RESEARCH ARTICLE

Descriptive Study on Selected Risk Factors and Histopathology of Breast Carcinoma in a Tertiary Care Centre in Kerala, India with Special Reference to Women Under 40 Years Old

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Abstract

Background: Breast cancer is the most common female cancer in Kerala, South India, with the incidence increasing in the past two decades, also in young women. However, there are limited data regarding the burden of disease, its epidemiology and histopathological characteristics in the state. Materials and Methods: This desciptive study covered 303 breast cancers evaluated during the period of December 2011 to August 2013 in the Department of Pathology, Government Medical College, Kottayam. The patients were also interviewed regarding selected risk factors. Results: The majority of the cases were 41-60 years of age with a mean at presentation of 53 years. Infiltrating ductal carcinoma was the most common subtype, followed by pure mucinous carcinoma and then lobular carcinoma. Of the cases, 6.6% were nullipara and 52.8% had fewer than or equal to 2 children. Median age at first child birth was 23 years (national value-19.8 years). A significant proportion (15%) had family history of breast cancer. Some 13.5% (41 cases) comprised the young breast cancer group (≤40years) with a mean age at first child birth in them was 27.4 years, 5 being nullipara and 6 having a positive family history. Conclusions: Breast cancer awareness, better availability of screening techniques and identification and targeting high risk groups all help to tackle the increasing load of breast carcinoma. A good proportion of cases comprised the young breast cancer group (under 40). Younger women should thus also be educated about breast carcinoma-risk factors, symptoms and diagnostic techniques to help in early detection and effective approach esto treatment.

Keywords: Breast cancer - risk factor - young women - histological subtype - South India

Introduction

One in ten of all new cancers diagnosed worldwide each year are carcinomas of the female breast, and it is principle cause of death from cancer among women globally. The age standardized incidence rate across the world is 43.3 per 100,000 female population. In India it was found to be 25.8 per 100,000 females (Globocan, 2012). The rise in incidence of 0.5-2% per annum has been seen across all regions of India and in all age groups but more so in the younger age groups (Khokar , 2012). As per the ICMR-PBCR 2001-2002 data, breast cancer is the commonest cancer among women in urban registries of Delhi, Mumbai, Ahmadabad, Kolkata, and Trivandrum in India.

In urban areas of developing countries, breast cancer is the most common cancer in women and due to increase in life expectancy, urbanization, and western lifestyles; the incidence has been rising up in low and middle income countries steadily in the last few years. Due to lack of awareness on early detection and barriers to health services, most women with breast cancer are diagnosed in late stages in India (Babu et al., 2013). Though the health indices in Kerala are far advanced in comparison to other states in India, the age adjusted incidence rate for breast cancer for the year 2006 was 30.5 in urban and 19.8 in rural areas (Jayalekshmi et al., 2009).

Breast cancers rarely occur in young women. Breast cancer at young age has been reported to have a more aggressive behavior and unfavorable prognosis compared to the older patients (Mathew et al., 2004). In the US, approximately 7% of women with breast cancer are diagnosed before the age of 40 years, and this disease accounts for more than 40% of all cancer in women in this age group (Anders et al., 2009). The incidence of breast cancer in Asia is increasing in young women (Keramatinia, 2014). In India the figures are expected to be much higher than the West, although exact values are not known.

To tackle with the increasing load of breast cancer in the state, a better understanding of the burden of cancer in

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the different regions of the state is required. This study was conducted in a Government medical college from central Kerala, South India and limited literature is available from this part of the state.

The purpose of this study was to describe selected risk factors of breast cancer (age, reproductive factors, and family history) in patients of different age groups with special reference to patients of 40 years and below. Also to study the proportion of various histopathological types of breast carcinoma in different age groups.

Materials and Methods

The study design is hospital based descriptive study conducted in the Department of Pathology, Government Medical College, Kottayam in Central Kerala, South India. Government Medical College, Kottayam gives tertiary care to Kottayam district (population of 1974551 as in 2011 census) and neighbouring districts- Pattanamthitta, Alapuzha and Idukki.

All cases which were diagnosed as carcinoma breast on histopathology and underwent mastectomy from December 2011 to August 2013 were included in the study. Exclusion criteria included *(a)* the patients who were diagnosed as in situ carcinoma *(b)* male breast cancer. Ethical clearance was obtained from the institutional ethics committee. All cases were reviewed and relevant clinical data were collected using a questionnaire regarding information on age , age of first child birth, number of children, attainment of menopause, family history of breast or ovarian cancers.

All the histopathology slides were also reviewed and typing of invasive breast carcinoma was done by WHO classification of tumours of breast 2012.

The data was entered into Microsoft Excel and statistical analysis was done using SPSS software version 13.0.

Results

Age

Of the 303 cases, most of the patients were between 41-60 years (63%). Minimum age was 26 years and the maximum age was 86 years. The mean age was 53 years (SD 11.7). 41 cases were ≤40 years(young breast cancer group), which constituted 13.53% of the total cases.

Histopathological types

Among the 303 cases, 259 cases (85.4%) are infiltrating ductal carcinoma which was the most common type. This was followed in decreasing order by 10 cases (3.3%) of Mucinous carcinoma, 9 cases (3%) of lobular carcinoma, 6 cases (2%) of IDC with medullary carcinoma, 5 cases (1.7%) of Metaplastic carcinoma, 4 cases (1.3%) of mixed IDC and ILC and 10 cases (3.3%) of other types of carcinoma (Table 2). Infiltrating ductal carcinoma was also the most common type (35 cases out of 41 cases-85.3%) in the young breast cancer group (≤40 years) (Table 3).

Reproductive and Family history

73.9% of cases were postmenopausal. 20 out of 303 cases (7%) were nullipara. Out of the 283 parous women, 20 (6.6 %) had only one child, 140 (46.2%) had 2 children and 123 (40.6%) had more than 2 children. The median age at first child birth of the total cases was 23 years. 44 cases (15%) had history of ovarian of breast carcinoma in their family (first and/or second degree relatives). The median age at first child birth among the young breast cancer group was 27 years. 5 cases out of 41 cases were nullipara and 6 cases had positive family history.

Table 1. Distribution of Cases According to Selected Risk Factors of Breast Carcinoma

Age (Years)	Number of cases	%
21-40	41	13.53
41-60	191	63.03
61-80	65	21.45
>80	6	1.98
Total	303	
Attainment of menopause		
Premenopausal	79	26
Postmenopausal	224	74
parity		
nullipara	20	7
1	20	6.00
2	140	46.20
>2	123	40.60
Family history		
yes	44	15
No	259	85
Age at first child birth		
<30	262	93
≥30	21	7
median age	23	

Table 2. Distribution of Cases According to Histological Types of Breast Carcinoma

Histopathological Type	Number of Cases, n=303	%
Infiltrating ductal carcinoma (IDC)	259	85.47
Invasive lobular carcinoma (ILC)	9	3
Mucinous carcinoma	10	3.30
Metaplastic carcinoma	5	1.70
Mixed IDC and ILC	4	1.30
Carcinoma with medullary features	6	2
Apocrine carcinoma	2	0.70
Adenoid cystic carcinoma	1	0.30
Invasive papillary carcinoma	2	0.70
Invasive solid papillay carcinoma	2	0.70
Encapsulated papillary carcinoma with invasion	3	1

Table 3. Distribution of Histological Types of Breast Carcinoma in Young Breast Cancer Group(≤ 40 years)

Histopathological type	Number of Cases, n=41	%
Infiltrating ductal carcinoma (IDC)	35	85.30
Carcinoma with medullary features	1	2.40
Mucinous carcinoma	2	4.80
Metaplastic carcinoma	1	2.40
Adenoid cystic carcinoma	1	2.40
Invasive solid papillary carcinoma	1	2.40

Discussion

Breast cancer appears to have a complex etiology with interplay of reproductive, environmental and genetic factors. Although many of these factors are well defined, the interactions between them are to be further studied. Burden of disease in the younger age groups in different populations need to be studied, to involve them in screening and follow up programmes. Also analysis of factors like family history may help to identify high risk groups and aid in screening.

Age is an important risk factor. The breast cancer risk increases as the age advances. In the present study, maximum numbers of cases were observed between 41-60 years (63.03%). The average age of patients was 53 years.

The average age of occurrence of breast cancer amongst US white females has been reported to be 61 years (Anderson, 2006). The average age of occurrence of the breast cancer seems to be lower as compared to western countries. (Leong et al, 2010). Other studies in India (Saxena et al, 2005; Pakseresht et al, 2009; Nigam et al, 2014) also showed lower values. A younger age at onset among the Asian population has been reported and it has been attributed to a cohort effect that has been decreasing in recent decades (Mousavi-Jarrrahi et al, 2013).The young breast cancer group (≤ 40 years) comprised 13.53% (41 cases) of the total cases.

IDC NOS is the commonest breast cancer followed by lobular carcinoma in the many of Indian studies (Saxena et al., 2005; Sofi et al., 2012). But in present study IDC NOS (82.9%) is the commonest breast cancer, pure mucinous carcinoma (10 cases, 3.3%) was second most common variant followed by lobular carcinoma (9 cases, 3%).Hence the occurrence of mucinous carcinoma was almost equal to lobular carcinoma in contrast to the above studies which showed much higher proportion of lobular carcinoma than mucinous carcinoma.

Various epidemiological studies carried out in India and western populations have identified various reproductive factors generally associated with breast cancer.

In the present study, majority of patients are postmenopausal (73.9%) followed by premenopausal (26.1%). Women who had menopause after 50 years had risk of breast cancer more as compared to women who had menopause before 45 years of age (Meshram , 2009).

20 out of 303 cases (7%) had history of nulliparity. Nulliparous women had a 2.2-fold higher risk of breast cancer than parous women. Three or more pregnancies were associated with a 40-50% reduction in risk (Meshram, 2009; Balasubramaniam et al., 2013).

International collaborative study of breast cancer and reproductive experience has been carried out in 7 areas of the world. In all areas studied, a striking relation between age at first birth and breast cancer risk was observed. It is estimated that women having their first child when aged under 18 years have only about one-third the breast cancer risk of those whose first birth is delayed until the age of 35 years or more (MacMohan et al., 1970). Many other studies in India also support this finding (Meshram, 2009 (Das et al, 2012). The median age at first childbirth for women aged 25-49 years in India during the years 2004-06 was 19.8years (NFHS, 2007). The median age at first childbirth

for women in Kerala, during the same period was 22.7 years (NFHS, 2006). The median age at first child birth in the present study was 23 years, which is higher than the national value and approximately equal to the state value.

Family history is another risk-factor for breast carcinoma. It has been noted that women who have first degree relative with breast cancer have a risk two to three times that of general population, the risk further increased if the relative was affected at an early age and/or had bilateral disease (Saxena et al., 2005). 44 (15%) out of 303 cases had history of breast or ovarian malignancies in their family in the present study. Studies conducted in other parts of India showed varied results. In studies by Aman Chauhan et al. in Karnataka, family history was seen in only 8% cases but in another study conducted by Saxena et al. (2005) in New Delhi, 20.7% of cases had family history (Saxena et al, 2005; Chauhan et al., 2011). *BRCA1* and BRCA2, located on chromosomes 17 and 13, respectively, are thought to account for the majority of inherited breast cancers. The estimated lifetime risks of developing breast cancer among *BRCA1* and *BRCA2*carriers are 47%-66% and 40%-57%, respectively, compared to a 12.5% risk among the general population. Although there is no universal approach, it is recommended that clinicians discuss intensive surveillance of the breasts and ovaries, chemo-prevention, and prophylactic surgery (i.e., bilateral mastectomy and bilateral salpingo-oophorectomy) with their patients diagnosed with a *BRCA* mutation, on an individualized basis (Anders et al., 2009). Inadequate knowledge of breast cancer risk factors and poor cancer screening practice among women with family history of breast cancer are reported from a study in Malaysia. Poor knowledge and practice of breast screening are likely to lead to late stage presentation of breast cancer disease (Subramanian et al., 2013). Hence efforts should be made to elicit family history of breast or ovarian cancers in the patients to identify high risk groups. These high risk groups should be educated and requires careful follow-ups with good screening modalities. Also improved ways of follow-up using identification of various putative genes like *BRCA* 1, *BRCA* 2 can also be employed. Hence study of family history in a population helps in screening of breast cancer and predisposition to breast cancer.

Breast cancer at young age is more aggressive and has lower survival rates. Young women with breast cancer are more likely to have higher rates of local and distant metastasis, be negative for estrogen receptors, and have tumours that are large with a high grade of anaplasia. Unfortunately, the specific mechanisms responsible for this tumor phenotype remain unclear (Mathew et al, 2004; Anders et al, 2009). In the West, approximately 7% of women with breast cancer are diagnosed before the age of 40 years, and this disease accounts for more than 40% of all cancer in women in this age group (Anders et al., 2009). In the present study the proportion of young breast cancer group was 13.53%. One another study from Manipur, India reported 31.6% of patients below 40 years (Thangjam et al., 2014). The exact incidence in different parts of the country is not known. The incidence of breast cancer is increasing in Asian population and seems to be higher than the Western statistics (Keramantinia et al., 2014).

Infiltrating ductal carcinoma was the most common

type of carcinoma in the young breast cancer group (85.3%). This was in accordance to other studies conducted in India on women less than 40 years (Thangjam et al., 2014). Across all histologic subtypes and stages, breast cancer survival rates are comparatively lower for women <40 years of age than for older women (Anders et al., 2009).

Most risk factors of women aged less than 40 years were similar to those described in breast cancer epidemiology at any age. Age at first childbirth, parity, family history, oral contraceptive use all proved significant associations with risk of breast carcinoma in the young in various studies (Tehranian et al., 2010; Ghiasvand et al., 2011). In the present study the mean age at first childbirth was 27, 6 cases were nullipara and 5 cases had positive family history. In a study from Italy, patients under 40 years old more frequently had a family history of breast cancer, more often used oral contraceptives and on average they had experienced menarche 1 year earlier than did older patients (Sidoni et al., 2006). Women who are diagnosed with breast cancer at a younger age are more likely to have a mutated (altered) *BRCA1* or *BRCA2*gene. Delays in diagnosing breast cancer also are a problem.

Many younger women who have breast cancer ignore the warning signs-such as a breast lump or unusual nipple discharge-because they believe they are too young to get breast cancer. Breast cancer screening awareness should be extended to the younger population also. High risk groups should be identified (e.g. positive family history) and educated about the risk of breast cancer and diagnostic modalities.

In conclusion, breast cancer awareness, better availability of screening techniques and identification and targeting high risk groups all help to tackle the increasing load of breast carcinoma. The younger women should also be educated about breast carcinoma-risk factors, symptoms and diagnostic techniques. This helps in early detection and effective approach to treatment.

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