

STUDY ON c-erbB-2 ONCOPROTEIN IMMUNO-EXPRESSION, EGF-R, AND OTHER OESTROGEN RELATED FACTORS IN BREAST CANCER

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Breast cancer is the most frequent cancer in women worldwide; whereas it is the second most common cancer among Indian women and an increasing trend in the incidence of this disease has been observed. The epidemiological evidences have strongly supported the hypothesis that genetic, environmental and hormonal factors affect the risk for development of breast cancer. Oestrogens are physiological mitogens for mammary cells. During malignant transformation, cells exploit this mitogenic action, which is involved in progressive accumulation of genetic alterations such as c-erbB-2 amplification, p53 mutation, overexpression of ER, etc.

In the present study, the immunohistochemical assays for the c-erbB-2 oncoprotein (p185), EGF-R and ER were carried out on histopathologically proven paraffin embedded tissue sections from 100 cases each of premenopausal and postmenopausal breast cancer (Part-I study). Out of the total 200 cases, 76 (38%) and 78 (39%) were positive for c-erbB-2 and EGF-R respectively; while 72 (36%) showed overexpression of ER. The c-erbB-2 oncoprotein significantly expressed in cases with lymph node metastasis, whereas both EGF-R, and c-erbB-2 revealed statistically significant overexpression in tumours of higher histological grades as well as in ER negative breast tumours. Moreover, concomitant expression of c-erbB-2 and EGF-R showed an association with lymph node involvement, histological grade of the tumour and ER status. Interestingly, a difference in overexpression of c-erbB-2 and EGF-R and their correlation with other investigated parameters was noticed between premenopausal and postmenopausal groups. The frequency of both c-erbB-2 and EGF-R expression was significantly higher in postmenopausal tumours.

Environmental factors like increased intake of total calories and fat consumption in women of higher socio-economic status appear to increase the risk. In a case-control study, serum samples of 175 patients with breast cancer (before initiation of any systemic treatment) and 182 control women were analysed for different lipid components (Part-II study). Among total subjects, 99 cases and 137 controls were premenopausal, while the remainder were postmenopausal. The mean serum levels of triglycerides, total cholesterol and LDL-cholesterol were found to be higher in breast cancer patients, whereas their HDL-cholesterol showed a lower level compared to controls. After dichotomy of the patients and controls on the basis of menopausal status, only premenopausal patients revealed higher serum levels of total cholesterol and LDL-cholesterol than corresponding controls; among postmenopausal cases, mean serum level of HDL-cholesterol was significantly lower in comparison with postmenopausal controls.

The study revealed an overall change in the levels of different blood lipid fractions in patients with breast carcinoma, also a difference was observed between pre- and

postmenopausal cases in this regard. These alterations may be the result of dietary factors or, due to metabolic and/or hormonal disturbances in the pathological process of breast cancer.

There are substantial experimental, epidemiological and clinical evidences, which show that breast cancer risk is influenced by endogenous hormones, particularly sex-steroid hormones. Physiologically, oestradiol is the most active oestrogen, whereas testosterone is the most potent androgen in women. The major and specific binding protein for testosterone and oestradiol in blood is SHBG. A case-control study was conducted on serum samples of 102 breast cancer patients and 100 control women to estimate the levels of testosterone, oestradiol and SHBG (Part-III study). Of these subjects, 52 were premenopausal patients and 65 were premenopausal control women. In breast cancer patients, the serum testosterone levels were significantly increased, while SHBG levels showed a significantly lower value. However, serum levels of oestradiol between cases and controls (overall) did not reveal any significant difference. Further, among breast cancer cases, a statistically significant inverse relationship was observed between levels of testosterone and SHBG, whereas serum testosterone and oestradiol levels showed a positive relationship. After division of the patients and controls according to menopausal status, only premenopausal patients revealed a higher serum mean level of oestradiol compared to corresponding premenopausal control women. Nevertheless, this study has indicated that testosterone and SHBG may have a role in breast cancer, possibly through their influences on the amount of bioavailable oestrogen.

Breast cancer is appearing to represent an enormous public health problem. The present study observed some important findings which support the involvement of genetic, hormonal, and environmental factors in the pathological process of breast cancer. Further, the study revealed a difference between pre- and postmenopausal cases. The difference in the pathological process between premenopausal and postmenopausal women, as revealed by this study, suggests that various oestrogen-related factors have some relation to the bimodal character of breast cancer. Only a clear pathophysiological understanding could lead to an efficient policy of breast cancer prevention and decrease in the mortality due to this cancer.