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Incidence and Clinical Profile of Triple Negative Breast Cancer (TNBC)

*Deepak Kumar rathi[1], Sarita Chaudhary[2], Mukta Sukhadia[3], Minaxi Sharma[3], Siddharth Verma[3], Garima Mehta[3]
[1]*Medanta the Medicity, Gurgaon (Haryana)*
[2]*SHKM medical college, Mewat (Haryana)*
[3]*R.N.T.Medical College, Udaipur (Rajasthan), India*
Corresponding Authour:Deepak Kumar rathi

Abstract
Objective: *To study the incidence and clinical profile of triple negative breast cancer (TNBC) patients.****Methods****Patients with histopathological evidence of breast cancer were evaluated for ER, PR HER-2 neu by immunohistochemistry. Their incidence and clinical profile were studied and result were analyzed statistically.*
Results: *196 out of 600 (32.67%) patients had TNBC. Patients with TNBC had younger age at presentation (51.48% were <50 years age) when compared to non-TNBC group (37.56% younger than 50). Patients with TNBC had significantly large tumor size (>5 Cm 24.85% vs 15.73%, p=0.012), higher node positivity (74.56% vs 64.86%, p=0.032), high recurrence whether distant or local (27.22% vs 16%, p=0.03), higher histopathological grade (55.90% vs 41.14%, p=0.05) when compared for non-TNBC group. 3 year DFS (Disease Free Survival) was significant lower in TNBC group (74.24% vs 85.66%, p<0.05). 5 year DFS rate was less in TNBC group, but not statistically significant.*
Conclusions:*TNBC was found more commonly in younger patients with large tumor size, high node positivity, more recurrence and less survival, suggesting an aggressive behavior when compared to non-TNBC group.*
Keywords*: TNBC (Triple Negative Breast Cancer), Non-TNBC(Non triple negative breast cancer), Hormone receptor, ER, PR, HER-2 neu.*

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I. Introduction

Breast cancer is being researched endlessly for past few decades. Rather than a single homogenous entity, it is now considered as a heterogeneous disease. Triple Negative Breast Cancer (TNBC) is a distinct clinical, histopathological and molecular sub-group of breast cancer which neither responds to tamoxifen nor to trastazumab andin general, associated with poor prognosis.Of all breast cancer diagnosed worldwide, TNBC found in about 10-17%[1]. Although TNBC accounts for a relatively small minority of breast cancer, it is important because it is responsible for a disproportionate high number of breast cancer deaths.Most of studies in TNBC have been done in western countries, who have entirely different clinical profile. So, we studied TNBC in R.N.T. Medical College, Udaipur, where majority of patients are from rural and tribal areas of southern Rajasthan.

II. Material & Methods

This study was conducted in Breast clinic of Department of General Surgery, RNT Medical College, Udaipur.The data of clinical profile of patients of breast clinic was studied retrospectively from 2001 to 2011.Patients with histo-pathological evidence of breast cancer were evaluated for ER, PR, HER-2 neu receptor status by immunohistochemistry (IHC).Breast cancer patients, who tested negative for ER, PR HER-2 neu i.e. TNBC were studied for their clinical profile.Results so obtained were evaluated and analyzed statistically.

III. Results And Discussion

Breast cancer is a heterogeneous disease. It was Perou et al (2000)[2] who, by using RNA expression assays, changed the landscape of breast cancer by defining its molecular types. Out of 1350 carcinoma breast patients seen in breast clinic, receptor status of 600 patients was known, in which 196 patients (32.67%) had TNBC, 37 patients were lost in follow up, which were excluded from the study.Most of the patients in our study

were from rural and tribal belt (58.19%).ReisFilho et al (2008)[3] found incidence of TNBC to be 10-17%. In 2011, an Indian study by Patil et al[4] on 1135 patient 19.9% of patients were triple negative.

In our study, we found that TNBC patients were significantly of younger age group (51.48% of <50 year age, p<0.05) than non-TNBC (38.08%).Table 1 demonstrate demographic & clinical characteristic of TNBC in Southern Rajasthan

Table 1 : Demographic & Clinical Characteristic of Triple Negative Breast Cancer (TNBC) in Southern Rajasthan

Variable	**No. of Patients (n=169) (%)**
Age	
Median Age	49.62 Years
< 35	14 (8.28%)
≥ 35	145 (91.72%)
Regional Distribution	
Rural	99 (58.56%)
Urban	70 (41.44%)
Histology	
Invasive Ductal Carcinoma	159 (94.08%)
Invasive Lobular Carcinoma	3 (1.78%)
Medullary Carcinoma	3 (1.78%)
Paget Disease	3 (1.78)
Invasive mucinous Carcinoma	1 (0.59%)
Duration of Recurrence (In years)	
< 3	27 (59.69%)
3-5	16 (34.78%)
> 5	3 (6.52)
Histopathological Grade	
I	8 (5.51%)
II	63 (43.45%)
III	90 (55.90%)

Table 2 demonstrates comparison between TNBC and Non-TNBC patients in our study.

Table 2 : Comparison between TNBC and Non-TNBC

Variable	No. of TNBC Patients (%) (n=169)	No. of Non-TNBC Patients (%) (n=350)	P Value
Age (Years)			
≤ 50	87 (51.48%)	131 (37.56%)	P=0.02
> 50	82 (48.52%)	219 (62.44)	
Tumor Size (Cm)			
≤ 5	127 (75.15%)	295 (37.56%)	P=0.012
> 5	42 (48.52%)	219 (62.44)	
Lymph Node Positivity	124 (74.56%)	227 (64.86%)	P=0.032
Recurrence (Metastasis and local)	46 (27.22%)	56 (16.00%)	P=0.03
3 Year DFS rate	74.24	85.66	P<0.05
5 Year DFS rate	73.63	81.55	P>0.05
5 Year OS rate	73.02	83.49	P>0.05

In 2007, a Canadian study on 1601 TNBC patients, Dent et al[5] found that they tend to have larger tumor at the time of diagnosis. In our study also, patients having tumor size >5 cm was more in TNBC (24.85%) than those of non-TNBC (15.73%). Rakha et al (2008)[6] in a study in U.K. reported higher prevalence of lymph node metastasis. Similarly in our study,73.22% of TNBC patients had lymph node (LN) positivity when compared to non-TNBC (64.86%).We found that more number of TNBC patients (27.22%) developed recurrence where local or distant, when compared to non-TNBC patients (16%) suggesting aggressive behavior of TNBC. The most common organ involved was lung (36.34%) followed by bone and liver. TNBC has a peculiar pattern of recurrence. Dent et al (2007) [5] found peak time of recurrence in TNBC patients at 2-3 years after diagnosis, then the risk subsequently declines over next 5 years. In our study 93.48% (43 out of 46) of TNBC patients had recurrence within 5 years of diagnosis, out of which 58.69% (27 patients) had it within 3 years. Dawood et al (2009)[7] in a study in Dubai found an increased risk of central nervous system metastasis (6-46% of those experiencing metastatic spread in TNBC). In our study out of 10 patients who had metastasis to multiple organ 3 developed brain metastasis (Total 3 out of 38 i.e. 7.89%).In Carolina breast cancer study in 2006[1], 90% of TNBC were of Ductal histology and 84% were of higher grade. We in our study found that 94.08% of patients had ductal carcinoma. Out of 169 patients 55.90% (P<0.05) were of grade III and were significantly more than those of non-TNBC (41.14%, P<0.05). So, TNBC tumors are of higher grade and mainly of ductal histology.Chemotherapy remains an iternal part of treatment for TNBC. Torrisiet al (2007)[8] found 5

year DFS rate in TNBC patients receiving CFF to be 84.61%.Eralp et al in 2008[9] found the patients receiving taxanesin combination therapy, 3 year DFS rate was 63%, while in our study it was 81.8%. 5 year DFS rate in patients receiving CAF was 62.85% indicating that TNBC have a higher chemosenstivity to epirupicinand taxane based chemotherapy, but generally have a worse prognosis mainly due to increased recurrence and metastasis .In a recent Chinese study in 2009 by Cao et al[10] on TNBC 5 year DFS rate was 73.81% and 5 year OS (Overall Survival) rate was 85.7%.When compared to above study we found decreased 5 year DFS rate (71.01%) and 5 year OS rate (78.02%) in our study most of patients are from rural background, which are diagnosed is relatively later stages when compared to western world. This is one of the facts of decreased survival is our study. We found statistically significant decreased 3 year DFS rate in TNBC patients (74.24%) vs non TNBC (85.66%, P <0.05), as we have seen that most of TNBC (58.69%) had metastasis or local recurrence within 3 years of diagnosis. 5 year DFS rate in TNBC (73.63%) was less than that on non-TNBC (81.55%), but was not statistically significant. This suggests that TNBC is overall more aggressive than non-TNBC group and has decreased survival.

IV. Conclusion

In our study in Southern Rajasthan most patients are from rural and tribal belt. In this population more number of carcinoma breast patients were TNBC when compared to western world. Survival was found to be less as more number of patients in our study presented in late stages. TNBC patients had larger tumor size, more lymph node positivity, were of higher grade, with more recurrence and decreased survival.

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