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An Overview of Male Breast Cancer in Western Odisha – A Hospital Based Retrospective Clinico-Pathological Study

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ABSTRACT: AIM- Male breast cancer is very rare, comprising 1% of all breast cancer with a male to female incidence ratio 1 : 100 . It comprises for < 0.2 % of all malignancies in men .. Rarity of disease and scarcity of data promoted us for retrospective clinico-pathological study, where to examine systemically regarding it's epidemiology, risk factors, clinical assessment, genetics, pathology and molecular markers. MATERIALS AND METHODS – This study was conducted in Department of Surgery, VIMSAR, Sambalpur, Odisha over a period of fifteen month (i.e. from August 2019 to October 2020), where male patients with aged between 30-75 years having clinical diagnosis of breast cancer were included. . The data regarding the incidence, presentation, histo-pathology, stage & grade of tumor, management and outcome were analysed. RESULTS – Out of 10 cases studied (which comprises 2.5% of all breast cancers seen in our department),8 (80%) cases had various risk factors for male breast carcinoma. Some cases were associated with multiple risk factors. Gynaecomastia (4 cases, 20%) comprises at the top, which was followed by obesity and breast cyst (3 cases,15% each) . Mean age at presentation for invasive group and non-invasive group were 54 years (range, 35 to 75 years) and 57 years (range, 50 to 65 years) respectively. Maximum number of cases (i.e 8cases , 80%) corresponds to invasive ductal carcinoma, which was followed by papillo-tubular carcinoma and adenocystic carcinoma (1 case each) . ER+ve andPR+ve comprises 8 (80%) cases and 7 (70%) cases respectively . 5(50%) cases were presented with Stage –III, which was followed by Stage–II and Stage-I having 3 cases and 2 cases respectively. None of them presented with Stage-IV carcinoma . Poor disease free survival rate corresponds to Triple negative cancers (24%). CONCLUSION - This study comprises higher Incidence rate (i.e 2.5%) of male breast cancers compared to national data , as it was done in a tertiary health care centre. Effort to increase awareness among patients, earlier presentation to clinicians, timely diagnosis before spreading to axilla and other organs, and evidence based treatment would be helpful in optimizing the management of this rare disease.

I. INTRODUCTION

Male breast cancer is very rare, comprising 1% of all breast cancer with a male to female incidence ratio 1 : 100 [1,2]. It comprises for < 0.2 % of all malignancies in men [3]. This is usually a disease of sixties. But in Middle East, China, South Asia and Africa male breast cancer is more common in fifties [4]. Incidence of male breast cancer increased by 26% over past 25 years. This disease may develop in a wide range of ages, i.e. the youngest patient was 9 years old and the oldest was above 90 years [5,6,7,8] . The mean age of presentation is 67 years, which is approximately 5-10 years older than females. Family history of first degree relatives, single marital status, previous benign disease of breast, and history of previous chest wall irradiation are the potential risk factors for male breast cancer. Smoking, alcohol use, obesity, hormonal therapy, and liver disease causing hyperestronism, and gynaecomastia are also additional risk factors [9]. Higher frequency rate corresponds to Jewish men (i.e 2.3 per 1 lakh cases), and country (like Egypt and Zambia) with higher incidence of malnutrition, parasitic liver diseasei.eschistosomiasis [10,11]. With exception of Tanzania and Central Africa (where higher proportion of male breast cancer cases are reported), male breast cancer is uniformly distributed throughout the world [12,13]. National Cancer Institute of United States reveals increasing incidence of male breast cancer from 0.86 to 1.08 per 1 lakh men [14]. However data on female breast cancers may not be completely relevant to men, particularly with regard to differences concerning the environmental environment, gender differences, medical / psychological side effects, and survival priorities. Rarity of disease and scarcity of data promoted us for retrospective study.

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II. AIM AND OBJECTIVE

This retrospective clinico-pathological study is done to examine systemically regarding it's epidemiology, risk factors,clinical assessment, genetics, pathology and molecular markers.

III. MATERIAL AND METHOD

Source of data- Patients admitted in department of General Surgery ,Veer SurendraSai Institute of Medical Science And Research (VIMSAR), Burla, Sambalpur, Odisha, India with clinical diagnosis of male breast cancer, were reviewed during our fifteen months study period. The data regarding the incidence, presentation, histo-pathology, stage & grade of tumor, management and outcome were analysed.

Study period - FromAugust 2019 to October 2020

Calculated sample size (n) – 10

Inclusion criteria-

- Male patients between 30 to 75 years of age with clinical diagnosis of breast cancer

Exclusion criteria-

- Age less than 30 years and more than 75 years.
- Immuno-compromised patients
- Patients with other diseases

Method of collection of data-Details of cases were recorded including history (including tumor size, histological grade, nuclear grade), clinical assessment, TNM tumor stage, immuno-histo-chemical study, molecular marker study. Complications encountered at and after surgery were evaluated.

Statistical Analysis-All groups were compared using Chi-square test and student's t test. P-value of < 0.05 indicated a statistically significant .

Ethical approval- Taken from Departmental Institutional Ethics Committee of Veer SurendraSai Institute of Medical Science And Research (VIMSAR), Sambalpur, Odisha before starting the study.

Funding – None funding sources

Conflict of Interest – None declared

IV. RESULTS

Table 1 :Risk factors for male breast cancinoma

Sl.no.	Testicular abnormalities	No. of cases (Out of total no. of cases = 10)
1.	Undescended testis	2 (10%)
2.	Congenital inguinal hernia	Nil
3.	Orchidectomy	1
4.	Orchitis	2 (10%)
5.	Testicular injury	1
6.	Infertility	1
7.	Klinefelter's syndrome	Nil
8.	Positive family history	1
9.	Obesity	3 (15%)
10.	Radiation exposure	1
11.	Breast cysts	3 (15%)
12.	Breast trauma	1
13.	Gynaecomastia	4 (20%)
14.	Other factors	0

Table 1 : Shows - out of 10 cases studied , 8 (80%) cases had various risk factors for male breast carcinoma. Some cases were associated with multiple risk factors. Gynaecomastia(4 cases,20%)comprises at the top, which was followed by obesity and breast cyst (3 cases,15% each), and then by undescended testis and orchitis (2 cases,10% each).Orchidectomy, Testicular injury, Infertility, Positive family history, Radiation exposure, Breast trauma were also risk factors for male breast carcinoma.

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Table 2 : Clinical features of male breast carcinoma (n=30)

Sl.no.	Clinical features	Invasive (n=07 cases)	Non-invasive (n=03 cases)
1.	Mean age (in years) (range)	54 (35-75)	57 (50-65)
2.	Mean duration of symptoms (months) (range)	4 (1 month -1 year)	8 (6 month -1year)
3.	Mass or lump	6/10 (60%)	1/10 (10%)
4.	Size of mass(in cms) (range)	3 (0.5-5)	1
5.	Site		
5a.	Retro-areolar	6/10 (60%)	1/10(10%)
5b.	Upper outer quadrant	3/10 (30%)	-
5c.	Skin & nipple retraction	4/10 (40%)	-
5d.	Lymphnode metastasis	4/10 (40%)	0

Table 2 : Shows –Mean age at presentation for invasive group and non-invasive group were 54 years (range, 35 to 75 years) and 57 years (range, 50 to 65 years) respectively. Youngest patient was identified at 38 years and oldest at 72 years.

In Invasive group (n=07 cases) , 6 (60%) patients presented with a painless breast mass, out of which retro-areolar (6 cases) presentation was the most common site followed by upper outer quadrant (3 cases). Nipple retraction and lymphnode involvement found in 4 (40%) cases each.

In non-invasive group (n=03 cases) , only 1 (10%) case was presented with retro-areolar painless breast mass, having size 1cm without anylymphnode metastasis and skin retraction.

Table 3 :Histo-pathological tumor profile(n=30)

Sl.no.	Types	No. of cases (%)
1.	Invasive ductal carcinoma	08/10 (80%)
2.	Papillo-tubular carcinoma	01/10 (10%)
3.	Solid tumor	00
4.	Schirrhous carcinoma	00
5.	Lobular carcinoma	00
6.	Adenoid cystic carcinoma	01/10 (10%)
7.	Paget's disease	00
	Total no. of cases	**10 (100%)**

Table 4 : Shows – On cytology of the aspirate smears, maximum number of cases (i.e 8, 80%) corresponds to invasive ductal carcinoma, which was followed by papillo-tubular carcinoma and adenocystic carcinoma (1 case each). None of them present with Solid tumor, Schirrous carcinoma, Lobular carcinoma, and Paget's disease.

Table 4 : Pathologic and genetic features of male breast carcinoma

Sl.no.	Pathological features	No.of cases positive or immune reactive
1.	Estrogen receptor	8/10 (80%)
2.	Progesterone receptor	7/10 (70%)
3.	HER-2/neu receptor	3/10 (30%)
4.	P^{53} protein	3/10 (30%)
5.	BRCA 1 gene	Nil
6.	BRCA 2 gene	4/10 (40%)
7.	Triple negative	1/10 (10%)

Table 4 : Shows –Estrogen receptor(ER) +ve and Progesterone receptor (PR) +ve comprises 8 (80%) cases and 7 (70%) cases respectively. BRCA 2 positive in 4 (40%) cases, but no immunoreactivity was seen with BRCA 1 gene mutation. HER-2/neu receptor and p^{53}protein +ve in 3 cases each (30%).

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Table 5 : Other features of male breast carcinoma (n=30)

Sl.no.	Features	Distribution (n=10)
1.	**Pathological stage**	
	I	02/10 (20%)
	II	03/10 (30%)
	III	05/10 (50%)
	IV	00
2.	**Treatment given**	
	Neo-adjuvant Chemotherapy	1 /10(10%)
	Adjuvant Chemotherapy	9 /10(90%)
	Adjuvant Radiotherapy	5 /10 (50%)
	Adjuvant Hormonetherapy	8 /10 (80%)
3.	**Recurrence Pattern**	
	Local recurrence	00
	Distant metastasis	01/10 (10%)
4.	**Death**	01/10 (10%)

Table 5 : Shows – 5 (50%) cases were presented with Stage –III, which was followed by Stage–II and Stage-I having 3 (30%)cases and 2 (20%)cases respectively. None of them presented with Stage-IV carcinoma. The treatment patterns includes were Neo-adjuvant chemotherapy (in 1 case), Adjuvant chemotherapy (in 9 cases), Adjuvant radiotherapy (in 5 cases), and Adjuvant hormonetherapy (in 8 cases). This study also involves recurrence pattern, where local recurrence (seen in 0 case) and distant metastasis (seen in 1 case) were taken into account. Out of the 10 cases studied, one death (10%)case was reported.

Table 6: Male breast cancer with survival outcomes

Sl.no.		No.of cases	Disease free survival	p-value
1.	Lymph node (-ve)	06	93%	< 0.005
2.	Lymph node (+ve)	04	70%	
3.	Early breast cancer (Stage- I, II)	05	95%	
4.	Locally advance breast cancer (Stage - III)	05	52%	
5.	Hormone receptor (+ve)	08	95%	
6.	Triple negative	01	24%	< 0.005
7.	All cases	10	80%	

Table 6 : Shows –Male breast cancers having Stage – I & II and Hormone receptor (+ve), correspond to higher disease free survival rate (95% each), followed by lymphnode (– ve) having 93%. Poor disease free survival rate corresponds to Triple negative cancers (24%).

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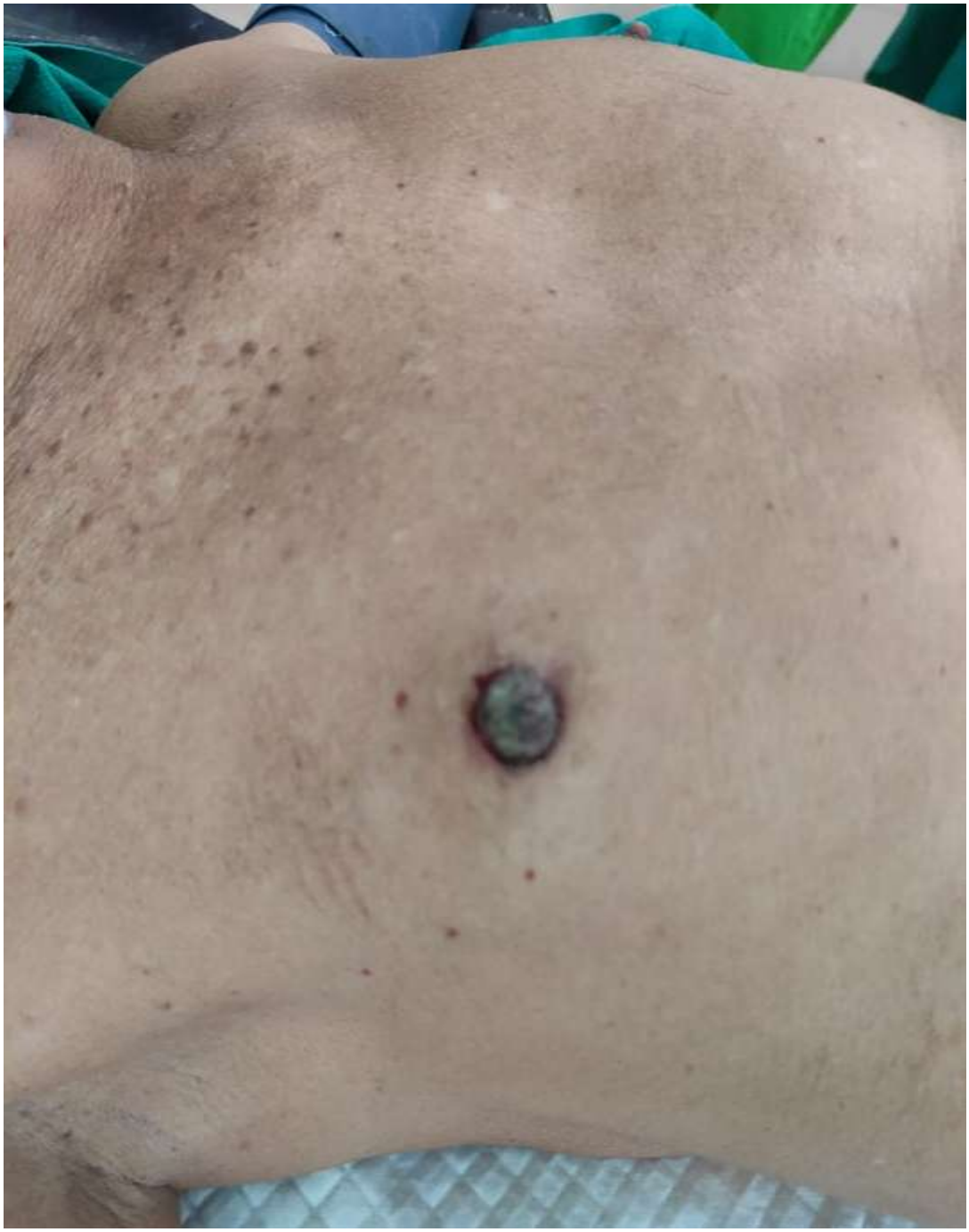

Fig: having feature of ulceration and retraction of nipple, red coloured nipple discharge with an underlying mass. no axillary lymphadenopathy

V. DISCUSSION

This retrospective study was done with 10 patients (majority belongs to 50-75 years age group) for the period of fifteen months in a tertiary health care to know the incidence of male breast cancers. The study of 60 patients by Sharma JD et al concluded, median age of presentation was 50 years which is near similar with present study. It also states left and right breasts were almost equally affected (51.65 vs 48.4%), 80% had nodal metastasis and 18.3% had distant metastasis at presentation, HR + ve in 53.3% cases, HER2/neu+ve in 15% cases, triple –ve in 18.3% cases . The histological profile was IDC in 31 cases, HR +ve in 26 cases, triple –ve in 4 cases and HER2/neu +ve in 6 cases [9].

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The study of 27 male breast cancers and 189 female breast cancers by Chaithanyababu et al concluded – mean age of presentation was 48.5 years, types include 8 cases ductal carcinoma in situ (4.19%), 6 cases infiltrating ductal carcinoma of medullary type (3.14%), 5 cases invasive lobular type (2.62%), 2 cases Paget's disease of nipple (1.05%). Male breast cancer were lymphnode –ve and HR +ve[15]. In present study - mean age at presentation for invasive group and non-invasive group were 54 years (range, 35 to 75 years) and 57 years (range, 50 to 65 years) respectively. Youngest patient was identified at 38 years and oldest at 72 years (Table-2).

Most of the patients presented in advanced stage in his study. During current years a protocol is followed i.e. management and treatment of male breast cancers are based on guidelines developed for female breast cancers. Though both have similarities , but they are different biologically, prognosis, risk factors and survival. Male breast carcinoma presents at higher clinical stage and with more lymph node involvement. It's incidence increases exponentially with age [16]. Many risk factors of breast cancers (both male and female) may be hormonally driven (i.e. hyperestrogenic state). Examples are – undescended testes, orchitis, testicular injury, infertility, obesity (especially that occurring before age of 30 years), cirrhosis, estrogen therapy,gynaecomastia, [12,13,17,18,19]. Positive family history (BRCA 2 mutation, localized in chromosome 13q12-13, first identified by Wooster) is also important risk factor where disease presents at an earlier age. The highest prevalence of BRCA 2 mutations in male patients with breast cancer is in Ireland, where it accounts for 40% of all cases [20]. In our study of 10 cases, gynaecomastia (4 cases, 20%) comprises an important risk factor, followed by breast cystand obesity (3 cases, 15% each) (Table - 1).

Histologic subtypes of breast carcinoma that found in women, also been reported in men. In men, approximatey 90% of all breast tumors are invasive and rest are non-invasive. In our study,, maximum number of cases (i.e 8, 80%) corresponds to invasive ductal carcinoma, which was followed by papillo-tubular carcinoma and adenocystic carcinoma (1 case each) (Table - 2). Ductal carcinoma in situ of male breast differ from of female breast , in that 75% of cases are papillary subtype and frequent are low to intermediate grade [21].Rare subtypes like medullary, tubular, mucinous, and squamous carcinoma are uncommon in men than women. But inflammatory carcinoma and Paget's disease have equal frequencies in man and women [22].

Irrespective of tumor grade, stage and patient's age , male breast carcinoma having a higher rate of hormone receptor (ER, PR) positivity than that of female breast , but similar percentages may be expressed for HER2 and p^{53}[23]. In present study, ER+ve andPR+ve comprises 8 (80%) cases and 7 (70%) cases respectively.Hormone expression up to 95% has been shown in a study by Wang-Rodriguez et al [24]. BRCA 2 positive in 4 (40%) cases, but no immunoreactivity was seen with BRCA 1 gene mutation. BRCA1 and BRCA2 mutation can cause breast cancer in females, but only BRCA2 mutation confers a significant risk to men. HER-2/neu receptor and p^{53}protein +ve in 3 cases each (30%)by immunohistochemistry (Table - 4). HER2 protooncogene is located in chromosome 17q21, expressed in 20%-30% of female breast cancers, and it's positivity is related to high grade tumor, lymphnode metastasis, high recurrence rate, high mortality, and poor prognosis [25,26].P^{53} mutation + ve, also indicates a poor prognosis [27,28].

VI. CONCLUSION

This study comprises higher Incidence rate (i.e 2.5%) of male breast cancers compared to national data , as it was done in a tertiary health care centre. Male breast cancers are associated with multiple risk factors. Hormone receptor + ve and BRCA2 mutation confers a significant risk to men. Effort to increase awareness among patients, earlier presentation to clinicians, timely diagnosis before spreading to axilla and other organs, and evidence based treatment would be helpful in optimizing the management of this rare disease.

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