ORIGINAL ARTICLE

Role of Nottingham Prognostic Index Scoring in Determining Prognosis of Breast Carcinoma in Different Age Groups

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ABSTRACT

The commonest malignancy among women is breast carcinoma world widely. It is the leading cause of death due to cancer among females in developing world but it remain second to lung carcinoma in developed world .The aim of this study is to determine the extent and spread of invasive breast carcinoma by applying Nottingham Prognostic Index (NPI) in patients of three different age groups for categorization into their respective prognostic groups thereby determining their morbidity and mortality.Out of total 140 mastectomy cases, 14 patients (10%) were under 35 years of age whereas 88 patients (62.85%) were in age group between 35 to 50 years. 38 patients were over 50 years of age (27.14%).The tumor size ranged from 1cm to 10cm in largest dimension with average size of 5 cm.

Out of the 140 cases, only one case (0.71%) was Grade-I, 126 (90%) were Grade-II, and 13 (9.2%) were Grade-III. Out of the 140 cases, 56(40%) cases showed no metastasis in axillary lymph nodes. In 32(22.8%) patients, 1-3 lymph nodes showed metastatic deposits. In 52(37.1%) patients, more than three lymph nodes were positive for metastasis. The largest number of lymph nodes received with mastectomy specimen was 16. NPI was applied to 140 cases. Out of total 140 cases, 75 cases (53.57%) were calculated as having prognostic index value between 3.5 and 5.4 and thus having moderate prognosis. Whereas 49 patients (35%) had Prognostic Index Value > 5.4 indicating Poor Prognosis. Only 16 patients (11.42%) had Prognostic Index less than 3.4 having Good Prognosis . It is concluded that it is very important to apply Nottingham Prognostic Index Scoring on Mastectomy Specimens of our patients to assess the prognosis and manage accordingly and also develop strategies to prevent it.

Key Words: Nottingham Prognostic Index (NPI), radical mastectomy, Bloom and Richardson Grading System, Carcinoma Breast, Lymph node metastasis.

INTRODUCTION

The commonest malignancy among women is breast carcinoma world widely. It is the second leading cause of death due to cancer among females[1].Widespread use of mammography enabling early early detection of breast carcinoma has reduced its mortality rate in western countries[2]. In Asia, Pakistan has the highest rate of breast cancer . Approximately 40,000 deaths per year occur due to breast carcinoma in Pakistan.Every1 in 9 women in Pakistan will have breast cancer [3]. In Karachi, the largest city of Pakistan, females usually presented at stage III or IV of breast carcinoma having incidence 69.1 per 100,000[4].

Risk factors for breast carcinoma include increased age, family history of breast cancer and no breast feeding. Females who have persistent and prolonged exposure to the sex hormones (estrogen and progesterone) are at increased risk of developing breast carcinoma.[5]. Early menarche (before age 12), late menopause (after age 55), no children and obesity in women over 50 are some of the risk factors of prolonged exposure to hormomes.[6].

Prognostic and predictive factors of breast cancer defines it management. The prognostic factor is a marker of poor outcome while predictive factors predict the response to therapy. The important prognostic factors are primary tumour size, tumour histological grade and lymph node (LN) stage[7].

The Nottingham Prognostic Index (NPI), developed in 1982 as an aid to the management of breast cancer, is a well established and widely used method of predicting survival of operable primary breast cancer. The NPI is concluded from tumor grade, tumor size and lymph node status.[9]. Nottingham Prognostic index has been validated

by further studies in Nottingham (UK) and by studies in several other countries[10].

The aim of this study is to determine the extent and spread of invasive breast carcinoma by applying Nottingham Prognostic Index (NPI) in patients of three different age groups for categorization into their respective prognostic groups thereby determining their morbidity and mortality.

Patients will be categorised into three age groups as follows:-

Group-1:   age <35 years
Group-1:   age 35-50 years
Group-1:   age >50 years

Prognostic Index: (Outcome variable). Based on three most important factors, i.e. tumour size, tumour grade and number of lymph nodes involved, prognostic index (outcome variable) will be calculated i.e.

G=tumour grade, L=Number of lymph nodes involved, S=tumour size in cm

The index will define the patients into three categories with different chances of dying from breast cancer. These categories are:-

Good prognosis: (score less than 3.4)
Moderate prognosis: (score 3.4 to 5.4)
Poor prognosis: (score greater than 5.4)

MATERIALS AND METHODS

This is a cross-sectional study is carried out at the Department of Pathology, Fatima Jinnah Medical College, Lahore.It was conducted on 140 cases in 06 months. A non-probability consecutive sampling technique was used for these patients. Patient of all ages having mastectomy with lymph nodes removal are included in this study while those having previous lumpectomy or mastectomy without lymph nodes removal or having benign lesions are excluded. Specimen after fixation in 10% buffered formalin is grossed and processed. Sections stained with Haematoxylin and Eosin are viewed by histopathologist for grading according to Nottingham modification of Bloom and Richardson Grading System and scoring according to Nottingham Prognostic Index.Data is tabulated and SPSS Version 17.0 is used for data entry and analysis.

RESULTS

Out of total 140 mastectomy cases, 14 patients (10%) were under 35 years of age whereas 88 patients (62.85%) were in age group between 35 to 50 years. 38 patients were over 50 years of age (27.14%). (Table I)

The tumor size ranged from 1cm to 10cm in largest dimension with average size of 5 cm(Table II).

Out of the 140 cases, only one case (0.71%) was Grade-I, 126 (90%) were Grade-II, and 13 (9.2%) were Grade-III (Table III).

Table – IV shows that out of the 140 cases, 56(40%) cases showed no metastasis in axillary lymph nodes. In 32(22.8%) patients, 1-3 lymph nodes showed metastatic deposits. In 52(37.1%) patients, more than three lymph nodes were positive for metastasis. The largest number of lymph nodes received with mastectomy specimen was 16.

NPI was applied to 140 cases. Out of total 140 cases, 75 cases (53.57%) were calculated as having prognostic index value between 3.5 and 5.4 and thus having moderate prognosis. Whereas 49 patients (35%) had Prognostic Index Value > 5.4 indicating Poor Prognosis. Only 16 patients (11.42%) had Prognostic Index less than 3.4 having Good Prognosis (Table – V).

Table-1: Frequency of breast carcinoma in different age groups (n=140)

Age	Number of patients	% age
< 35 years	14	10%
35-50 years	88	62.85%
> 50 years	38	27.14%

Table-2: Distribution of cases according toTumor size

Tumor Size	Number of patients	<35 years of AGE	35-50 years of AGE	> 50 years of Age
T1 <2cm	4	0	4	0
T2 2-5cm	105	11	61	33
T3 > 5cm	31	3	23	05

Table-3: Distribution of cases according to HISTOLOGICAL GRADE

Tumor Size	Number of patients	<35 years of AGE	35-50 years of AGE	> 50 years of Age
Grade-1	01	01	0	0
Grade-2	126	11	78	36
Grade-3	13	3	10	02

Table-4: Lymph node involvement (n=140).

Lymph nodes	Score	Number of patients	<35 years of age	35-50 years of AGE	> 50 years of Age
N0 no nodes	1	56	05	32	18
N1 (1-3)	2	32	02	21	10
N2 (>3)	3	52	07	35	10

Table-5: Nottingham Prognostic Index Scores (n = 140)

NPI	Number of pts	% age	Prognosis
<3.4	16	11.42%	GOOD
3.4-5.5	75	53.57%	MODERATE
>5.4	49	35%	POOR

DISCUSSION

Breast cancer has been rated as most common cancer in females[11]. It accounts for approximately 15% of female cancer deaths. In Asia, Pakistan has the highest rate of breast cancer . Approximately 40,000 deaths per year occur due to breast carcinoma in Pakistan. Every 1 in 9 women in Pakistan will have breast cancer.[3]

In western world breast carcinoma is more common in old age group [12] whereas in our study the most common age group presenting with breast carcinoma was 35-50 years. Variations in the incidence of breast cancer among different populations suggest different etiological factors. These etiological factors include genetic, environment, reproductive, endogenous and exogenous hormones in women, immune status, host vulnerability, socio-demographic differences, and behavioural characteristics across population.

One of the most important prognostic factor in breast carcinoma is tumour size[13]. It is independent of the lymph node status, although the risk of axillary lymph node metastasis increases with the size of the tumour [14]. Our study has shown that majority of tumors were T2 (75%) followed by T3 (22.12%) whereas only 2.85% were T1.According to the results, tumors are of large size in majority of patients in our study at first presentation.These findings are identical to results of two previous studies in which it was found that majority of cases with breast carcinoma had tumor size between 2cm and 5cm[2,15].

Axillary lymph node metastases is another important prognostic factor in breast carcinoma[20]. According to the results, axillary lymph nodes are positive for metastases in majority of patients in our study at first presentation.A study carried out by Ahmad Z, & Khurshid A, at Aga Khan Medical College showed that in 74.77% cases, lymph nodes were positive for metastases in mastectomy specimens [2] whereas another study shows axillry lymph node metastasis in 41% of their patients([17]).

Histological grade provides important prognostic and management information[18].It is extremely important to grade invasive breast carcinoma accurately. Modified Bloom and Richardson Grading System used to grade tumors measures three parameters i.e. tubule formation, nuclear pleomorphism and mitotic rate. Giving a score of 1 to 3 to each parameter, final grade is determined by adding scores of all the three parameters. Grade-I (score 3-5), Grade-II (score 6 or 7), Grade-III (score 8 or 9).

In our study, as shown in the results, majority of cases were Grade-II (90%). 13 cases (9.28%) were Grade-III, whereas only 4.17% cases were Grade-I. A similar study carried out by Emad A, Rekha in 2008 showed that majority of cases (i.e.

45.6%) were Grade-III, followed by 35.6% cases having Grade-II[7]. Another study carried out at Ayub Medical College revealed that 60.86% cases were Grade-III[1].

The Nottingham Prognostic Index (NPI) combines the three strongest prognostic factors and according to study results is a suitable model for prognosis of breast cancer. The Nottingham Prognostic Index categorized patients into three groups with different mortality rates on basis of three factors i.e. tumor size, tumor grade and lymph node status. The three groups include good prognostic category (score up to 3.4), moderate prognostic category (score 3.4 - 5.4) and poor prognostic category (score > 5.4). The prognostic categories have been shown to be useful in predicting outcome in treated patients with breast carcinoma in various studies.[19].

According to our results only 11.42% patients were in Good Prognosis Category with NPI scores less than 3.4. Thirty five percent (35%) patients were in Poor Prognosis Category with NPI score of more than 5.4. Large majority of patients i.e. 53.57% patients had NPI score between 3.4 and 5.4, falling in moderate prognosis category. Less than 3% are in the good prognosis category. This seems to be due to late presentation, presentation with bigger mass and many times presentation with lymph node metastasis in our patients. Another interesting finding was that in younger age group i.e. less than 35 years of age, majority of patients had NPI value of > 5.4 and therefore categorized in Poor Prognosis Category. This further emphasizes the advanced nature of disease and poor prognosis in young age group, as compared to middle age and old age group.

It is concluded that it is very important to apply Nottingham Prognostic Index Scoring on Mastectomy Specimens of our patients to assess the prognosis and manage accordingly and also develop strategies to prevent it.

REFERENCES

1. Naeem M, Khan N, Aman Z, Nasir A, Samad A, Khattak A, Pattern of breast cancer: Experience at Lady reading hospital Peshawar. J Ayub Med CollAbbottabad 2008;20(4): 22-24
2. Ahmad Z, Khurshid A, Qureshi A, Idress R, Asghar N, Kayani N, Breast carcinoma grading, estimation of tumor size, axillary lymph node status, staging, and nottingham prognostic index scoring on mastectomy specimens. Indian J PatholMicrobiol 2009; 52(4):477-81.
3. Nat Awareness Campaign Pakistan: (Article on internet): Available from: http://www.annieappleseedproject.org/natawca mpak.html
4. Ahmed F ,Mahmud S , HatcherJ and KhanSBreast cancer risk factor knowledge among nurses in teaching hospitals of Karachi, Pakistan: a cross-sectional study.BMC Nursing 2006;5: 6-8
5. Yager JD; Davidson NE. "Estrogen carcinogenesis in breast cancer".New Engl J Med 2006; 354(3): 270–82.
6. Pakseresht S, Ingle GK, Bahadur AK, Ramteke VK, Singh MM, Garg S, et al Risk factors with breast cancer among women in Delhi Indian J cancer 2009;46(2):132-138
7. Emad A. Rakha, Maysa E. El-Sayed, Andrew H.S. Lee, Christopher W. Elston, Matthew J. Grainge, ZsoltHodi, et al, Prognostic Significance of Nottingham Histologic Grade in Invasive Breast Carcinoma. *J ClinOncol* 2008;26(19):3153-3158
8. Blamey RW, Ellis IO, Pinder SE, Lee AH, Macmillan RD, Morgan DA, et al. Survival of invasive breast cancer according to the Nottingham Prognostic Index in cases diagnosed in 1990-1999.Eur J Cancer 2007;43(10):1548-55.
9. Decker T, Hungermann D, Böcker W. Prognostic and predictive factors of invasive breast cancer: , Der Pathol 2009;30(1):49-55
10. Lee AH, Ellis IO.TheNottingham prognostic index for invasive carcinoma of the breast.PatholOncol Res 2008;14(2):113-5.
11. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ. Cancer statistics, 2006. CA Cancer J Clin 2006;56:106-30.
12. Kollias J, Elston CW, Ellis IO, Early onset breast cancer-histopathological and prognostic considerations.British journal of cancer1997;75(9):1318-1323.
13. Chang JC, Hilsenbeck SG. Chapter 31: Prognostic and Predictive Markers, in Harris JR, Lippman ME, Morrow M, Osborne CK. Diseases of the Breast, 4th edition, Lippincott Williams & Wilkins, 2010.
14. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. Cancer 1989;63:181-7

15. C. T. Vallejo, J. A. Lacava, P. M. Cabaleiro et al, The Nottingham Prognostic Index (NPI) applied to 467 patients (pts) with a long-term follow-up that were treated in a single institution.Journal of Clinical Oncology. 2004;22: 9657

16. K McPherson, C M Steel, J M Dixon, Breast cancer—epidemiology, risk factors, and geneticsBMJ 2000;321doi: 10.1136/bmj.321.7261.

17. KW Jung, S Park, HJ Kong, YJ Won. Frequency and Predictors of Axillary Lymph Node Metastasis in Invasive Breast Cancer. ANZ J Rurg 2001; 71(12): 723-8.

18. Emad A Rakha, Jorge S Reis-Filho,Frederick Baehner,David J Dabbs, Thomas Decker , et al. Breast cancer prognostic classification in the molecular era: the role of histological grade. Breast Cancer Research2010, 12:207

19. D'Eredita' G, Giardina C, Martellotta M, Natale T, Ferrarese F, Prognostic factors in breast cancer: the predictive value of the Nottingham Prognostic Index in patients with a long-term follow-up that were treated in a single institution. Eur J Cancer. 2001;37(5):591-6