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CORRELATION OF RISK FACTORS WITH HPE GRADING IN BREAST CANCER

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ABSTRACT: OBJECTIVE: To correlate risk factors for breast cancer with Histopathological grading. **MATERIAL AND METHOD:** A four year retrospective study was carried out from 2009-2012. 46 cases which were reported as breast cancer in due course were reviewed with histopathological (Scarff-Bloom-Richardson) grade of the tumor and familial, hormonal and acquired risk factors. The correlation of risk factors and the histopathological grade is done by using 't' test. **RESULTS:** Among 46 cases of breast cancer, all were female. 16 cases were having familial risk factors, 12 cases were having hormonal risk factors and 12 cases were having acquired risk factors. 6 cases were having both familial and hormonal risk factors. In histopathological grading 12, 12, 22 cases were of grade I, II and III respectively. High grade was significantly correlating with familial and hormonal risk factors. There was a significant correlation with p value <0.001. **CONCLUSION:** Familial and hormonal risk factors are associated with high grade breast cancer than with that of acquired risk factors.

KEYWORDS: Breast Cancer, Risk factors, Scarff-Bloom Richardson grade.

INTRODUCTION: Breast carcinoma is the most common malignant tumor and leading cause of death in women, with more than 1, 00, 000 cases occurring worldwide annually.¹ In United States, each year approximately 1, 00, 000 new cases are diagnosed and approximately 30, 000 patients die from the disease. There has been a sharp increase in the detection of breast carcinoma, largely due to the wide spread use of mammography.² Most of these cases have a localized lesion with less than 2cm in diameter.³

Many risk factors for the development of breast carcinoma has been established, whereas many other remain questionable.⁴ The most common risk factor is prolonged estrogen stimulation operating on a genetically susceptible individuals.⁵

Nottingham's modification of Bloom Richardson grading system is the most widely used microscopic grading for breast cancer. It is based on architectural features and mitotic activity.⁶ The system was largely applied for Infiltrating ductal carcinoma NOS, but can also be applied to special types of ductal carcinoma and Lobular carcinoma.⁷ Higher the histopathological grade better will be the response to the chemotherapy.

AIMS AND OBJECTIVES:

1. To evaluate the risk factors for breast cancer.
2. To correlate the risk factors with histopathological grade in breast cancer.

MATERIALS & METHODS: A four year retrospective study was done from Jan 2009 – Dec 2012 in the department of Pathology, Karuna Medical College and Hospital, Kerala state, India. Patients who had undergone mastectomy for breast cancer and the patients with biopsy proven breast cancer were

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included in the study. Uncooperative patients and cases in which detailed history is not available were excluded from the study.

All the cases with breast cancer are reviewed. Detailed history with relevant risk factors was obtained from the case sheets. Patients are directly contacted wherever feasible and required.

Risk factors are conveniently categorized into:

- A. Familial risk factors - Family history
 - Genetic history
- B. Hormonal risk factors -Early menarche
 - Late menopause
 - Late age of first child birth
 - Nulliparity
 - Exogenous Estrogen.
- C. Acquired risk factor - Alcohol
 - Fatty Diet
 - Smoking
 - Radiation

Histopathological section of all the cases are examined and graded according to Nottingham modified Bloom Richardson system⁸ into Grade I, II & III. This System includes following parameters: Tubular formation, Nuclear Pleomorphism and Mitotic count.

Correlation of risk factors with that of histopathological grading is done with 't' test of statistical analysis.

RESULTS: A total of 46 cases were included in the study. All the cases were female. No male cases were there. Age of the patients were ranging from 30-87 years with a mean of 58.5 years (Table No.-1) Age of the youngest patient was 30 year and the oldest was 87 years.

Risk factors stratification is done based on the case sheets and on personal information. 16 cases were having familial risk factors, 12 cases were having hormonal risk factors, 12 cases were having acquired risk factors and 6 cases were having both familial and hormonal risk factors (Table No 2).

There was no correlation with the age & time of presentation to that of risk factors or HPE grade. Histopathological grading was done with Nottingham modification of Bloom Richardson grading. 12 cases were showing grade I (Fig. 1), 12 cases were showing grade II (Fig. 2) and 22 cases were showing grade III (Fig. 3).

In the above observation it was obvious that the familial risk factor & hormonal risk factors were associated with higher grade i.e. Grade III and Grade II respectively as compared to that of acquired factors with Grade I i.e. lower Grade.

On applying student 't' test of correlation the P value of <0.001 is obtained. It suggests that there is a significant correlation between the risk factors and histopathological grade. Good correlation of familial and hormonal risk factors with higher Grade and acquired risk factors with lower Grade is obtained.

Thus we conclude that the patients with familial and hormonal risk factors can get a high grade breast cancer as compared to that of acquired risk factors.

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DISCUSSION: The incidence of breast cancer rises throughout a woman's lifetime, peak incidence is seen at the age of 75–80 years with declining slightly thereafter. The most important risk factor is gender; only 1% of male patients will get breast cancer.⁹ Common risk factors for women identified by epidemiologic studies have been combined into the Breast Cancer Risk Assessment Tool (BCRAT), which also includes information from the Contraceptive and Reproductive Experiences study, women with early menarche i.e. at less than 11 years of age have a 20% increased risk¹⁰ as compared to that of women who are more than 14 years of age at menarche. Late menopause will increase the risk. Women who have a first full-term pregnancy at the age younger than 20 years have half the risk in comparison to nulliparous women or women over the age of 35 at their first birth.¹¹ It is hypothesized that the terminal differentiation of milk-producing luminal cells will occur in pregnancy, removing them from the potential pool of cancer precursors. The risk of getting breast cancer in an individual increases with the number of affected first-degree relatives (mother, sister, or daughter), especially if it occurs at young age. There is 1.2- 1.7 fold increase in the risk of getting breast cancer in case of postmenopausal hormone replacement therapy and adding progesterone increases the risk further.¹² Exposure to any kind of radiation to the chest, whether due to cancer therapy, atomic bomb exposure, or nuclear accidents, increases the risk of breast cancer. Correlations between breast cancer risk and dietary intake of any specific type of food is not yet proved even with large studies.¹³ Moderate or heavy alcohol consumption will increase the risk. There is significant reduction in risk with breastfeeding. Cigarette smoking is not been clearly associated with breast cancer.¹⁴

The most commonly used grading system, the Nottingham Histological Score (also referred to as Scarff-Bloom-Richardson), combines nuclear grade, tubule formation and mitotic rate to classify invasive carcinomas into three groups those are highly correlated with survival.⁸

In the present study we have compared the risk factors with that of histopathological grading. With extensive search of literature no similar study has been found. We obtained a good correlation of familial and hormonal risk factors with that of high grade & acquired factors with low grade. Carcinomas with high proliferation rates have a poorer prognosis but may respond better to chemotherapy.⁸

Based on these findings we can conclude that the patient with familial and hormonal risk factors needs neo-adjuvant chemotherapy for better outcome. And the prognosis of the patients with familial and hormonal risk factors is poor in comparison to others. However a prospective study on a large group of patients is necessary as further supporting evidence.

CONCLUSION: Familial and hormonal risk factors are associated with higher histopathological grade as compared to that of other risk factors.

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Age group	No. Of Cases
30-40	10
41-50	16
51-60	10
61-70	07
>71	03
Total	46

Table 1: Distribution of cases according to age group

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Risk Factors	No. of Cases
Familial (F)	16
-Family history	10
-Genetic history	06
Hormonal (H)	12
-Early menarche	04
-Late menopause	03
-Late age of first child birth	02
-Nulliparity	02
-Exogenous Estrogen.	01
Both F & H	06
Acquired	12
- Alcohol	04
- Fatty Diet	02
- Smoking	01
- Radiation	05
Total	46

Table 2: Distribution of cases according to risk factors

Fig. 1: Photomicrograph showing infiltrating ductal carcinoma grade I. (H&E, 100X)

Fig. 2: Photomicrograph showing infiltrating ductal carcinoma grade II. (H&E, 100X)

Fig. 3: Photomicrograph showing infiltrating ductal carcinoma grade III. (H&E, 100X)

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