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Original Research Paper

Pathology

INCIDENCE OF BREAST CANCER ACCORDING TO MOLECULAR CLASSIFICATION : A THREE YEARS STUDY AT RIMS, A TERTIARY CARE HOSPITAL IN RANCHI, JHARKHAND.

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ABSTRACT Breast cancer is a multifaceted disease, comprised of distinct biological subtypes with diverse natural history, varied spectrum of clinical, pathological and molecular features with different prognostic and therapeutic implications.Recent attention has been directed at molecular classification of breast cancer.This helps to appropriate specific and targeted therapy. In our institute we did a retrospective study of 3 years in the histologically diagnosed cases of breast cancer.We took 171 cases and classified them histologically as well as molecularly using immunohistochemical markers .i.e. ER, PR, HER 2, Ki67 and p53.

KEYWORDS : molecular, targeted therapy, immunohistochemistry, hormone receptor, human epidermal growth factor receptor etc.

INTRODUCTION:

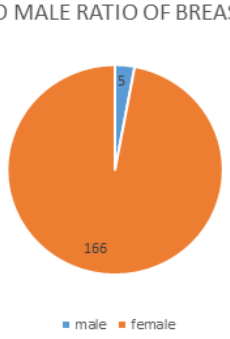
Breast cancer is the most frequent cancer among the females world wide accounting 23 % of all the cancers[1] and impacting about 2,1 million women each year.[2] In India the present rate is 25.8 per 100,000.[3]They are uncommon below the age of 35, but now the incidence is rapidly increasing between 35- 40 years.[4]A crucial development in the treatment was the recognition that the presence of hormone receptors in the tumor tissue co-rrelates well with the hormonal therapy and chemotherapy.[5]By the pioneering efforts of Perou and colleagues in 2000 to segregate breast cancer into distinct subgroups based on similarities in the gene expression profiles, has been enthusiastically embraced by the medical and scientific community. This was done with the hope that this approach will provide new insights into the biology of breast cancers and impact in the therapeutic strategies.[6,7] The subtypes of breast cancer most widely recognized by their gene expression signature includes, *luminal A, Luminal B, Her 2 enriched, Basal like and Normal breast like.*

MATERIALS AND METHODS :

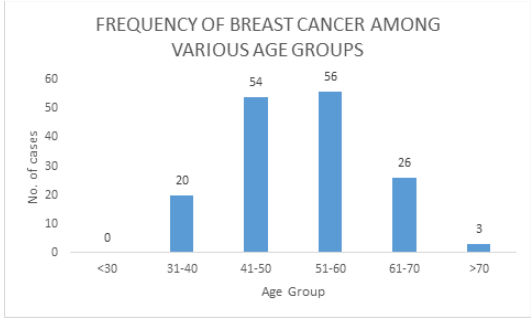
We did a retrospective study for a period of Three years .i.e. from January 2016 to December 2018. 171 paraffin blocks of diagnosed cases of breast cancer were subjected to ER, PR, HER 2, Ki67 and p53 IHC staining. Prior to this we did a histological assessment of grade using Nottingham modification of Bloom and Richardson grading system. ER, PR results were interpreted as positive and negative on the basis of *Allred score*.Ki 67 as high and low mitotic rate I.e.>14% and <14% respectively. P53 expression as positive and negative. Her 2 Neu scoring was done according to the ASCO/CAP guideline .However due to unavailability, Gene amplification study using FISH was not done.

OBSERVATIONS:

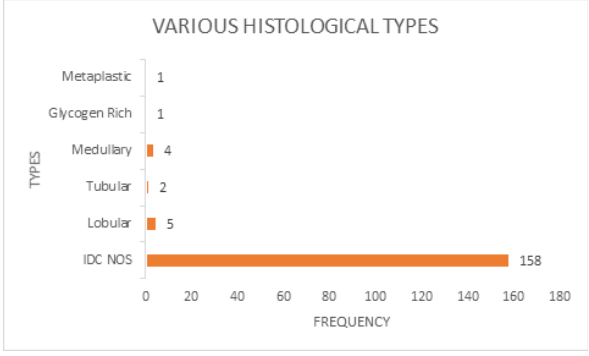
In our study of 171 cases of breast cancer 166(97.07%) cases were of female and 5(2.92%) cases of male breast cancer.Female: male ratio = 33.2:1.



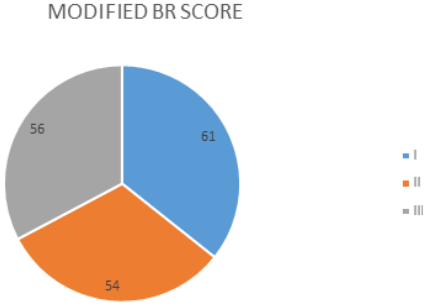
All the male breast cancer was above the age of 60 years.Among the females the most common age group effected was 51-60 years which had 56 (32.74%).



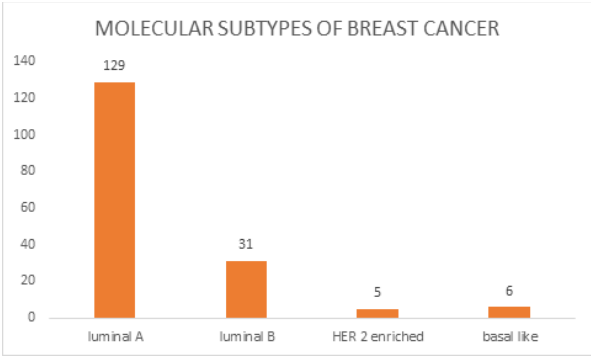
The most common histological type was infiltrative duct carcinoma NOS.I.e. 158 (92.39%).All the male breast carcinoma belonged to this category.



The cases were graded histologically using Nottingham Modification of the bloom Richardson Score as follows:



Molecularly the cases were classified in 4 subtypes as follows:
LUMINAL A : 129
LUMINAL B : 35
HER 2 ENRICHED : 5
BASAL LIKE : 6



We encountered two rare types of breast cancer I.e glycogen rich and metaplastic carcinoma both of which showed basal like molecular profiling..

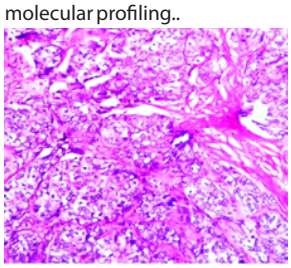


FIGURE 1: glycogen rich clear cell carcinoma

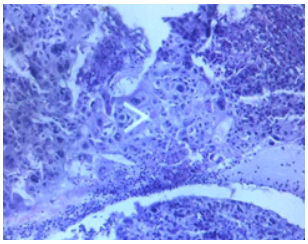


FIGURE 2: metaplastic carcinoma

DISCUSSION:

Perou and Sorlie proposed " *Molecular classification*" terminology in breast cancer for the first time.[8] Detection of difference in response to the treatment and metastatic pattern according to molecular subtype has further increased the value of molecular subtype.[9] A panel of ER, PR, HER-2, Ki67, p53 and basal markers like EGFR, CK14, CK5/6 are used. These are the ceratins points about the various molecular subtypes.[10]

LUMINAL A: They are usually 60% of invasive breast cancer.They are ER/PR positive and HER 2 negative and low ki67 (<14%). Histologically tubular, cribriform, low grade invasive NST, Classic lobular comes under luminal type A.They respond to endocrine therapy.Chemotherapy is not indicated .They have generally good prognosis.

LUMINAL B: They comprise about 10% of invasive breast cancer.ER positive PR low positive and HER 2 is variable and ki67 is >14%. Luminal B tends to be of higher histological grade than luminal A. Invasive ductal carcinoma NST and micropapillary carcinoma comes under this category.They respond to endocrine therapy but less than luminal type A.They respond well to Chemotherapy than luminal type A. The prognosis is not as good as luminal A.

HER 2 ENRICHED: They comprise about 15% of invasive breast carcinomas .They show high expression of HER 2 and low expression of ER/PR and associated genes.They show high proliferation rate and Tp53 mutation is also common. They are more likely to be of higher grade and are generally node positive. High grade invasive ductal carcinoma NST belongs to this category.They respond to anthracyclin based CT.

BASAL LIKE: These tumors show high expression of basal epithelial genes, basal cytokeratins. They comprise about 15% invasive breast carcinomas. They are triple negative,have high proliferation rate , Tp53 mutations are common and usually show BRCA1 dysfunction. These tumors are particularly common in African American people. High grade invasive ductal carcinoma , metaplastic carcinoma and carcinoma with medullary features belongs to this category. No response is seen with endocrine therapy or trastuzumab.They generally bear the worst prognosis among the four groups.

In our study we found that the HER 2 enriched cases had frequent lymph node metastasis I.e all 5 cases were lymph node positive. All tumors having basal like molecular profile were above 60 years of age and were histologically of grade III.

CONCLUSION:

Thus we conclude that breast cancers were usually encountered in women with only 2.92% in males.All the male breast cancers were of Grade III. Most frequently encountered histologically subtype is *infiltrative duct carcinoma not otherwise specified*.Whereas most frequently encountered molecular subtype is *Luminal A type*.

We had certain limitation in our study .The HER 2 positive cases which were equivocal could not be confirmed by FISH gene amplification due to the unavailability and Basal like markers like EGFR CK 14 and CK 5/6 could not be used as they were also unavailable too. Molecular subtype developed in breast cancer emphasized biological heterogenity which has been histopathologically defined by the pathologists for along time.We must not forget that molecular classification of the breast cancer is still in the developmental stage and has limitations of today.

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