VOLUME-6 | ISSUE-3 | MARCH - 2017 • ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

INCIDENCE OF TRIPLE NEGATIVE BREAST CANCER AND ITS CLINICOPATHOLOGICAL STUDY IN A TERTIARY CARE HOSPITAL OF CHATTISGARH STATE

General Surgery

KEYWORDS: Triple negative breast cancer ,hormone receptors, ER, PR, HER2Neu

Dr.Manju singh	Professor, Department of surgery, Pt JNM Medical College, Raipur, Chhattisgarh India-492001
Dr.Gambheer singh	Professor, Department of surgery, RIMS, Raipur ,Chhattisgarh India-492001
Dr.Sanjana Tiwari	Jr3, Department of surgery, Pt JNM Medical College, Raipur, Chhattisgarh India-492001
Dr.Brajendra kumar	Professor, Department of Medicine, RIMS, Raipur ,Chhattisgarh India-492001

ABSTRACT

Triple negative breast cancer is defined as being negative for the estrogen receptors progesterone receptors and Her2neu receptors .It affects younger age group , presents with more advanced disease has high nuclear grade ,higher relapse rate and overall poor survival. It is a recent concept and the burning topic of research todayThe purpose of my study is to know the incidence of Triple negative breast cancer in our institute and to increase the awareness about triple markers among general population and early detection of Triple negative breast cancer and prompt and aggressive treatment of cases so their survival can be increased.This prospective observational study was conducted in department of surgery Pt J.N. Medical college and Dr B.R.A.M. Hospital Raipur .50 cases were studied after taking proper consent ,incidence and clinicopathological variables evaluated. The incidence was found to be 20% ,maximum incidence was found in age group 29-39 years.It was associated with larger tumor size ,higher lymph node positivity and higher metastasisThus TN breast cancer should be integrated as a risk factor analysis for breast cancer

INTRODUCTION

Breast cancer is the most common female cancer, worldwide, more than a million women are diagnosed every year, however despite this increase, the mortality rate is declining, this is due to combination of factors including early diagnosis and effective treatment.[1]

Breast cancer is a common but very diverse disease with considerable survival heterogeneity. An ongoing challenge is to find improved methods of identifying and classifying groups of tumors with differing biological behaviours or responsiveness to specific therapies.

Triple negative breast carcinomas (TNBCs) are a group of primary breast tumors with aggressive clinical behavior. The importance of recognizing these tumors came to light largely as the result of gene expression profiling studies that categorized breast cancer into 3 major groups.[3] Two of these groups are defined by their respective expression of estrogen receptor and HER2. TNBCs represent a third group and are defined by negativity for hormone receptors and HER2.[4]

Yet there is paucity of data for clinicopathological features of triple negative breast cancer in Indian population. To the best of our knowledge no study has been performed in the Chhattisgarh populations.

MATERIAL AND METHODS

The prospective observational study was carried out in the department of Surgery, Pt.J.N.M. Medical College, Dr.B.R. Ambedkar Memorial Hospital over a period from February 2015 to September 2016 on 50 patients of >18 years age group with already known or suspected breast cancer. They were evaluated with trucut biopsy gun and sent for histopathological examination and immunohistochemistry for ER, PR and HER2neu after taking consent and ethical clearance from ethics committee Pt J.N. Medical college and Dr B.R.A.M. Hospital Raipur.

Statistical analysis

- Findings were expressed in percentage and mean.
- Kolmogorove-Smirnov analysis was performed to assess the linearity of data.
- Chi-square test or Fischer's exact test were used to compare the frequency distribution amongst different groups.
- Student's t test was used to assess the significance of difference between ordinal data.
- IBM SPSS® Statistics for Windows, Version 19.0. Armonk, NY: IBM® Corp. and Microsoft excel® Microsft corp. Ltd. Were used for statistical calculation.
- P<0.05 was considered as statistically significant.

Inclusion criteria:

- All the patients > 18 yrs referred to the department of surgery presenting with breast cancer.

Exclusion criteria:

- Patients unwilling to take part in the study.

RESULTS

Incidence of triple negative breast cancer in study subjects was found to be 20% i.e. 10 subjects out of 50 were found to be TNBC.

	Frequency	Percent
Other breast carcinoma	40	80.0
Triple negative breast carcinoma	10	20.0
Total	50	100.0

Table 1

Incidence of triple negative breast cancer in age groups was assessed. Significant difference I incidence of TNBC was found to exist difference age groups (p=0.006). Maximum subjects were found in age group 51-60 years (50%) while no subjects with TNBC were present in Age group >60 years. Amongst the age group maximum incidence was found in the age group 29-39 years (75%) while age group 51-60 years showed incidence of 31.2% and age group 40-50 years showed incidence of 9.1%.

Age group	Triple negative breast Cancer	Other breast cancer	Total
29-30 yrs Count	3	1	4
Percentage	75%	25%	100%
40-50 yrs Count	2	20	22
Percentage	9.1%	90.9%	100%
51-60 yrs Count	5	11	16
Percentage	31.2%	68.8%	100%
>60 yrs Count	0	8	8
Percentage	0%	100%	100%
Total Count	10	40	50
Percentage	20%	80%	100%

Table 2: Incidence of triple negative breast cancer in age groups

Association of family history with triple negativity was assessed using Fischer's exact test. Significant association was found to exist between two parameters (p=0021) indicating comparatively higher frequency of family history in TNBC subjects.

			Group		Total	p value
			Other breast carcinoma	Triple negative breast carcinoma		
Family history	Absent	Count	36	6	42	0.021
		% within Group	90.0%	60.0%	84.0%	
	Present	Count	4	4	8	
		% within Group	10.0%	40.0%	16.0%	
Total	Count		40	10	50	
	% within Group		100.0%	100.0%	100.0%	

Table 3: Association of family history with triple negativity

Association of tumor size with triple negativity

Triple negative breast cancer is associated with larger tumor size as evidenced by T4 lesions in 7 out of 10 patients ,although association of tumor size with triple negativity was performed using Fisher's exact test. No significant difference was noted in two groups (p=0.055).

			Group		Total	p value
			Other breast carcinoma	Triple negative breast carcinoma		
T	T1	Count	4	0	4	0.055
		% within Group	10.0%	.0%	8.0%	
	T2	Count	24	3	27	
		% within Group	60.0%	30.0%	54.0%	
	T3	Count	2	0	2	
		% within Group	5.0%	.0%	4.0%	
	T4	Count	10	7	17	
		% within Group	25.0%	70.0%	34.0%	
Total	Count		40	10	50	
	% within Group		100.0%	100.0%	100.0%	

Table 4: Association of tumor size with triple negativity

Triple negative breast cancer is associated with higher lymph node positivity as 9 out of 10 patients had lymph node involvement although association of lymph node status and triple negativity was performed using Fischer's exact test. No significant difference was noted between two groups (p=0.176).

			Group		Total	p value
			Other breast carcinoma	Triple negative breast carcinoma		
N	N0	Count	12	1	13	0.176
		% within Group	30.0%	10.0%	26.0%	
	N1	Count	11	1	12	
		% within Group	27.5%	10.0%	24.0%	
	N2	Count	16	7	23	
		% within Group	40.0%	70.0%	46.0%	
	N3	Count	1	1	2	
		% within Group	2.5%	10.0%	4.0%	
Total	Count		40	10	50	
	% within Group		100.0%	100.0%	100.0%	

Table 5: Association of lymph node status and triple negativity

Association of Metastatic status and triple negativity was performed using Chi square test. Significant association was noted between two parameters indicating higher frequency of metastatic disease in TNBC (p=0.008).

			Group		Total	p value
			Other breast carcinoma	Triple negative breast carcinoma		
M	M0	Count	35	5	40	0.008
		% within Group	87.5%	50.0%	80.0%	
	M1	Count	5	5	10	
		% within Group	12.5%	50.0%	20.0%	
Total	Count		40	10	50	
	% within Group		100.0%	100.0%	100.0%	

Table 6: Association of Metastatic status and triple negativity

DISCUSSION

We assessed fifty subjects with breast cancer for ER, PR and Her2 new receptors and noted various factors associated with triple negativity in breast cancers. We also studied various socio-demographic factors, risk factors and clinical features associated with TNBC Incidence of triple negative breast cancer in study subjects was found to be 20% i.e. 10 subjects out of 50 were found to be TNBC which is similar to Indian studies

Chun-Yan Li et al (2013) noted incidence of TNBC to be 10.4-13.5% in their hospital, author examined about 12,749 subjects.[6] **Faoulkes William D et al** (2010) in a review article on TNBC states that 12-17% of breast cancer subjects has TNBC.[7] . In India, the incidence of TNBC was found to vary from 12.5% to 29.8%.[9]

Incidence of triple negative breast cancer in age groups was assessed. Significant difference I incidence of TNBC was found to exist difference age groups (p=0.006). Maximum subjects were found in age group 51-60 years (50%) while no subjects with TNBC were present in Age group >60 years. Amongst the age group maximum incidence was found in the age group 29-39 years (75%) while age group 51-60 years showed incidence of 31.2% and age group 40-50 years showed incidence of 9.1%. This clearly indicate that the frequency of TNBC was significantly higher in lower age group,which is similar to wourldwide studies.

In a study by Alam et al (2016) the median age of patients was 39.5 years, quite younger than the Western data.[8] **Dent et al.**[5] have reported that the median age of TNBC patients were 53 years in their study. Younger median age in Indian population was supported by another two Indian studies.[10] This finding of younger median age most likely reflects the general trend of breast cancers occurring a decade earlier in Indian population than western data. **P suresh et al** Also reported population was slightly younger (median age 49 years)in their study on TNBC subjects, than the ones described in western data[9] (median age 53 years). The peak incidence was observed in the 5th decade (36.3%) in the study. Higher rates of triple-negative breast cancer have been observed in women who are younger, which may be associated with a greater likelihood of BRCA1 expression.

Association of family history with triple negativity was assessed and significant association was found to exist between two parameters indicating comparatively higher frequency of family history in TNBC subjects which is similar to wourldwide studies.

Li CY et al Also noted strong family history in TNBc during study of 21749 breast cancer the author states that One possible reason is the mutant BRCA1 gene.94 Phipps et al in their study also found that this increased risk of triple-negative breast cancer subtypes in subjects with family history. **Welsh et al** found that family history was

VOLUME-6 | ISSUE-3 | MARCH - 2017 • ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

associated with an increased risk of ER+ and ER-/PR-/HER2+ breast cancers but not triple-negative breast cancer; however, those findings were based on a sample size of only 53 triple-negative cases and a shorter duration of follow-up.

Association of history of OCP intake and triple negativity no significant difference was observed between two parameters in my study.

Comparison of duration of symptoms between TNBC subjects and others was performed No significant difference was noted between TNBC and other tumors. Distribution of lesions in quadrants of breast was assessed no significant difference was noted in TNBC and other tumors in my study Association of tumor size with triple negativity was performed no significant difference was noted in two groups. Maximum TNBC tumors were found in size T4 (70%) while next most common size was T2 (30%).This finding of large size tumors may be due to lack of awareness, ignorance and less availability of female surgeons in the region Association of lymph node status and triple negativity was performed no significant difference was noted between TNBC and others. Though lymph node positivity was found to be more in TNBC subjects the difference failed to reach statistical significance. Maximum frequency of lymph node status in TNBC was found in N2(70%).

Association of Metastatic status and triple negativity was performed . Significant association was noted between two parameters indicating higher frequency of metastatic disease in TNBC. Half of the TNBC lesions were found to be in metastasis stage M1.This is similar to wourldwide studies At diagnosis, TNBCs are commonly of larger tumor size. In study by **Fayaz et al** , the mean tumor size was 3cm in TNBC group; similar to that in **Dent et al**.[5] study and larger than other non-TNBC group in the same study (3.0 versus 2.1cm, respectively; *P*<0.0001). It was smaller (2cm) in **Tawfik et al**. study.

Most of tumors were T2 in Singapore study (70%). In another study and in Japan, T2 represents about 43% of cases of TNBC.

The presence of positive lymph nodes in the Lebanese study was 50%, while it was detected in 58% in study by **Fayaz et al** . With almost a similar percentage, **Dent et al**.[7] found that the rate of node positivity was slightly higher in the triple-negative group compared with the other group (54.6% versus 45.6%, respectively; *P*=0.02). In contrast, non-significant difference was documented by **Tawfik et al.**[15] in the study from Kansas (48 vs. 41%). Interestingly, the ratio was reversed in the Turkish study (29.4 in TNBC vs. 38.5% in non-TNBC)[18], found it to be higher in their study (68%) while it was much lower in Japanese patients (34%).

The high invasive nature of TNBC suggests higher risks of metastasis and local recurrence of TNBC. The result of our study and those of others all have shown that the risk of metastasis after tumor resection is much higher in TNBC patients than in non-TNBC patient.[20] However, **Li CY et al** did not find an increased risk of local recurrence in TNBC patients. A higher risk of metastasis would suggest a relatively lower disease-free survival and overall survival of TNBC patients.

In deed, **Yuan et al** have reported in their study of 305 TNBC cases that TNBC patients have a lower survival rate due to an increased risk of metastasis . **Li Cy et al** shows that the increased metastatic risk in TNBC patients is mainly caused by the increased metastasis to the liver and lungs because no difference in metastatic risk to the bones and brain was found between TNBC and nonTNBC. [14] This result further supports the indication of the tissue preference of TNBC metastasis. It is known that cancers are more likely to metastasize to certain tissues . The tissue preference of metastasis is related to the gene expression profile of the cancer cells as well as the gene expression pattern in the targeted tissue.

Status of ER, PR and HER2new receptors

Estrogen receptors, progesterone receptors and Her2New receptors were found to be absent from TNC subjects. Thus also significant difference in distribution of these receptors was noted in frequency of these receptors between TNBC and Other tumors.

Triple-negative breast cancer (TNBC) is characterized by a lack of expression of both ER and PR as well as HER-2. TNBC is often classified as a basal-like tumor associated with high malignancy, high recurrence rate and poor prognosis.[22] Unlike other types of breast cancer, TNBC is not responsive to conventional hormonal and targeted therapies due to the lack of the expression of receptors. Owing to lack of these receptors TNBC is associated with high rates of proliferation and has a poorer prognosis than other breast cancer subtypes, as demonstrated by diminished progression-free survival and overall survival rates.[23] A greater understanding of the molecular mechanisms of TNBC may facilitate the identification of therapeutic targets, as well as predictive or prognostic biomarkers, and enable an understanding of the mechanisms of response or failure to current cancer treatments.

CONCLUSION

Triple negative breast carcinomas (TNBCs) are a group of primary breast tumors with aggressive clinical behavior. Presence of triple negative markers correlate well with response to hormone therapy and chemotherapy. The study of triple negative markers has a direct bearing on the recurrence rate, disease free period and overall survival of the patient.It was associated with larger tumor size,higher lymph node positivity and higher metastasis.Thus triple negative breast cancers should be integrated as a risk factor analysis for breast cancer .

REFERENCES

1. Keshtgar M, Davidson T, Pigott K, Falzon M, Jones A. Current status and advances in management of early breast cancer. Int J Surg 2010;8:199– 202.
2. National cancer registry programme report (1981-2001) [Last accessed on 2011 Jan 24]. Available from http://www.icmr.nic.in/ncrp/cancer regoverrview.htm .
3. Tavassoli Fa, Devilee P (Eds.): World Health Organization Classification of Tumors. Pathology and Genetics of Tumors of the Breast and Female Genital Organs. IARC Press: Lyon 2003. ISBN 9283224124.
4. Diaz LK, Cryns VL, Symmans WF, Sneige N. Triple negative breast carcinoma and the basal phenotype: from expression profiling to clinical practice. Adv Anat Pathol 2007;14:419 ^ 30.
5. Dent R,Trudeau M, Pritchard KI, et al . Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res 2007;13:4429-4434.
6. Li CY, Zhang S, Zhang XB, Wang P, Hou GF, Zhang J. Clinicopathological and Prognostic Characteristics of Triple Negative Breast Cancer (TNBC) in Chinese Patients: A Retrospective Study. Asian Pacifc J Cancer Prev, 14 (6), 3779-3784
7. Foulkes WD, Smith IE, Jorge S. Triple-Negative Breast Cancer. n engl j med 363;20:1938-48.
8. Alam S, Bhuyan T, Mohanty R, Mohanty RC. Rising Triple negative breast cancer cases in Odisha, India:An ominous sign. Int J Sci Res Edu 4; 8: 5702-05
9. Suresh P, Batra U, Doval DC. Epidemiological and clinical profile of triple negative breast cancer at a cancer hospital in North India. Indian J Med Paediatr Oncol. 2013;34:89–95.
10. Prabu MP, Raina V, Shukla NK, Mohanti BK, Deo SV. A study of triple-negative breast cancer at a Cancer Institute in India. J Clin Oncol. 2011;29:15. Suppl; abstr e11548. 8. Suresh P, Batra U, Doval DC. Epidemiological and clinical profile of triple negative breast cancer at a cancer hospital in North India. Indian J Med Paediatr Oncol. 2013;34:89–95.