



ORIGINAL RESEARCH PAPER

General Surgery

“INCIDENCE AND CLINICO PATHOLOGICAL FEATURES OF TRIPLE NEGATIVE RECEPTORS STATUS IN CARCINOMA BREAST IN OUR INSTITUTION”

KEY WORDS: Triple Negative Breast Cancer , Trucut biopsy, Premenopausal, IntraDuctal Carcinoma, Metastasis

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ABSTRACT

AIM OF THE STUDY: To determine Incidence of Triple Negative Breast Cancer (TNBC) in Stanley, To analyze the Clinico Pathological features of Triple Negative breast cancer and to compare it with reports from other regions of the world.
MATERIALS AND METHODOLOGY: This was a prospective study was conducted in Department Of General Surgery in GOVERNMENT STANLEY MEDICAL COLLEGE AND HOSPITAL, CHENNAI. (October 2015 to September 2016). ALL NEW CASES OF CARCINOMA BREAST Patients were subjected to **Trucut Biopsy** for confirm of the diagnosis and receptor status, then its clinico pathological features were analyzed and compared.
RESULTS: Incidence rate Of Triple Negative Breast Cancer (TNBC) 28% is higher in our Study, Affecting younger females with no significant risk factors or family history, Associated with significant poor prognostic factors like Nodal spread positivity(83%), High grade tumor(59.6%), IntraDuctal Carcinoma type (94%), Lymphovascular invasion(58%) and metastasis (23%).
CONCLUSION: This study Shows TNBC is Very Aggressive tumor with increasing incidence rate among SouthIndian Population and this finding throws more light on the need for treatment strategies to be better tailored to effectively treat the TNBC patients.

INTRODUCTION

Breast cancer is the most common cancer among females in urban India and is rapidly catching up with cervical cancer in rural India(23).An estimated about 1 Million cases of breast carcinoma has been diagnosed annually worldwide. Of these, more than 170,000cases are diagnosed as Triple-Negative. (15)

Triple-Negative Breast Cancer (TNBC) is defined by the lack of protein expression of estrogen receptor (ER) and progesterone receptor (PR) and the absence of HER2 protein over expression.

Triple-negative breast cancer (TNBC) accountsfor approximately 15% of breast cancers.(21)

- TNBC is a Very aggressive tumour, poor prognostic factor for disease-free andoverall survival,
- No effective specific targeted therapyis available for TNBC,
- There is a clustering ofTNBC cases in premenopausal women.

The prevalence of TNBC is highest in premenopausal African American women; a recent report notes that 39% of all African American Premenopausal women diagnosed with breast cancer are diagnosed with TNBC. (16)

Currently, effective treatment options are limited to chemotherapy, but the majority of patients who fail to achieve pathologic complete response after chemotherapy has unfavorable prognosis.

Reliable data on TNBC in Indian setting is scarce(17), hence, we felt the need to study the clinical profile of these cancers in our setting.

AIMS & OBJECTIVES

- The aim of this study is to determine the
1. Incidence of Triple Negative Breast Cancer (TNBC) in Stanley,
 2. To analyze the ClinicoPathological features of Triple Negativebreast cancer.
 3. To compare it with reports from other regions of the world.

REVIEW OF LITERATURE

In 2007, Study Conducted in California TNBC affects younger, women with low SocioEconomicStatus. TNBC were diagnosed at later stage and were more aggressive with poorer survival.(8)

In 2009 Study conducted in Egypt concludes TNBC is more aggressive with IDC is most common along with 15%metastasis. (4)

In 2010 study from Japan states that TNBC is very aggressive with poor pathological features like IDC (95%), grade3 (92%). Stage II (86.5%) is very common in TNBC. (6)

In 2010, Study conducted in Singaporeconcludes that triple-negative breast cancers in an Asian population harbor adverse pathological features (IDC, grade3). (4)

In 2010mayo Clinic concludes TNBC associated with unique patient presentations, poor tumor characteristics. (7)

In 2012, According to study conducted at mulagohospital States that there is a fairly high prevalence of triple negative breast cancer (20%) among Ugandan African women attending breast clinic at Mulago hospital and TNBC was found to be associated with poor prognostic characteristics. (12)

In 2013 a study Conducted in North India showed Triple negative cancers are highly aggressive tumors that have distinct epidemiological, pathological and outcome characteristics. About 12.5% of breast cancers at this institute were TNBCs, and they affected younger females with no correlation between lymph node positivity and tumor size, had most of the recurrences distally in visceral organs within a period of 3 years. (14)

In 2014 study from Kuwait concludes that TNBC is very aggressive, more common in premenopausal status, T2 lesion is more common with poor survival. (1)

In Summary Review Of literature implies TNBC cases incidence increasing worldwide which are Very aggressive tumor affecting younger age group of premenopausal women along with poor pathologic features and high recurrence rate with poor survival.

MATERIALS AND METHODS

PLACE OF STUDY:

Department Of General Surgery And Dept Of Medical Oncology in GOVERNMENT STANLEY MEDICAL COLLEGE AND HOSPITAL, CHENNAI -1

DURATION OF STUDY:

12 months (October 2015 to September 2016)

STUDY DESIGN:

PROSPECTIVE STUDY

PATIENT SELECTION:
ALL NEW CASES OF CARCINOMA BREAST

METHODOLOGY

- Patients who attended Stanley Medical College , Chennai for Admission, Investigation, Treatment of Breast cancer (New Cases)
- Based on the Hospital Registry, Medical files of all patients diagnosed with Breast Cancer.

For all patients, **Trucut Biopsy** was Done (as shown in Figure 1) for confirm diagnosis and Receptor status

TRUCUT BIOPSY

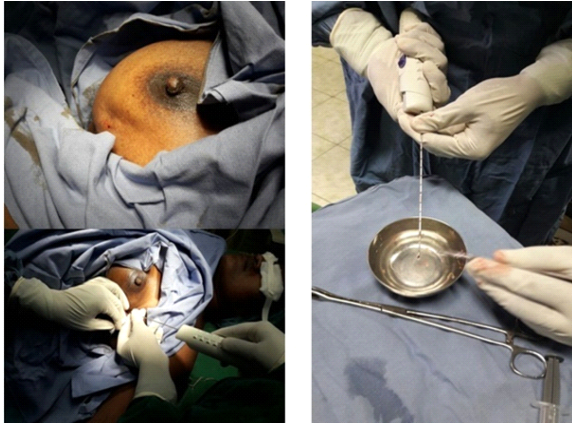


Figure 1:

Specimen sent to Pathology for

- HPE Report (Grade and Type of Tumour)
- ER/PR Status
- Her 2neu Status
- ER, PR and Her2neu Receptors status are assessed using Immunohistochemical Staining.
- Negativity was defined as absent Immunohistochemical stain in all the examined tissue.

The TNM staging was assessed based on clinical and radiologic findings(as shown in Figure 2).

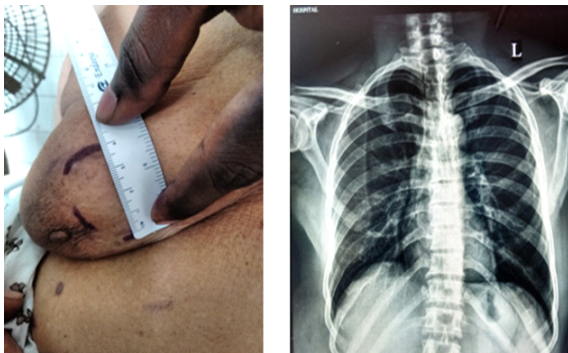


Figure 2:

Following Parameters are Analyzed in Triple Negative Breast Cancer :

- Incidence Rate
- In relation to Age
- In relation to Parity
- In relation to laterality
- In relation to Family history breast cancer
- In relation to PreMenopausal/PostMenopausal
- In relation to TNM Staging
- In relation to Grade and Type of Tumour
- In relation to Metastasis at Diagnosis
- In relation to lymphovascular invasion

- In relation to chemotherapy
- Comparison of Age with Grade of tumor
- Comparison Of Nodal spread with Lymphovascular Invasion
- Comparison of TNM Staging with Age and Menopausal status

RESULTS
INCIDENCE RATE

Incidence Rate 28.6 %

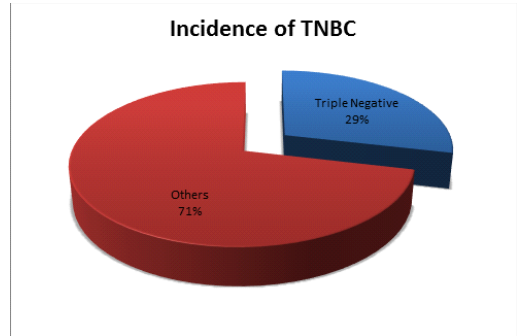


Chart 1:

In Our Study , the Incidence rate of Triple Negative breast Cancer is 28.6% (as shown in Chart 1) Total number of Carcinoma Breast are 164 cases, in which Triple Negative Breast Cancer was 47 cases others 117 cases.

AGE WISE DISTRIBUTION

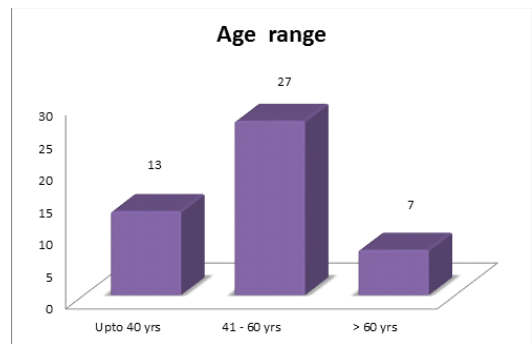


Chart2:

Table :1

AGE Distribution	Frequency	Percent	Valid Percent	Cumulative Percent
Upto40yrs	13	27.7	27.7	27.7
41 - 60yrs	27	57.4	57.4	85.1
> 60 yrs	7	14.9	14.9	100.0
Total	47	100.0	100.0	

In our study (total 47 cases), Almost more than 50% TNBC (27cases) comes under Age group of 41 to 60yrs, in which 19 cases out of 47 cases fall between 41 to 50yrs (as shown in Chart 2 & Table 1).

FAMILY HISTORY OF BREAST CANCER:

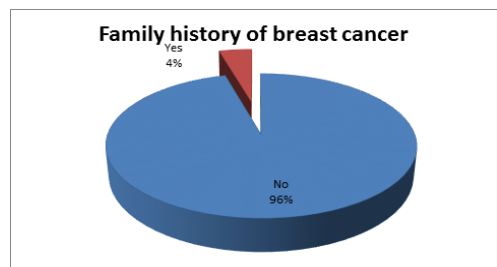


Chart 3:

In our study Family history cancer was present in only 2 Cases ,Total = 47Cases (as shown in Chart 3).

IN RELATION TO PARITY

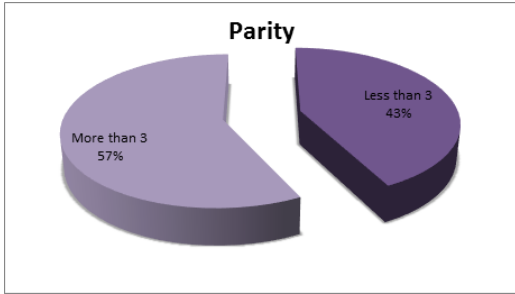


Chart 4:

In our study parity more than 3 (57.4%) was slightly common when compared to less than 3 (as shown in Chart 4)

MENOPAUSAL STATUS

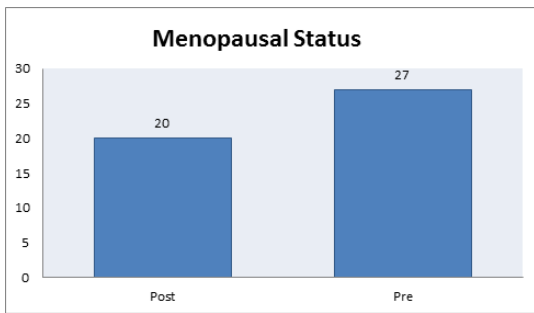


Chart 5:

In our study group (as shown in Chart 5), Premenopausal status is more common (57.4%) when compared to post menopausal status which was 42.6% (20cases)

LATERALITY

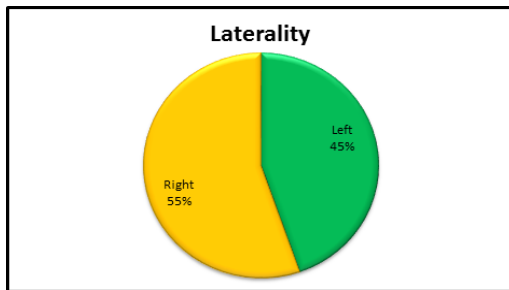


Chart 6:

This Chart 6 Shows Triple Negative cases have Right side laterality (55.3%)slightly higher when to compared left side (44.7%)

TYPE OF TUMOUR

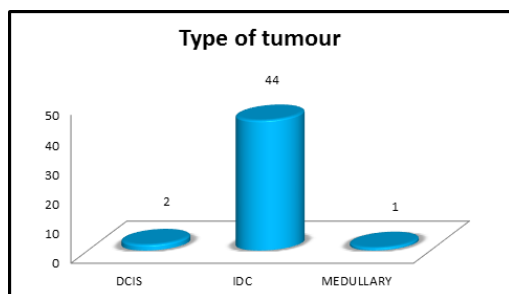


Chart 7:

Table 2:

Type of Tumour	Frequency	Percent	Valid Percent	Cumulative Percent
DCIS	2	4.3	4.3	4.3
IDC	44	93.6	93.6	97.9
MEDULLARY	1	2.1	2.1	100.0
Total	47	100.0	100.0	

In our study (as shown in chart 7 and table 2), IntraDuctal Carcinoma (IDC) is more common (93.6%) when compared to DCIS (4.3%) and Medullary Carcinoma (2.1%)

GRADE OF TUMOR

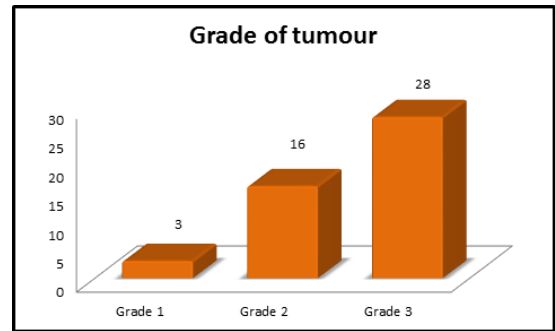


Chart 8:

Table 3:

Grade Of Tumor	Frequency	Percent	Valid Percent	Cumulative Percent
Grade 1	3	6.4	6.4	6.4
Grade 2	16	34.0	34.0	40.4
Grade 3	28	59.6	59.6	100.0
Total	47	100.0	100.0	

In Our Study group (as shown in chart 8 & table 3), Grade 3 (59.6%) tumor was more common followed by grade2 (34%). Grade 1 Tumour was very less (6.4%)

NODAL SPREAD

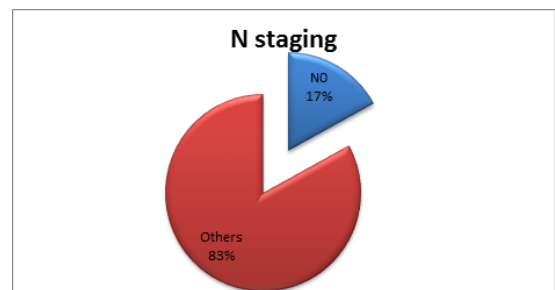


Chart 9:

In Our study (as shown in chart 9), Based on TNM Staging Nodal spread is more (83%) 39 cases.

TNM STAGING

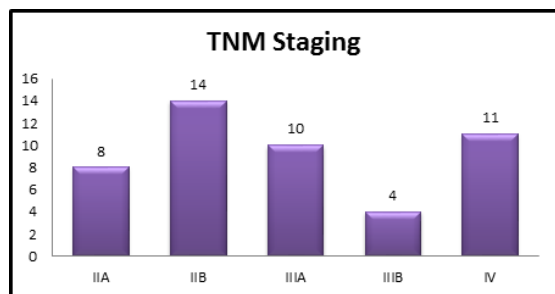


Chart 10

Table 4

TNM STAGING	Frequency	Percent	Valid Percent	Cumulative Percent
IIA	8	17.0	17.0	17.0
IIB	14	29.8	29.8	46.8
IIIA	10	21.3	21.3	68.1
IIIB	4	8.5	8.5	76.6
IV	11	23.4	23.4	100.0
Total	47	100.0	100.0	

In Our Study (as shown in chart 10 & Table 4), Based on TNM Staging Stage IIB is more common (29.8%) followed by Stage IV (23.8%), Stage IIIA (21.3%), Stage IIA (17%), StagelIIB(8.5%).

EARLY BREAST CANCER: Figure 3 on Right side is T2 N1 M0 lump inright lower outer quadrant, Figure 4 on left side is T2 N0 M0 lump in right upper outer quadrant



Figure 3

Figure 4

LOCALLY ADVANCED BREAST CANCER (LABC):

Figure 5:



METASTASIS AT THE TIME OF DIAGNOSIS

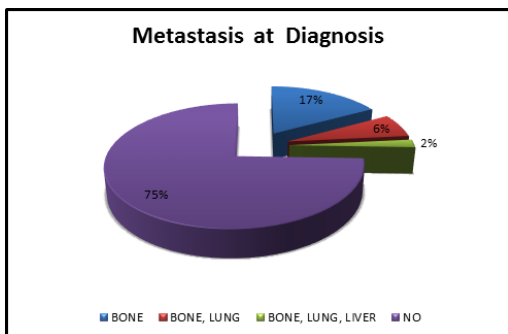


Chart 11

Table 5:

Metastasis at Diagnosis	Frequency	Percent	Valid Percent	Cumulative Percent
BONE	8	14.9	14.9	14.9
BONE, LUNG	3	6.4	6.4	21.3
BONE, LUNG, LIVER	1	2.1	2.1	23.4
NO	35	76.6	76.6	100.0
Total	47	100.0	100.0	

This chart 11 & table 5 shows Metastasis (23.4%) is common in Triple Negative ca breast cases in which bony metastasis was present in all cases followed by lung metastasis.

TREATMENT DETAILS

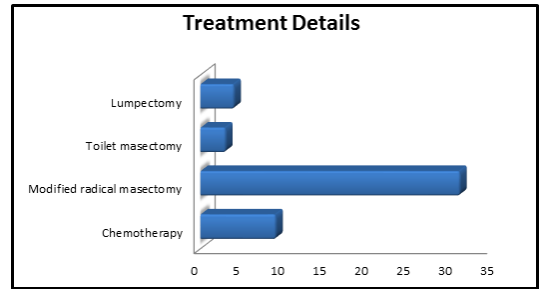


Chart 12

Table 6

Treatment details	Frequency	Percent	Valid Percent	Cumulative Percent
Chemotherapy	8	19.1	19.1	19.1
Modified radical mastectomy	32	66.0	66.0	85.1
Toilet mastectomy	3	6.4	6.4	91.5
Lumpectomy/WLE	4	8.5	8.5	100.0
Total	47	100.0	100.0	

In our study Majority cases underwent MRM 66% followed by palliative Chemotherapy 19.1%, Lumpectomy/Wide Local Excision (WLE) 8.5%, Toilet mastectomy 6.4% as shown in chart 12 & Table 6.

INTRA OP MRM - AXILLARY DISSECTION PICTURE SHOWING AXILLARY VEIN

MAHESWARI 50/F 1563894 RIGHT MRM

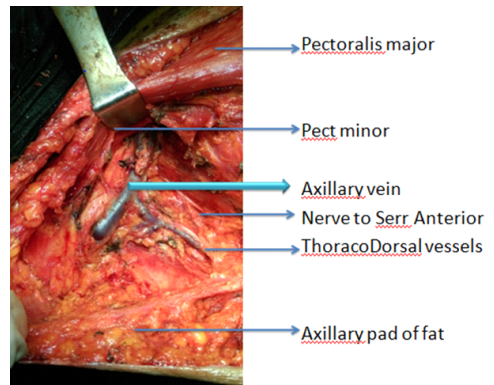


Figure :6



POST OP WOUND AFTER MRM SURGERY (Figure 7)

THAMARAI SELVI 48/F 1564796 RIGHT MRM POST OP WOUND

RIGHT MODIFIED RADICAL MASTECTOMY SPECIMEN :



Figure 8

TOILET MASTECTOMY FOLLOWED BY SSG COVER FOR STAGE IV DISEASE:

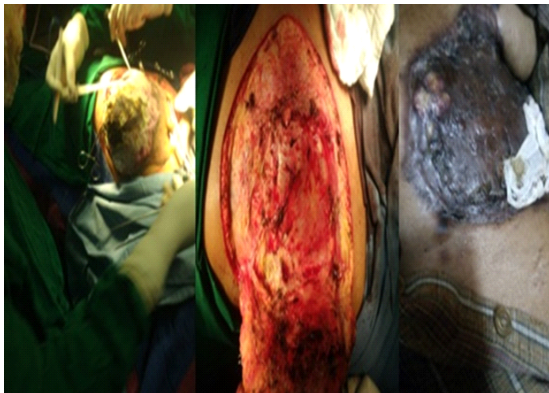


Figure 9

CHEMOTHERAPY

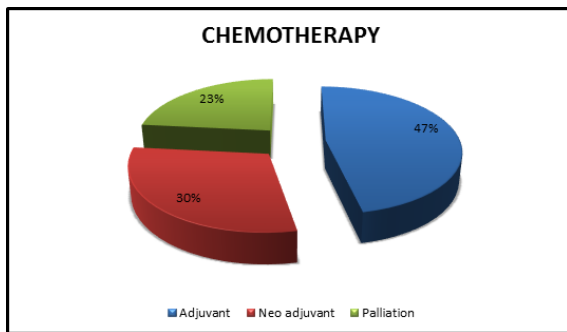


Chart 13

This chart 13 shows 46.8% cases received Adjuvant Chemotherapy, 29.7% NeoAdjuvantChemotherapy, 23.5 % Palliative Chemotherapy.

LYMPHOVASCULAR INVASION (LVI)

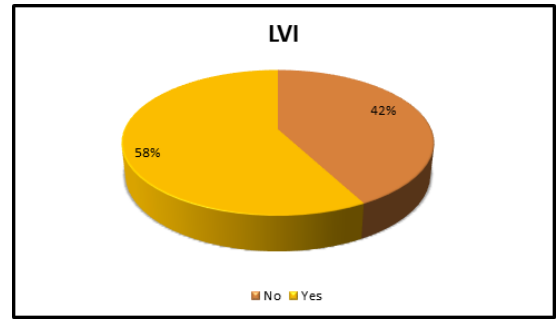


Chart 14

This chart 14 shows Lympho Vascular invasion (LVI) is more common in patient who underwent MRM/Toilet Mastectomy (58%).

AGE COMPARISON WITH TNM STAGING

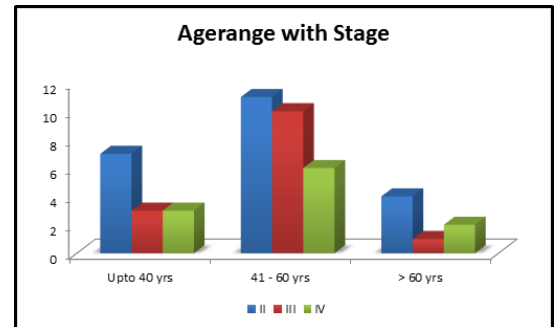


Chart 15

Table 7

		TNM Staging			Total
		II	III	IV	
Age range	Upto 40 yrs	Count 7	3	3	13
		% of Total 14.9%	6.4%	6.4%	27.7%
	41 - 60 yrs	Count 11	10	6	27
		% of Total 23.4%	21.3%	12.8%	57.4%
> 60 yrs	Count 4	1	2	7	
	% of Total 8.5%	2.1%	4.3%	14.9%	
Total		Count 22	14	11	47
		% of Total 46.8%	29.8%	23.4%	100.0%

From above comparison of Age with TNM staging, Stage II is more common in all age groups

STAGE COMPARISON WITH TUMOR GRADE

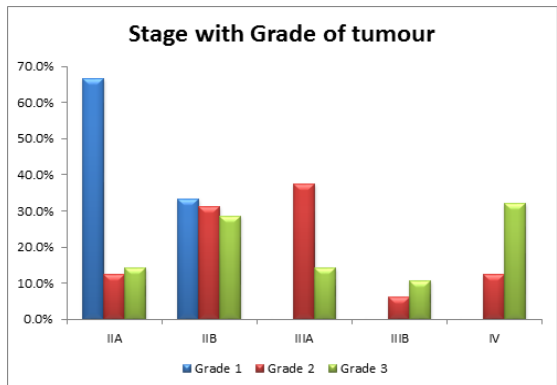


Chart 16

In Our study, Stage with Tumour Grade shows In Early breast Carcinoma Stage IIA (EBC) grade 1 is more common In Early Breast Carcinoma Stage II B (EBC) No Significant

In all locally advanced Breast cancer Stage (LABC) Grade3 is common

AGE COMPARISON WITH GRADE OF TUMOR

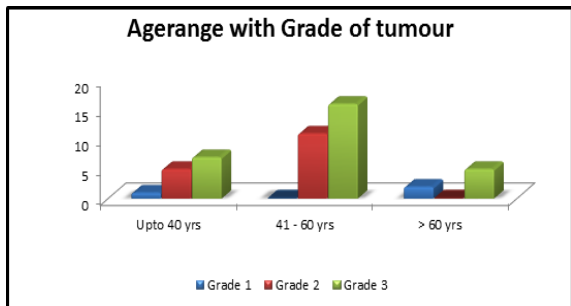


Chart 17

Table 8

		Grade of tumor			Total	
		grade 1	grade 2	grade 3		
Age range	Up to 40 yrs	Count	1	5	7	13
		% of Total	2.1%	10.6%	14.9%	27.7%
	41 - 60 yrs	Count	0	11	16	27
		% of Total	0.0%	23.4%	34.0%	57.4%
	> 60 yrs	Count	2	0	5	7
		% of Total	4.3%	0.0%	10.6%	14.9%
Total		Count	3	16	28	47
		% of Total	6.4%	34.0%	59.6%	100.0%

Table 9

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.208 ^a	4	.037

Grade 3 more common in all age group shows Significant p value 10.208 (<0.037)

GRADE COMPARISON WITH MENOPAUSAL STATUS

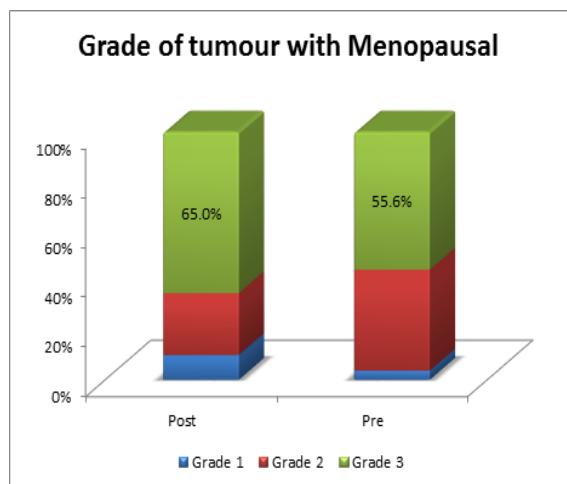


Chart 18

Chi-Square Tests

There is no significant between grade of tumor and menopausal status Pvalue is 1.844 (<.764)

NODAL SPREAD COMPARISON WITH MENOPAUSAL STATUS

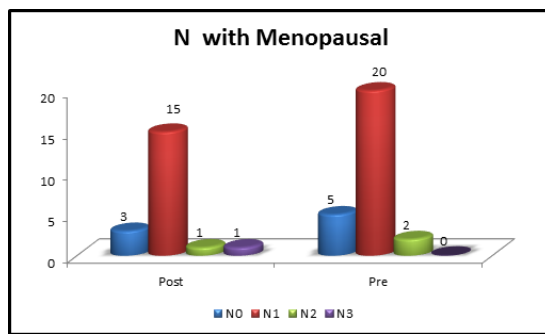


Chart 19

In Above chart 19 Comparison there is no significant between Nodal spread with menopausal Status P value is 1.539 (<0.673)

NODAL SPREAD COMPARISON WITH LVI

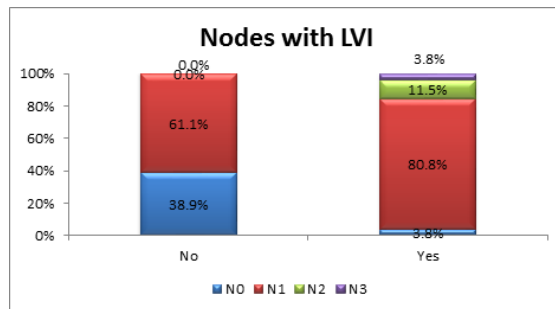


Chart 20

Table 10

	No	Yes
N0	38.9%	3.8%
N1	61.1%	80.8%
N2	0.0%	11.5%
N3	0.0%	3.8%

Chi-Square Tests

Table 11

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.518a	3	.015

In above Comparison there is significance between LVI positive in Nodal Spread cases. P value is 10.518 (<0.015)

DISCUSSION

- Our study Incidence rate in Stanley Medical College was **28.6 %** which was higher when compared to other studies
- **Most common age group is 40 to 50 yrs**(19 cases out of 47)
- Early age group is 30yrs and Older age group is 87 yrs.
- Mean Age group is 48.6yrs
- Family history breast cancer was seen in only 2 patients.
- Parity more than 3 was slightly higher in TNBC.
- TNBC is more common in Premenopausal Status (57.4%).
- Nodal Spread is more common in TNBC (83%)
- Grade 3 was more common in TNBC (59%)
- IntraDuctalCarcinoma is more common in TNBC(94%)
- Stage IIB is more common (29.6%)
- Metastasis 23% where Bone is more common(15%)
- Lymphovascular invasion is more common in TNBC (58%)
- Adjuvant 47% NeoAdjuvant 30% and Palliative chemotherapy 23%

CROSS COMPARISONS

- **Age with grade of tumor**
Grade 3 more common in all age group Significant p value <0.5
- **Lymphovascular invasion with Nodal spread**
80% nodal positivity has LVI Significant p value <0.15
- **Age with Stage**
Stage II is common in all age groups
- **Menopausal status with TNM Staging**
No significant
- **Menopausal status with grade of tumor**
No significant

COMPARISON TABLES

Patient characteristics in different studies. Table 12

	Incidence	Mean Age	Premenopausal	Parity more than 3
Stanley *	28%	48.6	57.4%	58%
North India(14)	15%	49	52%	71%
Kuwait(1)	13%	48	61%	50%
Turkey(11)	11%	44	70%	
Singapore(4)	11%	53		
Korea(5)	16%	45		
MayoClinic(7)	19%	59.7		
Bauer at all(8)	15%	50	64.6%	
Mulago(12)	20%		74%	
Egyptian(4)	15%	52%	48%	

In this Above table 12 Our study has been compared with various study groups done in various regions of world including North India.

Contd., (Table 1) Incidence was very high (28%) in our study when compared to all others, mean age was 48.6yrs which is slightly lower when compared to Study done in mayo clinic(59.7yrs) Singapore(53yrs) Egyptian(52yrs).

Premenopausal Status was lower(57.4%) when compared to Mulago(74%), Turkey(70%), Bauer et al (64.6%) and it was slightly higher when compared to NorthIndia (52%) and Egyptians(48%)

Parity more than 3 was lower (57.4%) when compared with North India study(71%)

Tumor characteristics in TNBC in different studies (Table 13)

	IDC	Grade 3	LVI	T2lesion	Stage II	LN +ve	Metastasis
Stanley *	94%	59%	58%	47%	47%	83%	23%
NorthIndia(14)	90%	61%	70%	62%	71%	40%	12%
Kuwait(1)	81%	57%	23%	43%	56%	58%	12%
Lebanon(2)	81%	63%			64%	50%	
Turkey(11)		53%	19%			29.4%	
Singapore(4)	93%	77%		70%			
Korea(5)		53.7%			90%		
Japan(6)	95%	92%		43%	86.5%	34%	
MayoClinic(7)	88%		18%				
Dent at all(3)		63%				54.6%	
Kanvas US(10)		75%	33%				
Egyptian(4)	93%				38%		15%

In above table 13 comparison IDC is More common in our Study group(94%) along with Japan(95%) Singapore(93%) and Egyptian(93%). Grade 3 was more in all study group highest in Japan (92%). Lymphovascular Invasion is also common (58%) in

our study highest seen in NorthIndia(70%). Stage II with T2 lesion is more common in our Study(47%) which was lower when compared to other studies. Nodal spread (83%) and Metastasis(23%) is more common in our study when compared to other studies.

CONCLUSION

Incidence rate Of Triple Negative Breast Cancer (TNBC) is higher in our Study, Affecting younger females with no significant risk factors or family history, Associated with significant poor prognostic factors like Nodal spread positivity, High grade tumor, IntraDuctalCarcinoma type, Lymphovascular invasion and metastasis.

Therefore this study Shows TNBC is Very Aggressive tumor with increasing incidence rate among SouthIndian Population and this finding throws more light on the need for treatment strategies to be better tailored to effectively treat the TNBC patients.

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