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Research Article

Metastatic Breast Cancer: A Correlation between Ki67, a Tumor Marker and Various Stages in Terms of age Groups

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ABSTRACT

Breast cancer is common most malignancy in multipara, premenopausal women The antigen Ki-67 plays important role in evaluating this condition biochemically. Being expressed in all phases of cell cycle (S, G1, G2, M) except GO.

METHODS: This cross-sectional design of the observational research on 283 patients was arranged and executed at JPMC (Jinah Postgraduate Medical Center). The hormone receptor status staging is done with immune-histochemical (IHC) staining. Ki-67, the nuclear antigen was assessed quantitatively as well as visually way using light microscopes.

Result: Most Cases belonged to stage -4 of the breast cancer followed by Stage -2 and stage-3. The biomarker KI 67 was more positive in 3rd and 4th stages.

Conclusions: Biological markers are good parameters to assess the progression of the breast cancer.

Keywords: Breast cancer, Metastasis, Stages, KI 67.

INTRODUCTION

Among the Asian countries Pakistan stands on the top in terms of prevalence of the breast cancer with around 90000 newly reported cases annually with a risk of 1/9 women. Tumor markers are the proteins which are expressed on the surface of cancerous or native cells. These biomarkers may be specific or non-specific and get detached from the tissues and may be found blood, urine and other body fluids. These proteins or tumor markers may help detecting various cancers in the human body as they rise in the early stages of the cancers. Ideally theses tumor markers need to have both the specificity as well as sensitivity to help in cancer screening and diagnosis [1]. Breast cancer is the most common among the women globally with unmarried and nulliparous women are at a greater risk [2]. Approximately 71.2% of the deaths among the breast cancer patients were reported to be for women with age group40-60 in 2016 from USA therefore, mammography screening is mandatory in this age group [3]. Menopause disturbs the balance of energy, hormones, various chemokines along with different cytokines and fat distribution that further promotes the tumor, focus on the menopause may alter the condition [4]. The TNM classification (Tumor, Node, Metastasis) for the malignant tumors is the recommended one by the UICC (The Union for International Cancer Control), based on anatomy based recording the nodal involvement metastases which describes the tumor staging from 0 to IV [5]. Cancer staging is very important in terms of classification of the cancer, its status at the time of diagnosis along with making a definitive management plan for the disease as well as the follow up for prognosis [6]. Ki-67, a nuclear protein was found to be associated with the cellular proliferation by Gerdes et al in 1980 with the help of mouse monoclonal antibodies. The Ki-67 antigen is frequently being assessed through the immune histochemical evaluation and has been reported to be expressed in S, G1, G2, as well as M phases of the cell cycle except the GO phase so it is helpful in the assessment of the growth fraction [7]. The estrogen has been documented to influence the progression of the breast cancer specially the estrogen receptor positive cancers [8]. Postpartum as well as the post-lactation associated involution along with associated inflammatory changes are also accepted to

promote the progression tumors. The Luminal tumors were reported to be the majority among the breast cancers while basal-like tumors as the 2nd followed by the unclassified whereas the HER2-tumors were the least frequent affecting the survival rates as well [9]. The tissues involved in breast cancer are lobular or ductal in their origin and appearance is lumpy or sometimes accidently diagnosed on imaging mammography is recommended as screening imaging modality in suspected as groups. Tissue biopsy is the definitive diagnostic technique providing the exact information about the nature of the cancer [10]. This study was designed to estimate the correlation between the Ki67 tumor marker and the age of the cancer patients to add in the diagnostic as well as the prognostic value in the breast cancer management. This is topic was not searched in this part of the world so we tried to generate and focus some new aspects in this field with some hope to improve in the future.

METHODS

This was a cross-sectional observational study carried out on 283 patients at JPMC. The hormone receptor status staging is done with immune-histochemical (IHC) staining. Specimen received in formalin coded as true-cut biopsy or mastectomy, submitted in single cassette. Sections were examined under light microscope. Breast cancer is typically described in stages, according to the presence and size of the tumor and its metastasis. Nuclear antigen Ki-67 was evaluated in a quantitative and visual way using light microscopes. Ki-67 values are acquired as the percentage of positively marking malignant cells using the anti- human Ki-67 mono clonal antibody MIB1. The Ki-67 percentage score is defined as the percentage of positively stained tumor cells among the total number of malignant cells assessed statistical analysis was carried out on SPSS version21 keeping level of significance below0.05.

RESULTS

Maximum number of patients belong to age group 51-60 which was 95(34%) followed by the age group of 30-40 years with79(28%) while the age group of 41-50 was at 3rd number with72(25%). The age group of 61-70 years was at 4th position frequency wise 30(12%) whereas the least frequent age group was 71-80 years 7(2%) shown in figure-1. The levels of KI67 were observed in 30 - 40Years age group as less than 15 in13(4.63%) patients, 15-30 in 17(6.00%) patients whereas more than 30 in49(17.31%) patients. The KI67 was found in age group 41 - 50 Years as less than 15 in 0(0%), patients 15-30 in 18(6.40%) patients and above30 in 54(19.08%) patients. These were in 51-60Years age group less than 15 in 28(9.89%) patients, while 15-30 in 13(4.63%) patients and above30 in 54(19.08%) patients. The age group 61 - 70 Years had less than 15 in 8(2.83%) patients, 15-30 in10(3.53%) patients and above 30 in12(4.24%) patients. KI67 levels in age group 71 - 80 Years were noted as below 15 in 01(0.35%) patients, 15030 in 03(1.06%) patients and more than30 in 03(1.06%) patients [Table-1].

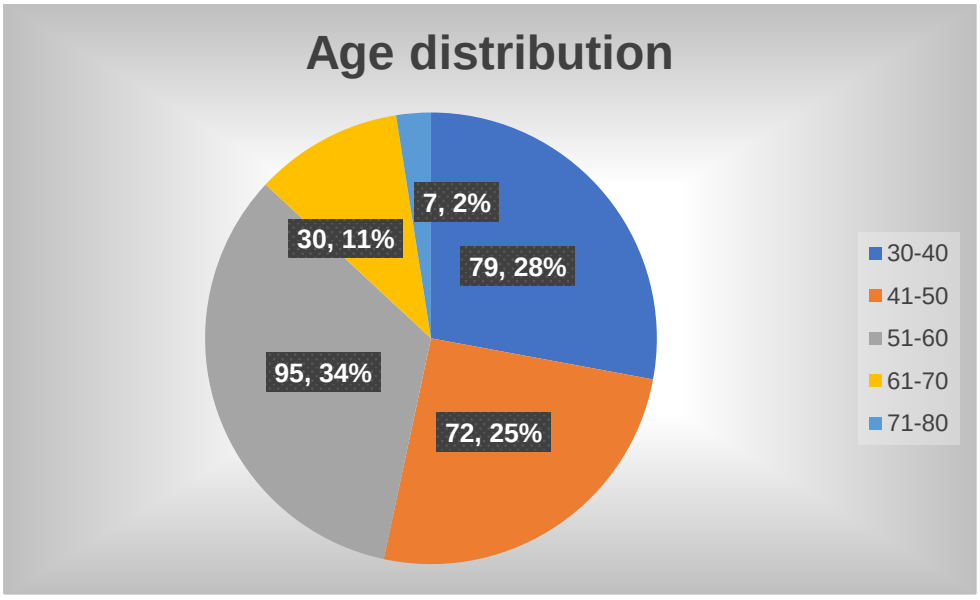

Figure-1: Pie Chart Representation of Various Age Groups

Table-1: Comparison between KI 67 Levels with Various Age Groups

Age Groups		KI 67 Max			Total
		Less than 15	15 - 30	More than 30	
30 - 40	Years	13(4.63%)	17(6.00%)	49(17.31%)	79(27.92%)
41 - 50	Years	0(0%)	18(6.40%)	54(19.08%)	72(25.44%)
51 - 60	Years	28(9.89%)	13(4.63%)	54(19.08%)	95(33.57%)
61 - 70	Years	8(2.83%)	10(3.53%)	12(4.24%)	30(10.60%)
71 - 80	Years	01(0.35%)	03(1.06%)	03(1.06%)	07(2.47%)
Total		50(17.67%)	61(21.55%)	172(60.78%)	283(100%)

DISCUSSION

Ki67 that tumor marker may predict the aggressive nature as well as the higher histopathological grades of the tumor [11]. The higher expression of Ki-67 tumor biomarker has association with the higher pT and pN stages along with ER/PR negativity whereas with HER2/neu positivity as well as ECE and LVI positivity [12]. Ki 67has been as an indicator for cell proliferation frequently with multiple diagnostic applications showing more Ki 67 expression in malignant tissues as compared to the normal ones. Studies have shown the positive correlation for Ki67/MIB-1LI and human malignancy. The routine histology-based examination of the tumor tissue has certain limitations in predicting the tumor behavior whereas the Ki67/MIB-1 immunostaining has improved the information regarding the grading system favoring the potential use of Ki67 in routine. The Judicious usage of Ki67 if combined with the histopathology of the malignant tissues may prove a reliable indicator for the tumor recurrence. Previous research has also confirmed the correlation of the Ki67 with the tumor size along with lymphatic invasion and metastases [13]. It was further observed and recommended in our study that Ki-67 may be considered as a future valuable biomarker for breast cancer. There were many limitations in our study from sample size to follow up but we tried to maintain the high quality of the research in our set up. Further studies are recommended for the field researcher. Breast cancer awareness programs are well run by the government with provide free evaluation, screening, diagnosis to treatment modalities. Further work is needed to train the health care professional with the advancement in techniques and skills.

CONCLUSIONS

It is concluded that the tumor marker Ki67 positive tumors may rapidly progress in advanced stages with tendency of metastasis.

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