breast carcinoma with breast imaging-reporting and data system. Malays J Med Sci 2022;29(4):65–72.
12. Iranmakani S, Mortezazadeh T, Sajadian F, Ghaziani MF, Ghafari A, Khezerloo D, *et al*. A review of various modalities in breast imaging: technical aspects and clinical outcomes. Egypt J Radiol Nucl Med 2020;51(1):1–22.
13. Zhang Y, Zhang B, Fan X, Mao D. Clinical value and application of contrast-enhanced ultrasound in the differential diagnosis of malignant and benign breast lesions. Exp Ther Med 2020;20(3):2063–9.
14. Luo WQ, Huang QX, Huang XW, Hu HT, Zeng FQ, Wang W. Predicting breast cancer in BI-RADS ultrasound category 4 or 5 lesions: a nomogram combining radiomics and BI-RADS. Sci Rep 2019;9(1):11921.
15. Raza S, Goldkamp AL, Chikarmane SA, Birdwell RL. US of breast masses categorized as BI-RADS 3, 4, and 5: pictorial review of factors influencing clinical management. Radiographics 2010;30(5):1199–213.
16. Borri F, Granaglia A. Pathology of triple negative breast cancer. Semin Cancer Biol 2021;72:136–45.
17. Hu Y, Yang Y, Gu R, Jin L, Shen S, Liu F, *et al*. Does patient age affect the PPV3 of ACR BI-RADS ultrasound categories 4 and 5 in the diagnostic setting? Eur Radiol 2018;28:2492–8.
18. Oktay M, Oktay NA, Besir FH, Buyukkaya R, Erdem H, Önal B, *et al*. Relation between radiographic BI-RADS scores and triple negativity in patients with ductal carcinomas. Int J Clin Exp Med 2014;7(8):2334–40.
19. Dawson SJ, Provenzano E, Caldas C. Triple negative breast cancers: clinical and prognostic implications. Eur J Cancer 2009;45(Suppl 1):27–40.
20. Ugras S, Stempel M, Patil S, Morrow M. Estrogen receptor, progesterone receptor, and HER2 status predict lymphovascular invasion and lymph node involvement. Ann Surg Oncol 2014;21:3780–6.
21. Boisserie-Lacroix M, Mac Grogan G, Debled M, Ferron S, Asad-Syed M, Brouste V, *et al*. Radiological features of triple-negative breast cancers (73 cases). Diagn Interv Imaging 2012;93(3):183–90.

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Address for Correspondence:

Dr. Azmat Ali, Department of Radiology, Ayub Medical College, Abbottabad-Pakistan
Cell: +92 331 120 3021
Email: drazmat772@gmail.com