Breast Carcinoma: Treat or Overtreat

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Breast carcinoma is the most common malignant neoplasm in women worldwide[1] and the second leading cause of death in developed world[2]. The lifetime risk ofbrcast cancer in developed world is estimated to be one case per eight women, making upto 32% of all female cancers; which is believed to be higher in the developing world[1]. Mammography and adjuvant systemic therapy have decreased the risk of recurrence and have improved disease free survival1. Breast cancer, in many, is a systemic disease at the time of diagnosis and cancer cells have already shed beyond the anatomical confmes of breast[3]. The woman having breast cancer is at an aboveaverage riskofhaving it in the contralateral breast in due course of time.

There is yet no prognostic marker better than axilla[7] lymph nodes having a direct bearing on treatment plan. Inspite of the similar treatment protocols and an axillary ndde negative status, the survival rate in younger patients is The older patients are less likely to have tumour recurrence due to much less expectancy[9]. Size of primary tumour is also a valuable indicator for predicting early recurrence[10,11]. The endocrine factors responsible for the development and progression of breast cancer[12]. are early pregnancy and early ovarian ablation (low risk); late menopause, early menarche, an early abortion, nulliparity, late first pregnancy and estrogen therapy (high risk factors).

In USA it is well established that black females have a 20% more mortality, as compared to their white counterparts having breast carcinoma[4,5] and the former group has a slightly little lower median age. Black women have a higher rate of medullary comedo, scirrhous, papillary and inflammatory carcinomas. The histologic subtypes of carcinoma breast exhibit wide range of differences in their relative frequency, site and prognosis[2]. Carcinoma breast appears to be a different disease process in black females, as compared to whites, in many respects even when the stage of disease presentation is controlled[4,13,14] The overall survival rate of breast cancer patients in black race is lower and they tend to do worse[15,16] Estrogen receptor positivity is also more in the European white female population having breast cancer37. Socio-economic status also plays a role, being inversely proportional to prognosis in a way yet to be understood and explored in detail[18]. There are differences in tumour composition and grade of differentiation amongst races[19,20] These differences are also highlighted in Pakistani population as compared to white population, the Pakistani population being close to black western population in this respect[21].

In Pakistan, over 75% breast cancer cases are in grade II and III Cases of premenopausal breast cancer are higher, which are usualiy estrogen receptor negative in contrast to western data[10,12]. Even within the premenopausal group, the percentage ofyounger patients (under 30 years of age) is much higher in Pakistani population, having a poor survival[7,8,23]. Tumour size and axillaiy node status are also important prognostic influences[11]. In Pakistannumberof positive lymph nodes is usually higher Multicentric tumour is also a bad prognostic indicator'. In our population the number of cases having a tumour >5 ems with axillary metastasis is over 75%. Patient survival, prognosis, disease free survival and response to treatment modalities offered is dependent on all these factors.

The tumour doubling time (TDT) is helpful in estimation of length of preclinical stage of disease and predicting the course. TDT is a functionof rate of cell mitosis, proportion of cell having active mitotic activity, rate of cell death, epithelial versus fibrous component of tumour, inter-mitotic time• interval, desquamation, dormancy, tumour burden and treatment effects. In early, acute, or progressive breast

cancer the TDT is in days, while in late or chronic breast cancerthe TDT may be in years. There is a direct relationship between TDT and survival, sometimes even after treatment

There are a number of newly identified prognostic factors under evaluation, which might show a different pattern among different populations enabling us to identify population subgroups on the basis of race, geography and life style. Some of these are tumour angiogenesis, microvessel density, PCNA (proliferating cell nuclear antigen), level of p53, cathepsin-D and procathepsin-D, genetic expression of heat shock protein, level of pS2, urokinase, transforming growth factors, nm23 a marker of metastatic potential, cyclic AMP binding protein, cyclin E, amplification of HER-2/neu oncogene and tumour necrosis[3].

Adjuvant treatment is given in even stage I disease to achieve a successful local control[24,28]. It is given regardless of nodal status and a skip axillary lesion is highly likely to be missed[24]. Chemotherapy is believed to be effective against distant metastasis and controlling the loco-regional recur rence[25]. Chemotherapy, if delayed, becomes less effective and less well tolerated[26]. Younger patients require a more intensive treatment due tobettertolerability andanaggressive form of disease[26]. Adjuvant therapy has clear benefits in terms of overall and disease free survival especially in young cases[27].

Our patients are usually young, who have a large multicentric tumour, are ER negative, have a high recurrence rate, poor socioeconomic status, high mortality, early lymph node involvement, and a systemic disease at the time of diagnosis with genetically committed cells already present outside the anatomical confines of breast. In addition, ER negative status mandates adjuvant treatment because of lack of response to hormonal manipulation. Chemotherapy if delayed, becomes less effective. The concept of chemoprevention in high risk population is also getting recognition and consideration with time. All these factors make it mandotory that a just and due consideration should be given in our population for enthusiastic and aggressive treatment even at the earliest stages of the disease.

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