ORIGINAL RESEARCH PAPER

Pathology

A STUDY ON CLINICO-EPIDEMIOLOGICAL PROFILE OF BREAST CARCINOMA IN EASTERN UTTAR PRADESH

KEY WORDS: Carcinoma, Clinico-epidemiological, Immunohistochemistry

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ABSTRACT

Introduction: Breast cancer is the most common female cancer worldwide representing nearly a quarter of all cancers. Public health measures require an understanding of pattern of disease and its clinical presentation. Therefore the current research was conducted to study clinico-epidemiological profile of reported breast carcinoma cases.

Methods: Sample consisted of 155 specimens of breast carcinoma received by Pathology department (retrospectively and prospectively), Hind Institute of Medical Sciences, Barabanki, Uttar Pradesh from June 2015 to May 2018. ER, PR and AR positive expression were defined as ≥10% nuclear staining and also HER2 (2+), FISH was performed. Nuclear staining was done for estimation of Ki-67.

Results: Among the study population, most of the breast carcinoma cases (67.1%) belong to 35-60 years age group. About 54.2% of the cases were from post-menopausal group. Left side of the breast carcinoma (54.5%) was more common. In about 20% of the breast carcinoma cases lymph nodes were involved. Lympho-vascular embolization was detected in 13.5% cases. Majority of cases had high Ki-67 grade (40.0%), absence of ER expression (77.4%), absence of PR expression (78.0%) and absence of HER2/neu expression (80.0%) respectively.

Conclusion: Breast carcinoma in India shows a quite different spectrum of presentation and behaviour both in early as well as advanced stage.

INTRODUCTION

Despite dramatic advances in cancer research, breast cancer remains a major health problem and it represents the current top biomedical research priority. Worldwide, breast cancer is the most common cancer affecting women and its incidence and mortality rates are expected to increase significantly the next few years. Recently the researcher`s interest has been attracted by high breast cancer rates among women aged <45 years. Also breast cancer is unquestionably the leading cause of cancer related deaths. Invasive breast cancer is documented to be the most common carcinoma in women. **[1]**

Breast cancer is the most frequent cancer among women, impacting 2.1 million women each year, and it also causes the greatest number of cancer related deaths among women. In 2018, it is estimated that 627,000 women died from breast cancer- that is approximately 15% of all cancer deaths among women. **[2]** About 2,550 new cases of invasive breast cancer are expected to be diagnosed in men in 2018. A man`s lifetime risk of breast is about 1 in 1,000. A woman`s risk of breast cancer nearly doubles if she has first degree relative (mother, sister, daughter) who has been diagnosed with breast cancer. About 5-10% breast cancers are linked to gene mutations inherited from one`s mother or father. Mutations in BRCA1 and BRCA2 genes are the most common.

About 85% breast cancers occur in women who have no family history of breast cancer. These occur due to genetic mutations that happen as a result of the aging process and life in general, rather than inherited mutations. The most significant risk factor for breast cancer are gender (being a woman) and age (growing older). **[3]** In order to improve breast cancer outcomes and survival, early detection is critical. There are two early detection strategies for breast cancer: early diagnosis and screening. In our study we attempted to make epidemiological observation of breast cancer patients in one of the tertiary care hospital for cancer treatment in Barabanki district. The purpose of this study was therefore to analyze the epidemiological and clinical profile of breast cancer cases attending a teaching hospital in Eastern Uttar Pradesh.

Material and Methods

Source of data: Cases of radical mastectomy received for routine Histopathological evaluation from the Department of Surgery, Hind Institute of Medical Sciences Barabanki, from May 2014 to June 2018 will form the source of data for the study.

Method of collection of data: The detailed clinical history and results of relevant investigations done were collected from the patients' case files. For study of prospective cases, the mastectomy and lymph node dissection specimen were received in the Pathology department in 10% formalin. In every case the standard protocol for surgical grossing of radical mastectomy specimens was followed. After a detailed specimen description, multiple sections were taken from the tumour, surgical margins, nipple and areola, non-neoplastic breast, and all the lymph nodes. After conventional processing, paraffin sections of 5µm thickness were stained by haematoxylin and eosin (H & E) for histopathological study. Additional 4µm sections were taken from single paraffin block of tumour tissue and plated on 4 glass slides coated with adhesive (polyLycine) for immunohistochemistry (IHC) to detect ER, PR, HER2/neu overexpression and Ki-67 proliferative index. For study of retrospective cases, the histopathology reports, slides and paraffin blocks were retrieved from the archives. Sections were taken from the paraffin blocks in the same manner. The technique for IHC included antigen retrieval in Tris buffer in a microwave oven, blocking endogenous peroxidase with 3% hydrogen peroxide, incubating with primary mouse monoclonal antibody (Biogenex), linking with rabbit anti mouse secondary antibody (Biogenex), enzyme labelling with streptavidin- horseradish peroxidase (Biogenex), developing chromogen with diaminobenzidine (DAB) and counterstaining with hematoxylin . Positive and negative controls were run with each batch of slides. The H & E stained slides were studied for the tumour histology, type, Scarff-Bloom-Richardson (SBR grade), lymph node metastasis etc. The immune-stained slides were examined for nuclear staining in case of ER, PR and Ki-67, and membrane staining in case of HER2/neu. In each case, the proportion of positive staining tumour cells (expressed in percentage) and the average intensity of staining (expressed as 0, 1+, 2+ or 3+) was evaluated. The relationship between various parameters such as age, menopausal status, duration of disease presentation, mammography findings, tumour size, tumour extent, histologic type, histologic grade, lymph node status, the expression of ER, PR, HER2/neu and Ki-67 index are studied.

Inclusion criteria: Radical mastectomy specimens from female patients of all ages, with breast carcinoma, are included in the study.

Exclusion criteria: Cases where only a tru-cut biopsy or limited surgery has been done, as in such cases all the parameters were not taken for assessment and cases where there is extensive tumour necrosis without sufficient viable tumours cells for accurate evaluation of the immuno-histochemical results.

Sample size determination: All the specimens available/provided during time frame of study were assessed for the study parameters keeping inclusion and exclusion criteria in view.

Statistical analysis: The data was analyzed using software Epi Info 7; **[4]** and the results were transferred to preformed tables in accordance to aims and objectives. Percentage expression for positivity of ER, PR, HER2/neu and Ki-67 has been estimated.

Ethical clearance: Ethical clearance was obtained from institution ethics committee before data collection.

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Result:

Among the study population, maximum number of breast carcinoma cases (67.1%) belonged to 35-60 years age group. According to the religion, Hindus suffered more from breast carcinoma (71.6%) as compared to Non-Hindu. Urban residents (46.4%) were less affected by breast carcinoma than rural folks (53.5%). Based on the menopausal status, post-menopausal (54.2%) females suffered breast carcinoma more in comparison with pre-menopausal ones. According to our study population, left side of the breast (54.5%) was more affected than right. Distribution of breast carcinoma lesions according to the quadrant, upper medial, upper lateral, lower lateral, lower medial and upper & lower lateral were 7.09%, 34.8%,32.9%,23.8% & 1.2% respectively. In our study population, only 20% breast carcinoma cases involved the lymph nodes. According to our study, lympho-vascular Embolization was detected in 13.5% cases only. **[Table No.1]** As per the distribution of breast carcinomas according to immune-histochemistry maximum number of cases were found with High Ki-67 grade(40.0%), absence of ER expression(77.4%), absence of PR expression(78.0%) and absence of HER2/neo expression(80.0%) respectively.**[Table No.2]**

Discussion:

The present study includes 155 cases of breast carcinoma cases which were classified into their molecular subtypes on the basis of expression of ER, PR and HER2/neu and Ki-67 score. In the present study majority (67.1%) of the cases were in 35-60 years age group with a mean age of 52.3 6.23 years. This is in coherence with the findings reported from other studies in Asia. [5,6,7] The reporting of majority of cases in later decades of life might be attributed to multiple factors like environmental factors, socioeconomic status, lack of comprehensive care approach and inadequate implementation of screening programmes. About 54.8% of the cases presented on left side while 45.1% of the cases were found in right side of the breast, which was in concordance with most of the studies in India and abroad.**[8,9,10,11]**

Majority of cases were of histological grade II (51.6 %) which correlated with studies by Nair et al andKakarala et al. **[10,12]** Lymph node metastasis were reported in only one-fifth of the cases of breast carcinoma. Similar findings were observed in almost all studies. **[13,14,15]** In this study, majority of the cases were ER, PR and HER2/neu negative (77.4%, 78.0% and 80.0% respectively. ER and PR negative were also reported in two other studies by Indian authors; **[10,16]** whereas in most international studies hormonal receptors were usually positive. **[9,14,15,17, 18]** Thus the study findings points towards a variable trend in Indian population where cases of breast carcinoma usually present with high grade of tumour in advance stage with lymph node metastasis. This finding suggests the explanation for ethnic variation related to difference in gene expression.

Conclusions:

Breast carcinoma in India shows a quite different spectrum of presentation and behaviour both in early as well as advanced stage. A greater understanding of the molecular classification of tumours based on triple markers helps in development of targeted therapies that lead to increased efficacy, decreased toxicities, and

better selection of patients who will benefit from treatment.

Table no 1: Distribution of breast carcinoma cases on the basis of biosocial and presentation characteristics

(N=155)

Biosocial characteristics	Number	Percentage
Age-group (years)		
≤35	15	9.6
35-60	104	67.1
≥60	36	23.2
Religion		
Hindu	111	71.6
Non-Hindu	44	28.3
Residence		
Urban	72	46.4
Rural	83	53.5
Menopausal status		
Pre-menopausal	71	45.8
Post-Menopausal	84	54.2
Side		
Left	85	54.8
Right	70	45.1
Quadrant		
Upper Medial	11	7.09
Upper Lateral	54	34.8
Lower lateral	51	32.9
Lower-Medial	37	23.8
Upper & Lower lateral	2	1.2
Lymph node Involvement		
Positive	31	20.0
Negative	124	80.0
Lympho-vascular Embolization		
Detected	21	13.5
Absent	134	86.4

Table No.2:- Distribution of breast carcinomas is according to Histopathological type, immunohistochemistry and Ki-67 grade.

(N=155)

Pathological profile	Number	Percentage
Histopathological Type		
Invasive Ductal CA	138	89.0
Papillary CA	5	3.3
Apocrine Differentiated CA	3	1.9
Paget`s disease of breast	2	1.3
Medullary CA	2	1.3
Lobular CA	2	1.3
Mucinous CA	4	2.6
TNM		
I	38	24.5
IIA	62	40.0
IIB	19	12.2
IIIA	24	15.5
IIIB	5	3.2
IIIC	7	4.5
IV	0	0
Histopathological grade		
Grade I	15	9.7
Grade II	80	51.6
Grade III	58	37.4
Ki-67		
Low	58	37.4
Intermediate	35	22.5
High	62	40.0
ER expression		
Present	35	22.5
Absent	120	77.4
PR expression		
Present	34	21.9
Absent	121	78.0
HER2/neo expression		
Present	31	20.0

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