International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Imaging Characteristics of Triple Receptor Negative versus Triple Receptor Positive Breast Cancer

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Abstract: ***Background: Triple receptor negative breast cancer (TNC) is defined as cancer negative for estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (Her2) and understanding the imaging characteristics of immunosubtypes of breast cancer may helpful in management of the disease. Objectives: To describe and compare the distinct imaging findings of TNC with triple receptor positive breast cancer (TPC) characteristics using mammography and ultrasound. Patients and methods: This is a retrospective observational analysis of the data extracted from the information system database belonging to the Iraqi National center for cancer Research-Baghdad University during a 4-year period starting from January 2011 until November 2014. Sonographic and mammographic findings had been acquire from breast imaging reports. Results: From overall 620 patients were included in this study, only 192 patients had full tumor receptor analysis, there were 55 women diagnosed as triple positive breast cancer and only 22 patients with triple negative breast cancer. 36.4% of TNC was found in young women aged under 40 years and shows positive family history of breast cancer. All patients with TNBC were detected clinically and was palpable. Pathologic grade-II and stage-IIwere more often observed in TNC (68.1% and 50% respectively) and 91% of TNC were ductal carcinoma. 7.1% of TNC were occult on mammography versus 10.4% of TPC. Mass without calcification was commonest mammographic presentation in both groups of breast cancer (64.3% and 62.5% respectively). Breast cancer was visible in patients with TNC and 3.6% of lesions were occult in TPC. Well circumscribed, oval or round hypoechoic mass was most commonly presentation of TNC on ultrasound whereas TPC was frequently found as poorly circumscribed, irregular hypoechoic mass. Conclusions: being familiar with distinctive imaging features of TNC compared to TPC would assist in evaluation of particular immune subtypes of breast cancer and because of TNC lesions were may mimic a benign breast lesions therefore, using mammography combined with ultrasound will minimize false-negative cancer particularly in TNC subgroup of breast cancer.***

Keywords: breast, cancer, triple, ultrasound, mammography

1. Introduction

Triple receptor negative breast cancer is unique clinical entity and distinctive phenotype of breast cancer and currently defined as breast cancer cells will test negative for estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2, [1, 2] which is characterized by more violent clinical course and poor survival rate. [3, 4]for that reason, early diagnosis of this aggressive subtype of breast cancer has significant prognostic value. At present, there is focusing on imaging characteristics of each molecular phenotype of breast cancer to emphasis the hypothesis that triple negative breast cancer reveals distinct findings on diagnostic imaging. [5]

The main purpose of the current study was to define individual radiological and clinicopathological appearance of TNChas been documented by using mammogram and breast sonography and compared these findings with those of TPC according to the breast imaging reporting and data system (BIRADS). [6]

2. Patients and Methods

This is a retrospective observational analysis of the data extracted from the information system database belonging to the Iraqi National center for cancer Research-Baghdad University during a 4-year period starting from January 2011 until November 2014. Sonographic and mammographic findings had been acquire from breast imaging reports. Routine examination of patients by mammography and ultrasound were conducted before the surgery and any other therapy.Institutional approval for this study was obtained and verbal and/or written consent was obtained from each of the patient at each visit during which their database was updated. All results were confirmed by postoperative histopathology.

From overall620 patients were included in this study, only 192 patients had full receptor analysis, there were 55 women diagnosed as TPC and only 22 patients with TNC. The inclusion criteria for this survey was patients diagnosed as breast cancer with negative expression of ER, PR and HER2 and patients with TPC and data belonging to these patients were analyzed and tabulated separately.

Parameters are evaluated for this survey included data pertaining to patient identification, age at presentation, marital status, educational level, age at first child birth, number of delivery, history of lactation and hormonal intake, family history, mode of detection (asymptomatic by clinical breast examination or by screening mammogram) and clinical features (pain, lump, skin changes, ulceration, bloody nipple discharge, axillary nodes and features of distant metastasis), hormone receptor status of the tumor (ER, PR and HER2), laterality of tumor and its maximum size, tumor grade at diagnosis (using Bloom-Richardson grading system) and prognostic stage at presentation and histological subtype of breast cancer.

Mammographic findings of TNC and TPC were evaluated included BIRADS category (BIRADS-IV, V and others), mass without calcification (margin, shape and density), mass with calcification, calcification alone, occult lesion and focal asymmetry or distortion.

Sonographic findings acquired included mass (shape, echopattern, margin, orientation, boundary, posterior acoustic enhancement, edge shadowing, vascularity and resistive index), perilesional echogenic halo and lymph node; in addition occult lesions.

Both ultrasound images and mammograms for sample of the study reviewed if available, some of cases contained only sonographic images, only mammogram or both. From overall patients were enrolled in this study; 77 sonographic and 62 mammographic images are available for review.

Main limitations for this study were unavoidable selection bias in retrospective study and only patients had available ER, PR and Her2 data were involved in the statistical analysis and sample of the study was relatively small in size and depended on the accuracy of the data entries like other database studies.

Microsoft office Excel 2010 was used for data collection and statistical analysis was performed by SPSS version 18 and comparisons of demographic data, tumor characteristics and imaging (sonographic and mammographic) features were made between triple negative and triple positive breast cancer.

3. Results

Cancer phenotype:
From total 620 patients reviewed in the current study, only 192 (31%) of cases have been performed full hormonal phenotype analysis, 22 (11.5%) of these patients did not express ER (estrogen receptors), PR (progesterone receptors) or HER2 (human epidermal growth factor receptor 2) and 55 (28.6%) of patients were express triple receptors positive outcomes as shown in Figure (1).

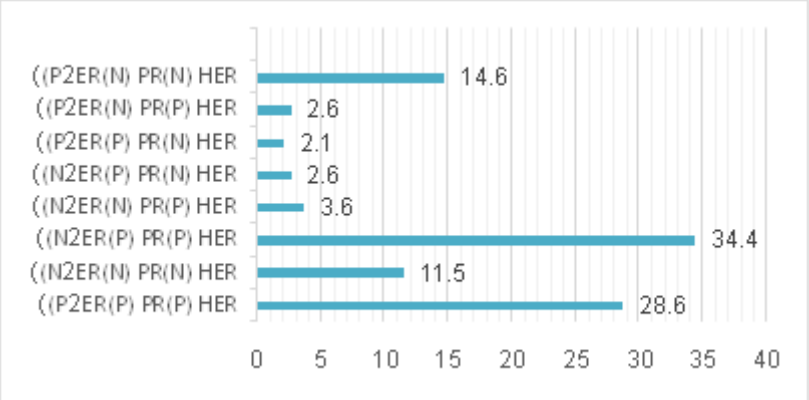

Figure 1: Shows distribution of breast phenotypes of sample of the study, N (negative) and P (positive)

Demographic and pathologic profile:
Demographic and histopathological characteristics of patients with TNCwere reviewed and compared it with results of TPC in table (1). 36.4% of TNC was found in young age group (age less than 40 years) whereas 87.3% of triple receptor positive patients were occur in age above 40 years. 36.4% of TNC shows evidence of family history of breast cancer and 9.1% for non-breast cancer. Family history of breast cancer was found in 27.3% of TPC. All patients in this study were detected clinically either by self-breast examination or by alarming symptoms like bloody nipple discharge or pain or discovered by clinician during clinical examination. Palpable breast lesion was detected in all triple receptor negative patients while it's seen in 92.7% of patients with triple receptor positive expression. Axillary nodes were positive in 31.8% of triple receptor negative patients versus 18.2% of TPC. Maximum diameter of breast lesions in majority of women in both groups was ranged from 20-49 mm. TNC was more commonly associated with pathologic grade-II in 68.18% of cases versus 65.5% in TPC. At time of diagnosis, stage-II tumor was more frequently occur than other stages and recognized in 50% of TNC and in 50.9% of TPC. Regarding histological subtype of TNC, 91% of cases were ductal carcinoma (81% of them wereinfiltrating duct carcinoma, NOS [C50), 4.5% of them were comedocarcinoma, NOS (C50), 4.5% of them weremedullary carcinoma, NOS) and 4.5% of patients were infiltrating duct and lobular carcinoma (C50) and 4.5% of patients were lobular carcinoma, NOS (C50). Concerning histological subtype of TPC, 98.2% of cases were ductal carcinoma (94.6% of them were infiltrating duct carcinoma, NOS [C50),1.8% of them were intraductal carcinoma, non-infiltrating, nos., 1.8% of them wereadenocarcinoma in situ, NOS) and 1.8 % of patients were lobular carcinoma, NOS (c50).

Table 1: Shows clinicopathological characteristics of TNC versusTPC.

Parameter		Triple negative Total no.=22		Triple positive Total no.=55	
		Number	%	Number	%
Age group (years)	20-29	-	0.0	1	1.8
	30-39	8	36.4	6	10.9
	40-49	9	40.9	21	38.2
	50-59	5	22.7	15	27.3
	60-69	-	0.0	10	18.2
	70-79	-	0.0	2	3.6
History of Hormonal intake	yes	1	4.5	11	20.0
	No	21	95.5	44	80.0
Family history of cancer	None	12	54.5	34	61.8
	Breast	8	36.4	15	27.3
	Other	2	9.1	6	10.9
Mode of detection	Asymptomatic	-	0.0	-	0.0
	Symptomatic detection	22	100	55	100
Presenting features	pain	3	13.6	7	12.7
	Lump	22	100	51	92.7
	Skin changes	3	13.6	6	10.9

	Ulceration	2	9.1	2	3.6
	Bloody nipple discharge	-	0.0	2	3.6
	Axillary nodes	7	31.8	10	18.2
	Features of Distant metastasis	-	0.0	-	0.0
Laterality	Right	14	63.6	27	49.1
	Left	8	36.4	27	49.1
	Bilateral	-	0.0	1	1.8
Maximum size of tumor (mm)	< 20	2	9.1	9	16.4
	20-49	19	86.4	43	78.2
	50+	1	4.5	3	5.4
Tumor grade	I	2	9.09	3	5.4
	II	15	68.18	36	65.5
	III	5	22.72	16	29.1
Stage at first presentation	0	-	0.0	1	1.8
	I	2	9.1	4	7.3
	II	11	50	28	50.9
	III	8	36.4	16	29.1
	IV	1	4.5	6	10.9
Histology	Ductal	20	91	54	98.2
	Lobular	1	4.5	1	1.8
	Mixed ductal and lobular	1	4.5	-	0.0

Mammographic outcome:
Mammogram was not available in 8 out of 22 patients with TNC and 7 out of 55 patients with TPC because of age limitation for mammographic examination and all these patients were under age of 40 years where the mammogram is not routine radiological examination therefore statistical analysis applied only for remaining available cases and mammographic findings are summarized in table (2) and (3). In 7.1% of TNC were occult on mammogram and in 10.4% of TPC; the lesion was not clearly visible. Mass without calcification was commonest mammographic presentation in both triple receptor negative and positive cancer (64.3% and 62.5% respectively) and mass with microcalcifications were detected in (7.1% and 12.5% respectively). Suspicious microcalcifications alone were only seen in TPC (4.2%). Focal asymmetry were seen in 7.1% of TNC whereas only in 4.2% of TPC. Breast density among TNC categorized as: fatty breast (7.1%), scattered fibroglandular density (28.6%), heterogeneous density (57.2%) and dense breast tissue (7.1%). In triple receptor positive cancer, the breasts density were classified as type I in (20.8%), type II in (37.5%), type III in (29.2%) and type IV in (12.5%). BIRADS 4 was most commonly category in TNC (57.2%)while BIRADS 5 was the commonest category among TPC (50%).

Table (2) shows mammographic outcomesof TNC versusTPC.

Mammographic findings	Triple negative Total No.=14*		Triple positive Total No.=48**	
	Number	%	Number	%
Occult lesion	1	7.1	5	10.4
Mass alone	9	64.3	30	62.5
Mass with microcalcifications	1	7.1	6	12.5
Suspicious microcalcifications alone	0	0	2	4.2
Focal asymmetry	1	7.1	2	4.2
Architectural distortion	2	14.3	3	6.2
Density: Type 1 (Fatty)	1	7.1	10	20.8
Density: Type II (Scattered)	4	28.6	18	37.5
Density: Type III (Heterogeneous)	8	57.2	14	29.2
Density: Type IV (Dense)	1	7.1	6	12.5
BIRADS category: ACR BIRADS 4	8	57.2	16	33.3
BIRADS category: ACR BIRADS 5	4	28.6	24	50
BIRADS category: Other or not available	2	14.2	8	16.7

*8 out of 22 triple receptor negative cancers had no mammogram study.
**7 out of 55 triple receptor positive cancers had no mammogram study.

The study found that 10 out 14 of TNC (71.4%) and 36 out of 48 of TPC (75%) presented with mass with or without calcifications on mammogram. The contour of TNC were irregular in shape in 40% of cases, 60% were rounded or oval in shape whereasTPC most frequently had an irregular contour (75%). The borders of TPCwere usually spiculated (58.3%) while only 30% of triple receptors negative cancers were speculated margin as shown in table (3).

Table 3: Shows mammographic features of breast mass of TNC versus TPC.

Mass		Triple negative Total No.=10		Triple positive Total No.=36	
		Number	%	Number	%
Contour	Oval	3	30	6	16.7
	Round	3	30	3	8.3
	Irregular	4	40	27	75
Border	Smooth	1	10	0	0
	Spiculated	3	30	21	58.3
	Macrolobulated	2	20	2	4.7
	Microlobulated	3	30	4	8.3
	Ill-defined	1	10	9	18.7

Sonographic findings:
Breast tumor was visible in all TNC whereas 2 out of 55 of TPC (3.6%) were occult during ultrasound examination. Contour of TPC cancer was frequently irregular (62.3%) but 59.1% of TNC had an oval or rounded shape. Spiculated border were seen in 54.7% of TPC versus 22.7% of TNC. Hypoechoic tumors were most commonly echopattern in both TNC (90.9%) and TPC (90.6%). Long-axis of TNC was parallel to the skin surface in (63.6%) of cases whereas not parallel in (60.4%) of TPC. The lesion in TNC had abrupt boundary in majority of cases (72.7%) whereas seen in (41.5%) of TPC. Posterior acoustic enhancement of the lesion was seen in (63.6%) of lesions in TNC and only in (22.6%) of TPC and edge shadowing was detected only in (18.2%) of TNC. Color Doppler interrogation of breast lesions revealed that positive internal vascularity was found in (63.6%) of TNC and 45.4 % of them had high resistive index equal or higher than 0.7 whereas positive internal vascularity was seen in (52.8%) of TPC and 37.8% of them had high resistive index. Positive ipsilateral axillary lymph nodes with suspicious morphology were recognized in (27.3%) of TNC and in (15.1%) of TPC.

Table 4: Shows sonographic findings TNC versus TPC

Sonographic findings		Triple negative Total No.=22		Triple positive Total No.=53*	
		Number	%	Number	%
Contour	Oval	7	31.8	14	26.4
	Round	6	27.3	6	11.3
	Irregular	9	40.9	33	62.3
Border	Smooth	2	9.1	2	3.8
	Spiculated	5	22.7	29	54.7
	Macrolobulated	3	13.7	5	9.4
	Microlobulated	7	31.8	7	13.2
	Ill-defined	5	22.7	10	18.9
Echogenicity	Hypoechoic	20	90.9	48	90.6
	Isoechoic	0	0	0	0
	Hyperechoic	0	0	0	0
	Mixed	2	9.1	5	9.4
Alignment	Parallel to skin	14	63.6	21	39.6
	Non parallel	8	36.4	32	60.4
Boundary	Echogenic halo	6	27.3	31	58.5
	Abrupt	16	72.7	22	41.5
Post acoustic enhancement	Positive	14	63.6	12	22.6
	Negative	8	36.4	41	77.4
Edge shadowing	Positive	4	18.2	18	34
	Negative	18	81.8	35	66
Vascularity	Positive	14	63.6	28	52.8
	Negative	4	18.2	7	13.2
	Not available	4	18.2	18	34
Resistive index	< 0.7	4	18.2	8	15.1
	0.7 or more	10	45.4	20	37.8
	Not available	8	36.4	25	47.1
Axillary LN	Negative	15	68.2	43	81.1
	Benign morphology	1	4.5	2	3.8
	Suspicious morphology	6	27.3	8	15.1

* 2 out 55 of triple receptor positive cancers were occult on ultrasound and statistics applied only on 53 cases.

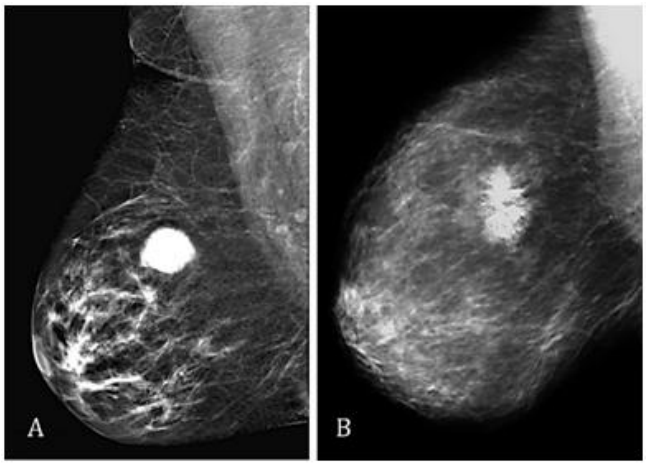

Figure 2: A. Mammogram of right breast [MLO view] of 49-year-old woman with triple receptor negative breast cancer showed a well-circumscribed lobulated smoothly marginated dense breast mass. B. Mammogram of right breast of 53-year-old woman with triple receptor positive breast cancer showed an irregular dense spiculated breast mass.

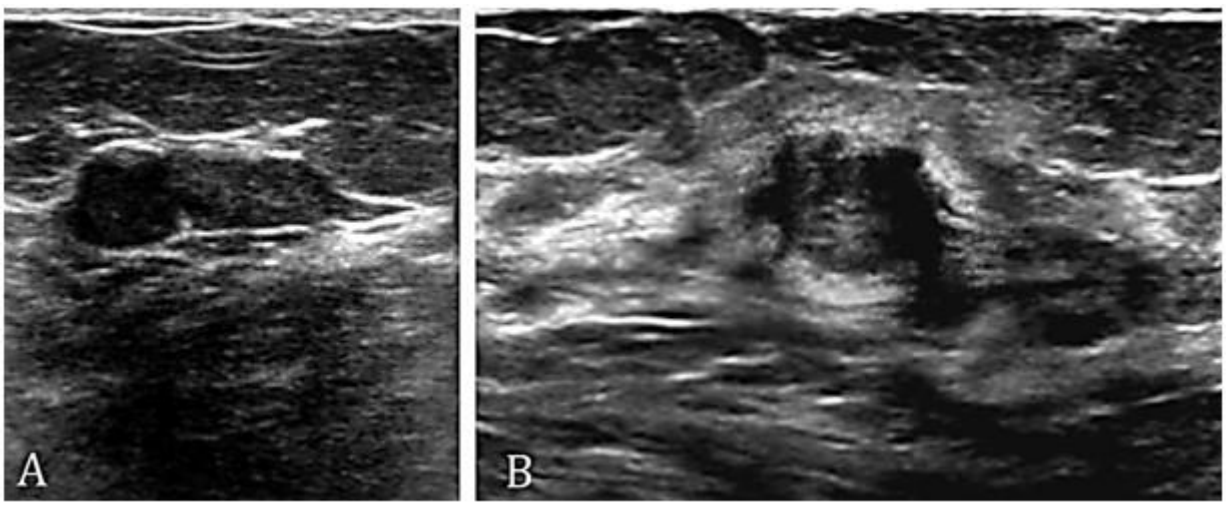

Figure 3: A. Ultrasonography of left breast of 44-year-old woman with triple receptor negative breast cancer showed a well-circumscribed lobulated smoothly marginated hypoechoic breast mass. B. Ultrasonography of right breast of 49-year-old woman with triple receptor positive breast cancer showed an irregular spiculated heterogeneous hypoechoic breast mass with edge shadowing and echogenic halo

4. Discussion

Triple receptor negative breast cancer own distinctive molecular and clinicopathological behavior and study of mammographic and sonographic appearance may potentially suggest individual features of the disease and assist in management. [4, 5] it's crucial to notice this group of breast cancer in its early stage ever since it has a poor prognosis so well understanding of imaging peculiarities of TNCuseful in treatment decisions. [2]

The current study was found that TNC account for 11.5% of all subtypes of breast cancer and 28.6% of cancers was triple receptors positive breast carcinoma. This incidence is in agreement with results that obtained by Dent et al [7] and Reis-Filko and Tutt study [8] where the incidence of TNC was 11.2% and 10-17% respectively whereas the incidence was 12-26% in Chen et al. [9]

The present study found that TNC were younger than women with TPC, 36.4% of triple negative cancer was affected women under age 40 years compared to 12.7% in TPC. This is consistent with results acquired by Bauer et al [10], Carey et al[11] and Dent et al [7]. This finding suggests that TNC is more aggressive disease in nature. Family history of breast cancer was slightly higher incidence in TNC than TPC which is in concordant with resultsachieved by Horvathet al [12]; however, no genetic mutation or BRCA analysis studied in patients in this survey.

No significant difference was found in detection of TNC in comparison with TPC and all patients on this survey were discovered clinically either on breast examination achieved by the patient herself or by clinician or detected by presenting clinical symptoms; however, this result is in disagreement with results that acquired by Krizmanich-Conniffet al [3], Dent et al [7]and Collett et al [13], where, significant difference are seen in mode of detection of the cancer and TNC more likely detected clinically whereas most TPC detected by mammogram.

Palpable breast lump was found in patient with TNC more frequent than in TPC (100% vs. 92.7 respectively) may be because of the rapid growth rate and aggressive nature of TPC which is concordant with Stadalnykaiteet al [1]and Krizmanich-Conniff et al [3] studies.

Regarding axillary lymphadenopathy in the two subtypes of breast cancer, the patients with TNC more likely to have positive axillary lymph nodes than the patient with TPC (31.8% vs. 18.2% respectively) which is consistent with different series acquired similar results. [4, 6, 12] No comparison was made in the current study between size of the tumor and status of regional lymphadenopathy.

Maximum diameter of breast carcinoma in majority of patients in the both groups of breast cancer was in between (20-49 mm), this is dissimilar with Burnside et al[6] that identified the mean size of tumor in theTNCwas significantly larger than in other subtypes.

With respect of tumor grade and stage of the disease, majority of tumor in the two groups were found in stage-II and grade-II, in contrast to many literatures reported that TNC had higher stage and grade than other form of breast cancer. [14, 15]About the differentiation of tumors, Burnside et al [6] stated that grade-III was significantly more often observed in TNC than in non-triple receptor negative cancer.

No significant difference was detected between the two subtypes of breast cancer concerning the histological subtypes since majority of tumors were ductal carcinoma as mentioned in the other literatures that found same conclusion. [5, 6, 13]

Although mammography is a gold standard for breast cancer screening; however, 7.1% ofpatients with TNC were not visible on mammography and 10.4% of TPC were occult. Dogan et al [16]reported that TNC were mammographically occult in 9% of the patients. Nevertheless, no significant different was found in incidence of occult lesion on mammography between TNC and TPC which is in agreement with Yang et al [2] noticed that mammographic tumor visibility was similar among all immunophenotypes.

With respect ofmammographic findings, both triple negative and positive immunotypes of breast cancer often present as a mass with or without calcifications (70.4% vs. 75% respectively) and no significant statistical difference were detected. Yang et al [2] found that TNC most commonly presented as a mass in mammography (85%). The same observation was recognized by Kojima and Tsunda [17] and Dogan et al [16].

Regarding microcalcifications, lower proportion of patients with TNC experienced mass with microcalcifications (7.1%) versus 12.5% of patients with TPC whereas no patients were presented by isolated microcalcificationsamongTNC but 4.2% of patients with TPCrevealedmicrocalcifications. This low association between microcalcifications with TNC may explained by rapid development of the cancer to an invasive stage due to aggressive nature of the disease and no reported ductal carcinoma in situ. Same observations were reported by Ko et al [18] and Yang et al [2].

Focal asymmetry of breast on mammography was seen in TNC more than TPC (7.1% vs. 4.2% respectively) which is in agreement with Ko et al [18] study concluded same finding and is not consistent with results obtained by Stadalnykaiteet al [1] that found TNC were less associated with focal asymmetric density.

Though Ma et al [19] and Yang et al [2] series stated that breast density was not a specific indicator of any of the subtypes of breast tumor; however, with respect the patients in this study, breast density type 3 and 4 (heterogeneous and dense breast) was more common in TNC than in TPC (64.3% vs. 41.7%) and approachable results were achieved by Burnside et al [6]and Huiyan et al studies. [20], whichis may be explained that TNC affect younger population than the TPC.

BIRADS-IV was the commonest category in TNC (57.2%) whereas 50% of TPC classified as BIRADS-V and only two

patients with TNC categorized as BIRADS-III because of benign morphological appearance on mammogram and lesions were microlobulated on ultrasound and biopsy was recommended. The same observation was detected inKrizmanich-Conniffet al study [3].

Concerning the appearance of the breast mass on mammogram, TNC often present as a round or oval in contour (60%) and less frequently being irregular in shape (40%), in contrast to TPC, 75% of the mass were irregular in shape; many literatures were concluded similar findings. [1, 8, 16] nevertheless, Ko et al [18] and Stadalnykaite et al [1] concluded that most TNC were usually irregular in shape (87% and 65%) respectively.

The margin of TNC on mammogram were ill-defined or speculated in 40% of masses and smooth, microlobulated or microlobulated in 60% whereas 77% of masses in TPC were ill-defined or speculated in margin. These results were consistent with findings observed by Kojima and Tsunoda study [18] and Dogan et al [16].

Ultrasound examination of breast was the mainstay in provisional diagnosis of the TNC since many authors and literatures observed that breast cancer has no specific imaging findings typical or breast cancer and no all cases of TNC are visible on mammogram.[1, 2, 16, 21]Breast cancer was visible in all patients with TNC and only 2 out of 55 patients with TPC (3.6%) were occult on ultrasound in patients presented with isolated microcalcifications on mammogram. Dogan et al reported that 7% of TNC were occult on sonography [16].

Ultrasound of TNC presents a mass with irregular profile in 40.9% and remaining masses presented with oval or round shape (60.1%) while 62.3% of TPC were irregular in shape. Similar observations were obtained by Wojcinskiet al [5], Dogan et al [16] and ko et al [18]. 54.6% of TNC showed circumscribed margin (smooth, microlobulated or microlobulated) and 73.6% of TPC presented with ill-defined or speculated margin. Wang et al [21]showed that TNC are less likely to be associated with speculated margin and other comparable observations were concluded by different authors in many literatures. [1, 5, 16, 18]
With respect of echo pattern of the breast mass on ultrasound, most TNC were hypoechoic (90%) and no significant difference was found in echo pattern of the lesions in between TNC and TPC as seen in Wojcinski et al.[5]

Regarding the orientation of the longest axis of the lesions, most triple negative masses was parallel to the skin surface on ultrasound (63.6%) whereas 60.4% of TPC were non-parallel. The parallel orientation is one of characteristics of benign breast lesions and these results support the hypothesis that ascertained benign morphology of TNC on sonography. [5, 22]

Triple negative cancer most frequently had an abrupt boundary (72.7%) while 58.5% of TPC had an echogenic halo at its boundary this may indicates aggressive biological behavior of the triple negative masses. Comparable findings were achieved by other authors as Krizmanich-Conniffet al [3] and Wojcinskiet al. [5]

Posterior acoustic enhancement was found in majority of TNC and less frequently in TPC (63.6% vs. 22.6%) and edge shadowing was less often found in TNC. Posterior acoustic echoes may indicate internal necrosis or fluid which is reported in many pathological evaluations. [5, 22]

With patients had color Doppler analysis of breast masses, most of TNC and TPC has positive internal flow (63.6 vs. 52.8%) and high resistive index (0.7 0r more) was found in 45.4% of TNC and in 37.8% of TPC and no significant difference was found in between two group regarding the vascularity of the lesions which is comparable to results that acquired by Kojima and Tsunoda study. [17]

Axillary nodal involvement at time of presentation was positive in 31.8% of TNC compared to 18.9% in TPC; however, majority of these LNs showed more suspicious morphology in TNC compared to TPC which is in agreement with Bo et al [4] and Wojcinskiet al. [5]

5. Conclusions

Although mammography is considered a gold standard screening tool for breast cancer, TNC lacks the characteristic criteria of breast cancer on mammogram and to less extent on ultrasound and may be occult on mammogram and may even mimic a benign lesion therefore mammography alone is generally suboptimal investigation tool in diagnosis of TNC and combined with ultrasound become useful to lower rate of missed diagnosis and can help in pretreatment planning and donate to a well understanding biological behavior of the each subtypes of breast cancer.

On mammogram, breast density was heterogeneous or extremely dense in majority of TNC and usually classified as BIRADS-IV category, more often presented as mass alone and less frequently as mass with microcalcifications or isolated microcalcifications and mass usually well circumscribed and less frequently irregular.

On ultrasound, most of TNC characterized by visible well circumscribed mass with oval or round shape, hypoechoic, and abrupt boundary, parallel to skin surface and frequently show posterior acoustic enhancement with high-resistive internal vascularity.

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