www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i4.162

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Incidence and clinical profile of Triple negative breast cancer in Kashmir

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Introduction

Breast cancer is a heterogenous disease, encompassing a plethora of entities which not only have distinct morphological features but also clinical behaviour. In recent years it has become apparent that this diversity may be underpinned by distinct patterns of genetic, epigenetic and transcriptomic abberations[1].

Tiple negative breast cancer (TNBC) is defined by a lack of expression of both estrogen and progesterone receptors as well as human epidermal growth factor receptor-2. It is charecterised by distinct molecular, histological and clinical features including a particularly unfavourable prognosis despite increased sensit-ivity to standard cytotoxic chemotherapy regimes.

The epidemiological risk factors of TNBC compared to non TNBC appear to differ significantly. Overall, the prevalence of TNBC in large unselected breast cancer patient cohorts is 11-20%[2,3], whereas in selected cohorts of patients with advanced breast cancer or patients of African-American ethnicity, TNBC may be diagnosed among as many as 23-28% of all patients[4,5] and in Asian populations upto 25-31%.[6]

Methods

The study was conducted in Department of Radiation Oncology and Department of Medical Oncology SKIMS SRINAGAR.

Inclusion criteria were breast cancer patients registered at Hospital Based Cancer Registry SKIMS from 2008-2012, who were documented as cases of TNBC by immunohistochemistry. Only patients having IHC documentation being ER-ve, PR-ve and HER2 1+ were taken for the study. Since data was collected retrospectively no patient having HER2 2+ was subjected to FISH testing as all the patients had already completed treatment and were on follow up.

Exclusion criteria were patients with double malignancy and male breast cancer patients.

Results

All the patients were evaluated jointly by Radiation Oncologists, Medical Oncologists and Pathologists. During this period of 5 years, total number of breast cancer patients registered at HBCR SKIMS SRINAGAR was 804 out of which TNBC accounted for a total of 94 patients which gives an incidence of 11.94% for TNBC in Kashmir. Simple statistics was used to evaluate the data.

Table 1: Distribution of cases according to various age paramenters.

Age group(yrs)	**N**			**Percent**	
21-30	6			6.38	
31-40	24			25.53	
41-50	32			34.04	
51-60	24			25.53	
61-70	6			6.38	
71-80	2			2.12	
Age Parameters (yrs)	**n**	**minimum**	**maximum**	**Mean**	**Std. deviation**
Age at menarche	94	12	14	13.07	+/- 0.626
Age at marriage	92	17	27	19.91	+/- 1.551
Age at Ist childbirth	90	18	28	21.16	+/- 1.260
Age at menopause	55	39	54	45.24	+/- 2.494

Most common age group at Presentation was 41-50 yrs accounting for 34.04% of the patients. Mean age at Presentation was 47.5 years. Mean fertile period in our patient population was 32 years.

Table 2: Distribution of cases according to Clinical Presentation.

Presenting symptom	**N**	**Percent**
Breast lump	79	84.0
Nipple discharge	3	3.2
Mixed	12	12.8

Most common presentation in this study group was Breast Lump.

Table 3: Distribution of cases according to site of involvement

Breast quadrant involved	**N**	**Percent**
Upper outer	63	67.0
Upper inner	12	12.8
Lower inner	4	4.3
Lower outer	10	10.6
Central	5	5.3

Upper outer quadrant was most common site of involvement in our cases.

Table 4: Distribution of cases according to lactational history and its duration.

Lactational history	**N**	**Percent**
Present	90	95.7
Absent	2	2.1
Not applicable	2	2.1
Duration	**N**	**Percent**
<1 yr	30	33.3
1-2 yrs	48	53.3
>2 yrs	12	13.3

Majority of our patients with children had a positive history of lactation and duration of lactation in most cases was 1-2 years.

Table 5: Distribution of cases according to Parity.

No. of live births	**N**	**Percent**
0	2	2.1
1	7	7.4
2	32	34.0
3	36	38.3
4	10	10.6
5	5	5.3
Not applicable	2	2.1

2 of our patients were unmarried and most common parity was 3.

Table 6: Distribution of cases according to any co-morbid conditions or family history of breast cancer.

Co-morbidity	**N**	**Percent**
Diabetes mellitus	3	3.2
Hypertension	11	11.7
Both DM/HT	3	3.2
Nil	77	81.9
Family history of breast cancer	**N**	**Percent**
Present	2	2.1
Absent	94	97.9

Hypertension was more common in our patients but both hypertension and diabetes mellitus which is considered as a part of metabolic syndrome was present in only 3.2% of our patients. History of Radiation exposure a risk factor for breast cancer

was absent in all of our patients. Only 2.1% of our patients had a positive family history of breast cancer.

Table 7: Distribution of our cases according to histopathology and stage of disease.

HPE	**N**	**Percent**
IDC	96	100
Stage	**N**	**Percent**
I	2	2.1
IIA	32	34.0
IIB	25	26.6
IIIA	13	13.8
IIIB	11	11.7
IIIC	11	11.7

All of our patients had infiltrating ductal carcinoma on histopathology and most common Stage at presentation in our patients was II followed by III.

Discussion

This study was undertaken to investigate incidence and clinical profile of triple negative breast cancer patients registered in our Hospital Based Cancer Registry at SHER-I-KASHMIR INSTITUTE OF MEDICAL SCIENCES(SKIMS) from 1st January 2008 to 31st December 2012. No advanced statistics was used to evaluate the data as same was not needed for this study. Most of our observations are in accordance with international published data but not so much with data from indian subcontinent as is discussed in detail below. There have been quite a few studies in triple negative breast cancer from indian subcontinent but kashmir being geographically, culturally and ethnically different from rest of India, this study was undertaken to see the similarities and differences in incidence and profile of triple negative breast cancer in Kashmiri populace when compared to rest of Indian subcontinent as well as international published data.

Total number of breast cancer patients registered at our institution in the said period was 804, out of which 94 patients had IHC documented triple negative breast cancer, so the incidence of triple negative breast cancer in this patient cohort was 11.69% which is in accordance to what Chaeng et al[3] observed but quite less when compared to general indian population in which triple negative breast cancer is found in as high as 31% of breast cancer patients[6].

Lin NU et al[7] observed the mean age at presentation in triple negative breast cancer of 47.5 years same as we observed in our study. Most common mode of presentation at the time of diagnosis was Lump followed by mixed symptoms of lump and discharge as illustrated in Table 2. Most frequent site of involvement in our patients was upper outer quadrant in 67% followed by upper inner quadrant in 12.8%. 95% of our patients were parous and had positive lactational history and most being para 3 as illustrated in Table 4 and 5. Majority i.e. 95% of our patients had lactational history of 1-2 year duration. None of our patients had a previous history of therapeutic radiation exposure or any history of significant radiation exposure due to serial chest x-rays/fluoroscopy as in case of hodgkins lymphoma or tuberculosis. History of both Diabetes mellitus and Hypertension was present in only 3.2% of our cases which can be a part of metabolic syndrome a risk factor for triple negative breast cancer[8].

Young age at menarche, high parity and short duration of lactation are found to be associated with triple negative breast cancer[4]. In our study mean age at menarche was 13 which is not completely in concordance with published data, mean parity was 3 which is in concordance but majority of our patients had lactational period of 1-2 years which again is not in complete concordance with the international published data. Family history of breast cancer was present in only 2.1% of our patients, 2.1% had history of other malignancy in family and 95.8% had no history of malignancy in family. Kandel et al[9] observed that among triple negative breast cancer patients 11% carry BRCA1 mutation and so present at a young age with family history but only 2.1% of our patients had such family history, BRCA1 testing was not done in any patient as no patient fit the BRCA1 testing criteria.

All of our patients had infiltrating ductal carcinoma and most frequent stage at presentation was IIA in 34% followed by IIB in 26.6% i.e. stage II in 60%, IIIA in 13.8%, IIIB in 11.7% and IIIC in 11.7% i.e. stage III in 37%. None of our patients presented in stage IV as illustrated in Table 7. Lin NU et al[7] observed that triple negative breast cancer patients presented in stage II(42%) and stage III(28%) trend being same as in our study most common stage at presentation was II.

This study shows the data of 5 year period and only 94 patients were found to have triple negative breast cancer. A larger cohort of patients is needed to replicate the observations to be high powered study statistically, but Kashmir being a small place when population is considered we think this sample of patient population likely represents the whole kashmiri populace. Further studies are underway to see the treatment outcome of these patients and results will be out soon to see the whole treatment profile, metastatic profile and survival analysis.

Aim

Triple negative breast cancer being a relatively aggressive form of breast cancer, aim of this study was to see the similarities and differences in clinical profile of TNBC in our representative population when compared to published national and international data.

Conclusion

In our study mean age at presentation was 47 years and 57% patients were postmenopausal, majority of our patients were multiparous with positive history of lactation. Family history of breast cancer was found in only 2.1% cases and most of our patients presented in localised stages most common being stage II. Some of our observations were in concordance with published data and some were not in complete concordance. A larger study is needed to clear the differences.

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