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Clinicopathological Features of Triple Negative Breast Cancer: A Perspective Analysis

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Abstract:
Aim
- *The aim is to study various clinicopathological features of TNBC in Northern part of INDIA.*

Background:
- *Molecular classification of breast cancer is based on gene expressing profile.*
- *They subgroup [luminal A, luminal B, HER2, and basal like] have distinct gene expression pattern and phenotypical characteristics.*
- *TNBC shares phenotypical features with basal like breast cancer, which is in turn the most aggressive and with worse outcome.*
- *There is a growing evidence of the heterogeneity of such entity on the molecular level that may cause discrete outcomes*
- *They are associated with aggressive histology, poor clinical outcome, associated with BRCA1 mutation and unresponsive to endocrine therapy and short survival.*

Material And Method:
- ***Study Design:*** *Hospital based retrospective, descriptive type of observational study.*
- ***Study place:*** *Dept. of general surgery SMS hospital Jaipur.*
- ***Study population:*** *338 cases of diagnosed breast cancer.*
- ***Statistical Analysis:*** *Descriptive statistics.*

Result:
- *Total breast cancer patients studied = 338*
- *30 patients [9.7%] were found to have TNBC*
- *Most [56.6 %] were before the age of 45 years.*
- *More common in pre menopausal women[60 %]*
- *Most of TNBC [96.6 %] had histological features of IDC*

Conclusions:
- *TNBC represents around 10 % of breast cancer.*
- *TNBC is commonly associated with pre menopausal status before the age of 45 years.*
- *TNBC is commonly occurs in UOQ with infiltrative duct histology.*

I. Introduction

Only a decade ago, breast cancer was considered a relatively 'simple' disease in many respects, with focus essentially on quantifying whether a tumour was, or was not, estrogen dependent—a situation that had lasted for a century [1]. A quiet revolution has taken place so that in modern times breast cancer is characterized by its molecular and clinical heterogeneity. Molecular classification of breast cancer is based on gene expressing profile, theysubgroup [luminal A, luminal B, HER2, and basal like] have distinct gene expression pattern and phenotypical characteristics. TNBC shares phenotypical features with basal like breast cancer, which is in turn the most aggressive and with worse outcome. There is a growing evidence of the heterogeneity of such entity on the molecular level that may cause discrete outcomes. Breast cancer is a heterogeneous disease, encompassing a number of distinct biological entities that are associated with specific morphological and immunehistochemical features and clinical behavior. Triple-negative breast cancer (TNBC) accounts for 10–20% of all breast carcinomas. Triple-negative cancers have a tendency to affect Pre-menopausal and African-American/Hispanic women more frequently [5].

Triple-negative tumors (estrogen receptor (ER), progesterone receptor (PR) and HER-2 negative) have aggressive clinical behavior and poor prognosis. Most TNBC shows a basal-like phenotype [4].More advanced stage at diagnosis and larger median tumor size are characteristic for TNBC. Triple-negative tumorshave high histological and nuclear grade, high mitoticindex, low local relapse rate, and more distant recurrence [5].

Relapses and deaths commonly occur within the first 5 years following diagnosis [2, 7]. Breast cancer survival at 3 and 10 years is correlated closely with histological grade, size, and lymph node involvement. In this study, we try to investigate some demographic, clinical, and pathological characteristics of the triple-negative breast cancers in Northern part of INDIA.

II. Patients And Methods

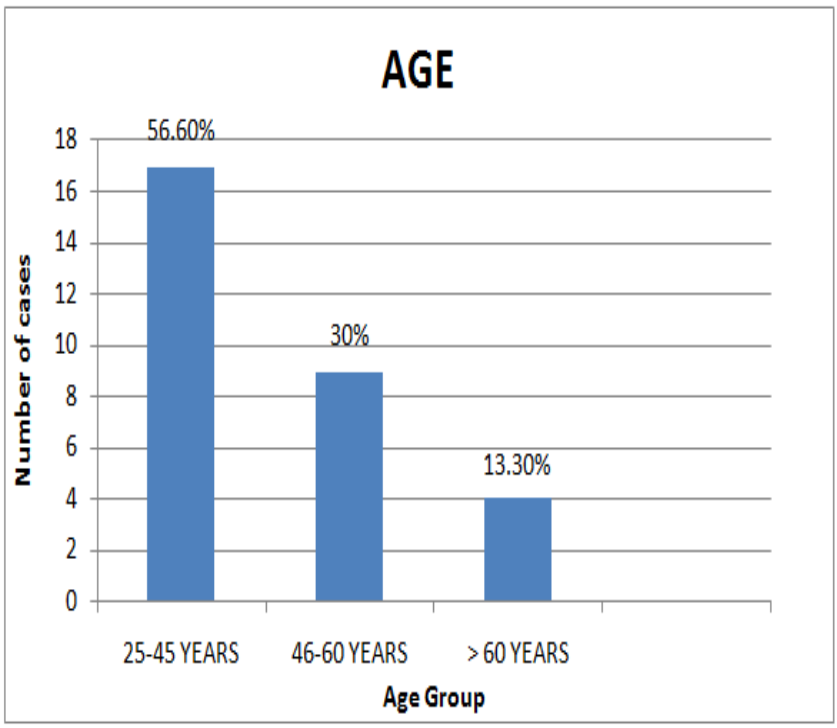
Study Design: Hospital based retrospective, descriptive type of observational study.
Study Place: Dept. of General Surgery SMS hospital Jaipur Rajasthan.
Study Population: 338 cases of diagnosed breast cancer.
Statistical Analysis: Descriptive statistics
This analysis included women with diagnosed breast cancer at SMS hospital Jaipur.
Patient demographics were obtained.
Tumors were staged according to the TNM criteria.

The data on ER, PR, andHER2/neu was obtained through standard clinical testing, Tumors scored as 2 were not included in this study. We further categorized the patients as triple-negative if they were negative for estrogen receptor, progesterone receptor, and Her2/neu.

III. Statistical analysis:

Table 1: Patient characteristics

		N	%
Age	**25 to 45 years**	17	56.6%
	46 – 60 years	9	30%
	>60 years	4	13.3%
Menstrual status	**Pre Menopause**	18	60%
	Post Menopause	12	40%
Laterality	**Right**	14	46.6%
	Left	16	53.3%
Locality	**UOQ**	16	53.3%
	REST	14	46.6%
Parity	**Parity □3**	19	63.3%
	Parity <3	11	36.6%
OCP use	**Yes**	5	16.6%
	No	25	83.4%
Smoking history	**Yes**	3	10%
	No	27	90%



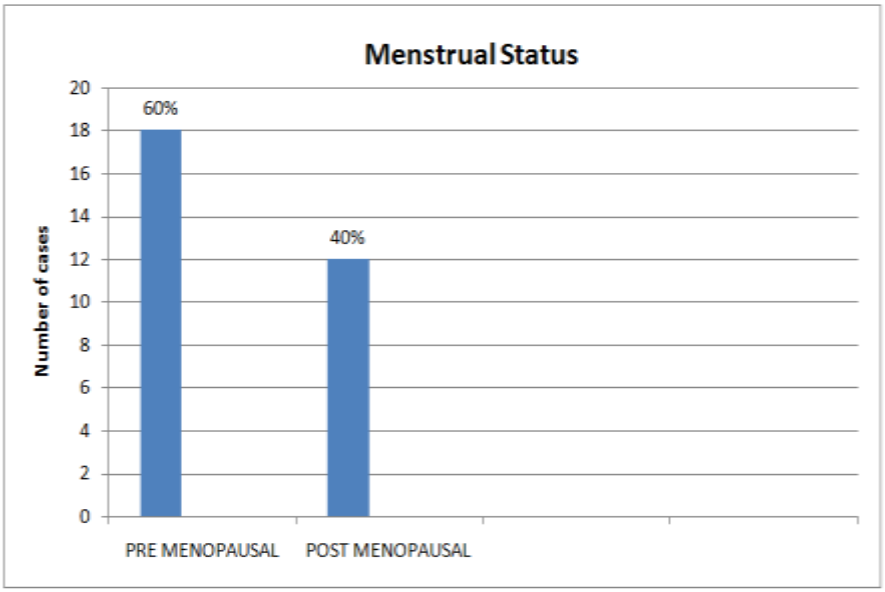


Table 2: Histological Pattern of TNBC:

Characteristic		**N**	**%**
Histological type	IDC	29	96.6 %
	OTHER	1	3.3 %

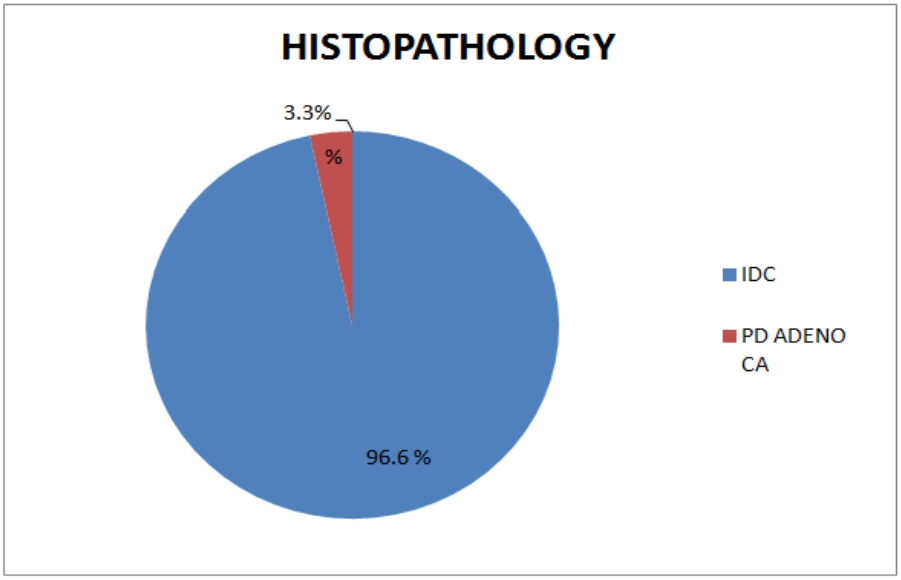
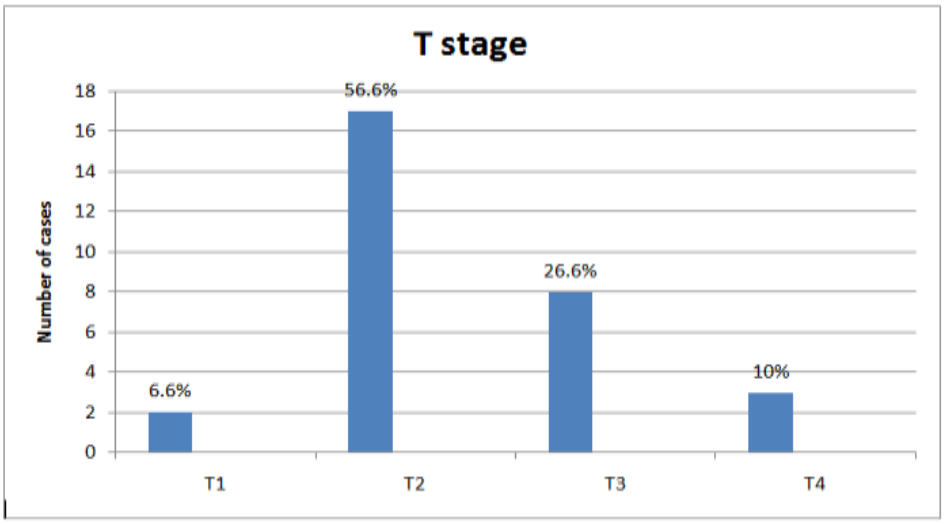
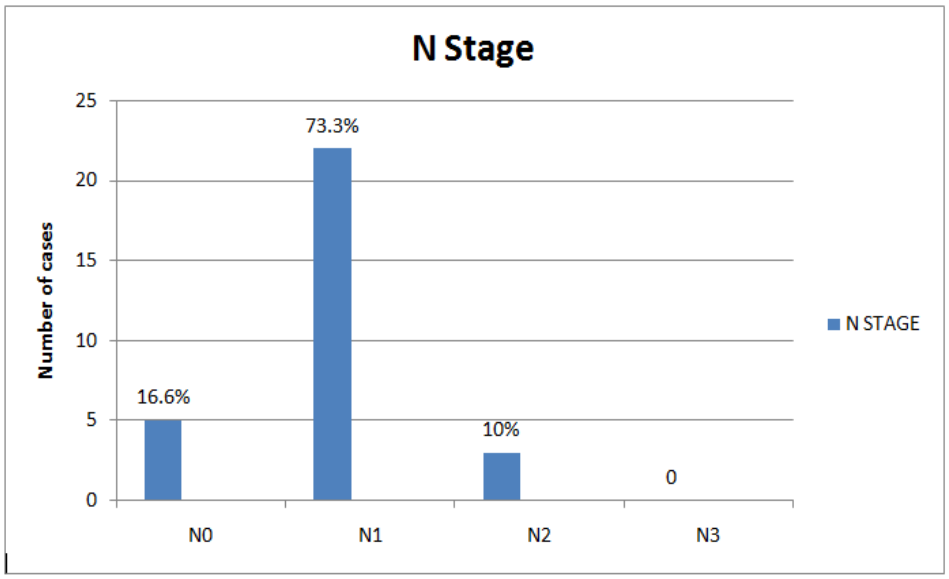


Table 3: Tumor characteristics

Characteristics		**N**	**%**
T STAGE	**T1**	2	6.6%
	T2	17	56.6 %
	T3	8	26.6 %
	T4	3	10%
N STAGE	**N0**	5	16.6 %
	N1	22	73.3 %
	N2	3	10 %
	N3	0	0 %
TNM STAGE	**1**	1	3.3
	2nd	17	56.6 %
	3rd	11	36.6 %
	4th	1	3.3 %
METASTATIS AT PRESENTATION	**YES**	1	3.3%
	NO	29	96.6.%


T stage
Number of cases
18
16
14
12
10
8
6
4
2
0
56.6%
26.6%
10%
6.6%
T1
T2
T3
T4


N Stage
Number of cases
25
20
15
10
5
0
73.3%
16.6%
10%
0
N0
N1
N2
N3
N STAGE

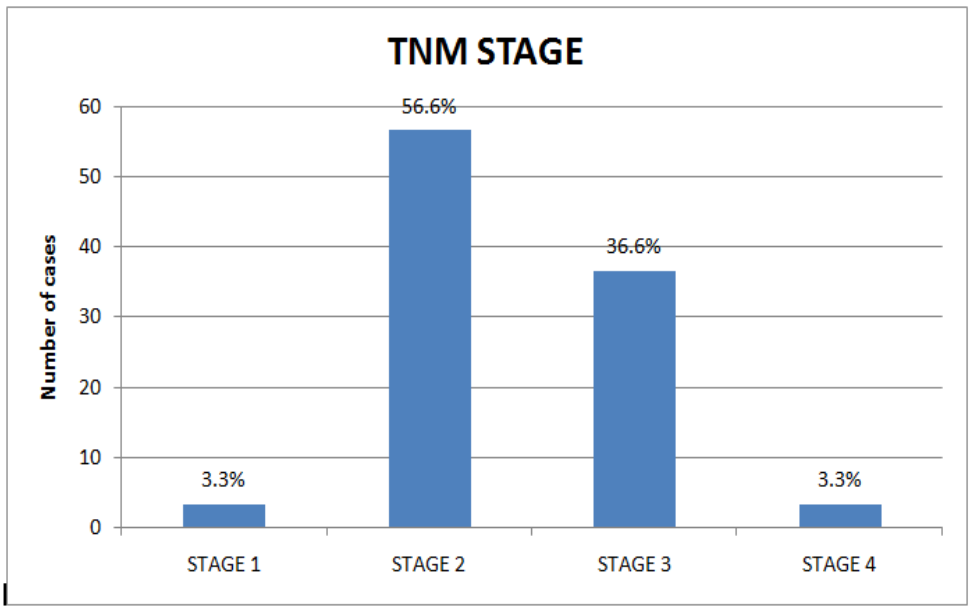

TNM STAGE
Number of cases
60
50
40
30
20
10
0
56.6%
36.6%
3.3%
3.3%
STAGE 1
STAGE 2
STAGE 3
STAGE 4

Table 4: Comparison with other studies

Studies	Prevalence (%)	Mean age	Post Menopausal (%)	Parity □3 (%)	OCP (%)	Smoking history (%)
Present study	9.7	46.8	40	63.3	16.6	10
Kuwait[33]	12.2	18	39	50.2	44	7.7
Lebanon[34]	9.3	52	52			
Turkey[11]	10.6	44	30		35	
Singapore[17]	11	53				
Korea[8]	16	45				
Japan[26]		56				
Mayo[35] **Clinic**		59.7				
Bauer et.[16] **al.**		50		664.6		
Dent et.al.[36]		50				
Phipps[19] **et.al.**				57	55	
Kwan[18] **wt.al.**				34	72	49

IV. Discussion

The demographic, clinical and pathological features of the patients with TNBC are different from other molecular type of cancer breast. The **prevalence** of TNBC in the northern part of India [Rajasthan] is 9.7% as shown in our study, Korea [16%] seems to have the highest and Lebanon [9.3%] the lowest[8,34] prevalence. In comparison to other breast cancer subtypes, pt of TNBC presents earlier than other molecular type of breast cancer, and in premenopausal women. In our study the average **age** of TNBC presentation was 46.8 years. Korea and Turkey have the youngest cohort the TNBC [44-45years], [8, 11]While Japan has the oldest [mean age was 56 years].[26] However many studies documented 50 years as the mean age at diagnosis of TNBC. 60% of the pt were **Premenopausal** which is comparable to the study done in Turkey [70%], [11]and 48% in Lebanon In our study 16.6 % patients gave history of **oral contraceptives** [OCP] as compared by 72% in Kwan et. al[18], 44 % in Kuwait[33], 55 % in Phipps et al study[19] and 35 % in the Turkish study.[11] In our study 10 % patients gave history of **smoking** as compared by 7.7 % in Kuwait[33] and 49 % in Kwan et al. In TNBC more than 90 % exhibit an invasive ductal **histology** [IDC]. In our study, 96.6% pts were of IDC which is almost comparable to that of Singapore and Japan [93 % and 95 % respectively]. At diagnosis, TNBCs are commonly presents with larger **tumor size**. In our study, the mean tumor size was 3.5 cm in TNBC group near about to that in dent et al [36] and Kuwait [33]. It was smaller [2 cm] in Tawfik et al. [17] study.

V. Results

Total 338 breast cancer patients were studied, out of them 30 patients [9.7] were found to have TNBC. Age of presentation of triple negative breast cancer is earlier than other sub groups of breast cancer. Pre menopausal women with breast cancer are more likely to have TNBC. Triple negative group have more aggressive behavior and present at more advanced stage.

They are mainly IDC.

Smoking, OCP intake and parity do not have any extra impact on triple negative type of breast cancer. The presentation in UOQ is more as compared to other quadrant which is same with other group of breast cancer. So TNBC is a different entity than other breast cancer and is an area for further research to develop novel treatment.

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