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RESEARCH ARTICLE

HISTOPATHOLOGICAL STUDIES ON BREAST CANCER AMONG DIFFERENT POPULATIONS IN AN AROUND CHENNAI

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ABSTRACT

Breast cancer is a very heterogeneous disease that is characterized by a number of histopathological subtypes. The major histological types of breast cancer were estimated. The 180 samples were analysed. The majority of breast carcinomas fall into the category ductal carcinoma (39%) and Tubular Carcinoma (23%) followed, and by Infiltrating Lobular Carcinoma (9%), Medullary Carcinoma (8%), Inflammatory Carcinoma (8.5%) and Pagets (6%). The histopatholgical showed breast cancer are mostly ductal carcinoma and tubular carcinoma.

INTRODUCTION

Histopathology plays an important part in determining the treatment strategy for women with breast cancer with the evaluation of breast specimens determining the surgical and the enological therapeutic option used. Relation between the amount of breast core needle biopsy material examined and agreement between preoperative and postoperative histopathology parameters in invasive breast cancer has been established (Hanby, 2005). O'Leary *et al.,* (2004) reviewed surgical specimen histopathology reports of 113 patients with invasive breast carcinoma. The histopathological characterization of primary breast carcinoma admittedly is a finite and perfect source of information for an ideal prognostic and predictive evaluation (Viale, 2003) for tailoring the most appropriate intervention for each individual patient. Middleton *et al.,* (2003) reported African - American women with breast cancer have a poorer survival rate than white women and are more likely to die of breast cancer in almost every age group. Diagnosis of pure Ductal carcinoma *in situ* (DCIS) and retrospective evaluation was made in a series of breast cancer patients who had a histologic diagnosis of pure ductal carcinoma *in situ* with micro invasion (Zaragno *et al.,* 2005).

Breast Cancer incidence rates vary according to estrogen receptor expression and histopathology. Anderson *et al.,* (2006) reported that annual mortality rates from breast cancer after initial diagnosis (hazard rates) might also vary by histopathology. Atri *et al.,* (2002) assessed the prognostic value of family history of malignancies in patients afflicted with breast cancer and examined family history and histopathologic characteristics of 542 Iranian primary breast cancer patients. Histologic and imunophenolyping characterization of primary breast carcinoma can be consistently evaluated by simple histologic examination and immuno histochemical assays (Viale, 2003 and Hamby, 2005). The histopathology plays an important part in determining the treatment strategy for women with breast cancer. The present histopathology study was carried out to determine the breast cancer among the in an around the Chennai populations.

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MATERIALS AND METHODS

Collection of tissue sample

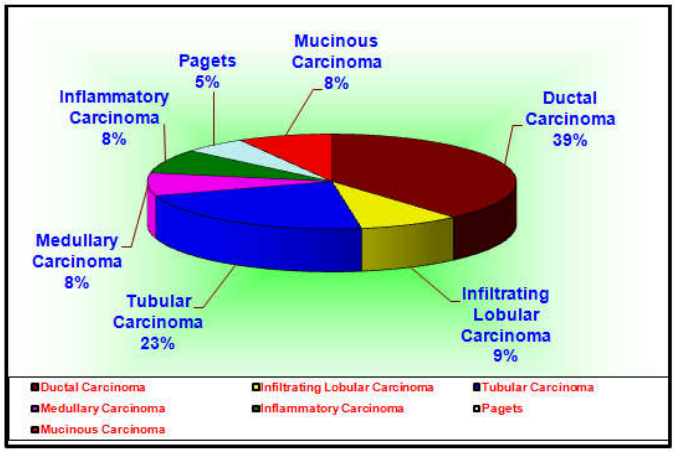
The breast cancer sample was collected from the different places in an around Chennai *viz.* Government General Hospital, Royapettah Government Hospital and Adyar cancer Institute, Chennai, India.

Breast cancer tissue analysis

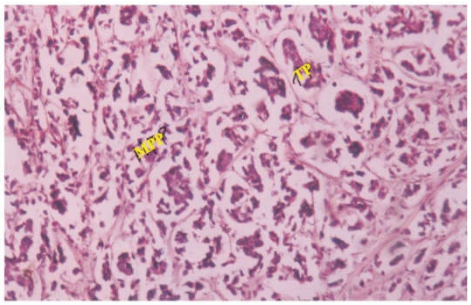
One hundred and eighty breast cancer subjects were considered and classified into three groups according to their age: 31-40, 41- 50 and 51- 60 years. The collected cancer tissue samples were prepared with the protocol of Lowe and Teffrey (1990) and Ahmed *et al*. (1990). The final slides were examined under the microscope and classified with different breast carcinoma. The microphotograph was taken and assessed.

RESULTS

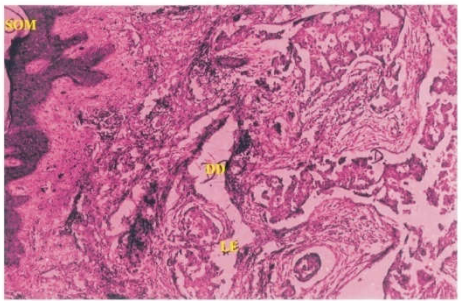
Among 180 breast carcinoma subjects, 38.33% had ductal carcinoma either in the infiltrating form or papillary form. 22.55% showed infiltrating tubular carcinoma and 8.8% were observed to have lobular carcinoma type. Medullary



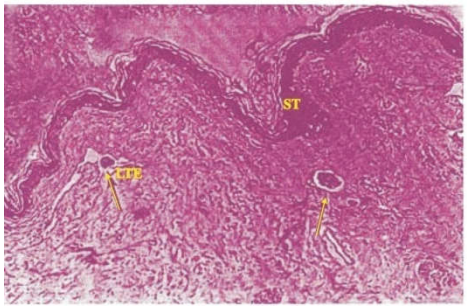
Graph 1: Histopathology incidence in Breast Cancer



A. Infiltrating Tubular

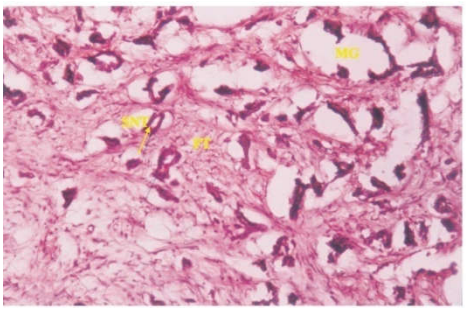


B. Ductal carcinoma

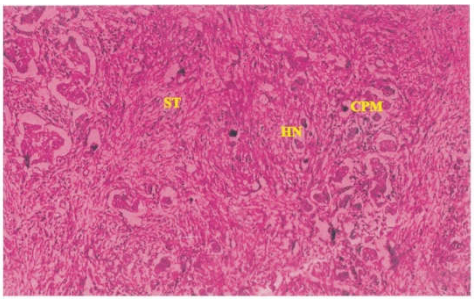


C. Inflammatory

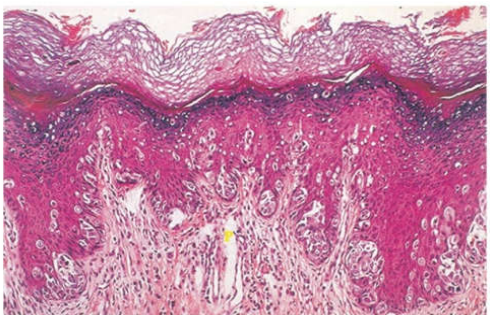
carcinoma was found in 7.7% of the subjects. Inflammatory carcinoma and mucinous carcinoma of the breast were found to have similar incidence, according 8.25% pagets disease of the breast was found to be the least occurring with 5.5% (Graph 1) (Fig A-M). The pathological examination of the breast carcinoma tissues revealed usual infiltrating – neoplastic ductal cells inside and outside the ducts-which were



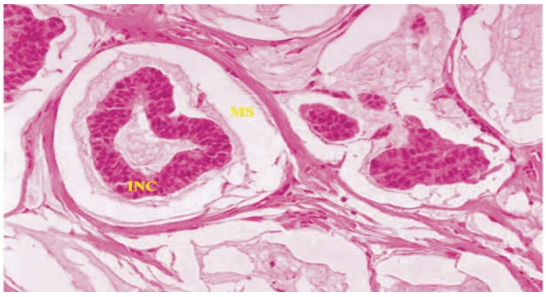
D. Tubular carcinoma



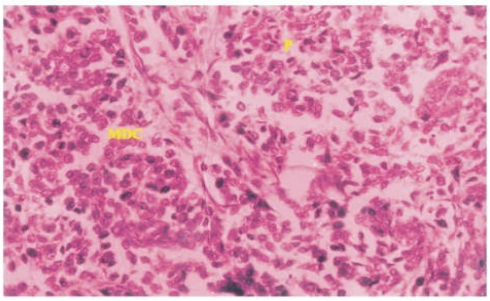
E. Schirrous type



F. Paget

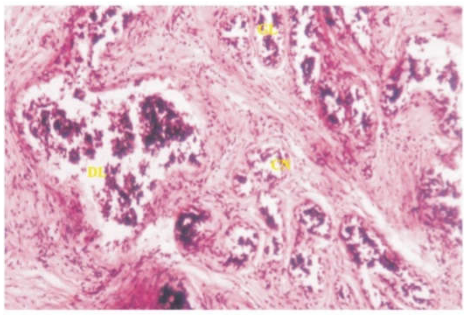


G. Pappillary Patte

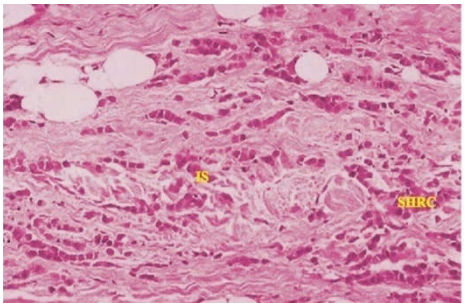


H. Mucinous carcinoma

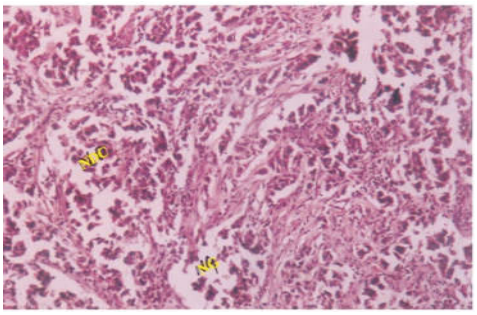
MPP- micropappilary pattern, ST- Skin thickening, LTE- Lymphotic with tumour emboli, TP- Tubulo papillary, SOM- Skin overlying malignant, DD- Dilated ducts, LE- Lymphotic Invasion



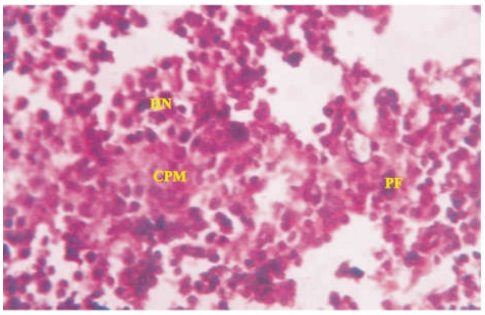
I. Intraductal carcinoma



J. Lobular carcinoma



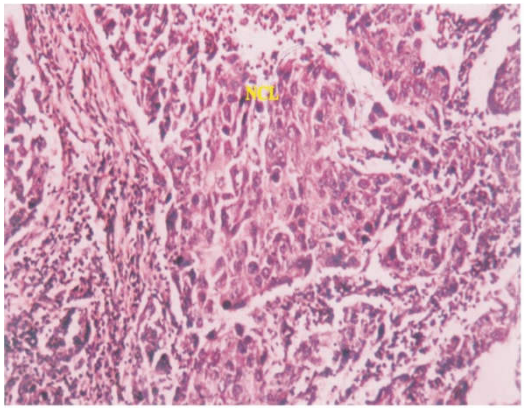
K. Dutal carcinoma-papillary pattern



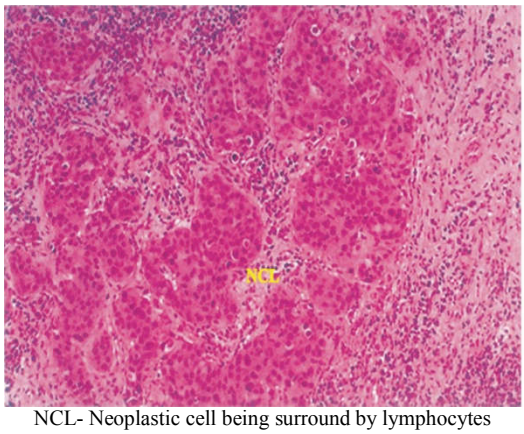
L. Infiltrating ductal

MPP- micropappilary pattern, ST- Skin thickening, LTE- Lymphotic with tumour emboli, TP- Tubulo papillary, SOM- Skin overlying malignant, DD- Dilated ducts, LE- Lymphotic Invasion

infiltrating into the stroma. Neoplastic glands and cells arranged in cords and sheets, infiltrating the stroma showing infiltrating ductal carcinoma (Fig A &B) in the breast tissues, were also characterstic. Inflammatory carcinoma of breast is defined by its clinical features and its mode of spread within the breast, and not by architectural pattern or cytology (Fig. C). Ductal carcinoma was associated with small calcification within tumour gland or stroma. Furthermore infiltrating tubular carcinoma with dense stroma and tubulo-micro papillary structures with less stroma were also noticed. In the majority of cases, the infiltrating tubular carcinoma was



NCL- Neoplastic cell with lymphocytes



NCL- Neoplastic cell being surround by lymphocytes

M. Medulary carcinoma

accompanied by cribriform or micropapillary intraductal carcinoma. Infiltrating tubular carcinoma found in (Fig. D) the section showed small hyperchromatic round cells arranged in linear cord, (Indian file pattern) infiltrating into stroma. The tubules appeared to be distributed at random rather than arranged in any particular pattern. Tubular carcinoma cells of the breast (Schirrous Type) were also observed (Fig. E) in breast cancer subjects. The tumour was composed of low grade malignant cells in a tubular configuration. Compressed malignant glands surrounded by dense fibrous tissue (desmoplastic reaction) was also characteristic touch pathological manifestation. Hematoxylin and Eosin stained sections showed malignant neoplasm composed of small neoplastic tubules (tubules lined by hyperchromatic cells) surrounded by dense fibrous stroma. The angulate shape of some tubules and luminal cytoplasmic protrusions were also noticed. Eczematous changes of the nipple (Fig. F) called the pagets were also not worthy. The pathological condition of the tissue showed skin with pagetoid cells (pagets disease of the breast). Large cells with clear cytoplasm (vacuolated appearance), representing the migration of malignant cells from adjacent mammary ducts in the nipple was trend in 10 among 180 subjects. Besides, histopathological changes were also observed in the malignant cells with hyperchromatic nuclei arranged as papillary structures (Fig. G) and Clusters of pleomorphic cells. Axillary deposit was observed in the lymph node with dilated sinusoids being filled with malignant cells. Mucinous carcinoma (Colloid carcinoma of the ductal type) disclosed (Fig. H) islands of neoplastics (malignant) with pools of mucin secretion around. Mucinous carcinoma was found in 15 subjects with strands of cells and delicate fibrovascular septa traversing the mucus. The breast tissue

involved in this type of tumour was usually a small cluster of epithelial cells, constituting mucinous or colloid carcinoma. Intraductal carcinoma of breast (Fig. I) indicated malignant cells proliferating within the glandular lumina and comedo pattern-dilated ducts with lumen containing central necrosis lined by neoplastic ductal cells were also observed. Lobular carcinoma of the breast, otherwise called infiltrating lobular carcinoma, arises from the lobular and terminal duct epithelium and accounts for approximately 5-10% of all breast cancers (Fig. J). Ductal carcinoma - papillary pattern (Fig. K) showing malignant ductal cells - round to oval cells with vesicular nuclei and prominent nucleoli were also observed in certain breast tissues. Indeed 69 breast carcinoma subjects were identified to be suffering from ductal carcinoma. Medullary carcinoma (Fig. M) syncytical masses of large neoplastic cells surrounded by lymphocytes. Lymphocytes were seen to have as small dots in the cytoplasma and associated with large neoplastic ductal cells. Fibrous tissue and heavy infiltrate of lymphocytes and plasma cells sharply delineated the neoplasm from adjacent fatty breast tissues in 14 breast carcinoma subjects.

DISCUSSION

The human mammary gland was once thought to actively develop during puberty under the influence of estrogen and other growth hormones, but once fully developed, it entered a resting state unless stimulated by the hormones of pregnancy. But in the 1980's, investigators described the histologic features of cyclical changes that occur in the breast with ovarian hormonal periodicity and distinguished those changes from the abnormal alterations observed by pathologists. The combined information derived from these studies defined the functional unit of the adult female breast from which the majority of both benign and malignant lesions arise as the terminal duct lobular unit.

Histologically, DCIS is described as malignant epithelial cells found inside the mammary ducts and lobules, showing no evidence of invasion through the basement membrane of the ducts or lobules into the surrounding breast tissue (Waston, 2001). It is the most common cell type, comprising 70-80% of all cases of breast cancer. The tumours occur throughout the age range of breast carcinoma, being most common in women in their middle to late 50s. Among 180 breast carcinoma subjects taken for the present study, the pathological analysis revealed that 38.33% of them showed ductal carcinoma either in the infiltrating form or papillary form. DCIS can also extend into a lobular unit and enters into the differential diagnosis of lobular carcinoma *in situ* (LCIS) or atypical lobular hyperplasia (ALH). Distinguishing lobular involvement by DCIS with a low nuclear grade from LCIS or ALH can be difficult because the cytologic features of the cells are often similar. Formation of small secondary lumens and a resetting arrangement of cells suggest ductal differentiation. The presence of distinct cell margins in foci of solid growth has also been identified as a ductal feature. Cytoplasmic vacuolization, intracytoplasmic lumens and singlet ring cells are more typical of LCIS or ALH, but they can be seen in DCIS. According to Zavagno *et al.,* (2005) retrospective evaluation on a series of breast cancer revealed a fine histologic diagnosis of pure ductal carcinoma insitu patients with microinvasion.

The use of the term "carcinoma" in LCIS is misleading, because LCIS is not viewed as a cancer. Rather, LCIS serves as a "marker" for subsequent development of invasive cancer. It has the ability to convert in to invasive ductal form of breast cancer, rather than the invasive lobular type. Women have an increased risk of developing this invasive cancer for approximately two decades after diagnosis of LCIS 8.8% of the breast carcinoma subjects have been are observed to have lobular carcinoma type in the present investigation. LCIS generally lacks specific clinical or mammographic signs, and occurs more frequently in premenopausal women. By definition, these cancer cells are confined to the mammary lobules without microsopic evidence of invasion (Morrow and Schnitt, 2000). LCIS is characterized microscopically by a solid mass of small cells. The cells have a low proliferative rate and are typically oestrogen receptor positive, rarely over express the HER-2/neu oncogene and there is a reported risk of disease occurring in both breasts.

Lobular carcinoma of the breast, otherwise called infiltrating lobular carcinoma, arises from the lobular and terminal duct epithelium and accounts for approximately 5-10% of all breast cancers (Watson, 2001). Invasive lobular carcinomas are characterised by greater proportion of multicentricity in the same or the opposite breast. The lesions tend to have ill-defined margins, and occasionally the only evidence is subtle thickening or induration. Patients with infiltrating lobular carcinoma are especially prone to have bilateral carcinoma. Invasive lobular carcinoma has a similar prognosis to infiltrating ductal carcinoma. Lobular carcinoma is less common than the carcinoma of duct origin. Some invasive lobular carcinoma may accumulate considerable cytoplasmic mucus, resembling the singlet ring cells of poorly differentiated carcinoma of gastrointestinal tract origin (Gad and Azzopardi, 1975). Patients who have had lobular carcinoma *in situ* diagnosed by breast biopsy, have an approximately 20% risk of subsequently developing infiltrating carcinoma of the breast.

The initial description of ILC (invasive lobular carcinoma) presented by Foote and Stewart in the 1940s was that of classic infiltrating lobular carcinoma and most clinical pathology studies published afterward followed their definition. In the 1970s, the variant histologic patterns were recognised, and subsequent series of ILC included these subtypes. A trabecular variant, consists of classic lobular carcinoma cells infiltrating in trabeculae one or more cells in thickness. This particular variant has not gained wide acceptance because of its significant morphological overlap with the classic and mixed patterns. Most ILC's are not composed completely of any one histologic pattern. The proportion of a single histologic pattern required for classification as a particular histologic subtype has varied from 70% to 80% (Tavassoli, 1992 and Rosen, 1997). More recently, a pleomorphic variant of ILC has been described. This variant exhibits the classic pattern of infiltration, but it is composed of cells with pleomorphic nuclei and often relatively abundant eosinophilic cytoplasm. It has been demonstrated to behave more aggressively than classic ILC (Eusebi *et al.,* 1992., Weidner and Semple, 1992 and Bentz *et al.,* 1998). The reported incidence of variant subtypes has varied with the histologic criteria employed, but it ranges from 23-70% (Dicostanzo *et al.,* 1990 and Rosen, 1997).

Tubular carcinoma is typically present as a well-differentiated carcinoma. The frequency of axillary lymph node metastases is approximately 10%, lower than that of ductal carcinoma. The prognosis is considerably better than for invasive ductal carcinoma. This neoplasm is defined by a tubular growth pattern and low cytological grade. Its overall incidence among breast cancers has been reported as about 2%. However, the incidence is about 9% of tumours are 1 cm or less in diameter and 8% are mammogram-detected cancers (Rosen *et al.,* 1981). In the present investigation, 22.55% of the population under study showed infiltrating tubular carcinoma as per histology. Most authors recognize pure and mixed variants of tubular carcinoma and mixed tubular carcinomas are those in which a major tubular component coexists with ordinary ductal carcinoma. Occasionally, a tubular pattern coexists with a classic lobular carcinoma and have been termed tubulolobular carcinomas. Most tubular carcinomas are not more than 1 cm in diameter. This suggests slow growth, evolution to ordinary ductal carcinoma, or both. The gross appearance is that of a stellate or relatively well-circumscribed mass indistinguishable from ordinary ductal carcinoma. Small tumour may produce only stellate retraction, similar to that of benign radial sclerosing lesions. It has been suggested that some tubular carcinomas may arise from benign radial sclerosing lesions, but there is lack of evidence. Microscopically tubular structures, some of which are characteristically sharpe, angular, snouts compose most of the neoplasm. Some authors require 100% tubular growth pattern for a diagnosis of pure tubular carcinoma, and 75% to greater than 95% tubular growth pattern for a diagnosis of mixed tubular carcinoma (Tavassoli, 1992; Norris, 2001 and Deos, 1992). Others accept over 75% or 80% of tubular growth pattern for a diagnosis of pure tubular carcinoma, (Winchester *et al* ., 1996) and 50% to 75% tubular growth pattern for a diagnosis of mixed tubular carcinoma, (McDivitt *et al.,* 1982., Elson *et al.,* 1993) since indolent behaviour seems to characterize those tumours in which 75% or more of the neoplasm demonstrates a tubular growth pattern.

First described by Ewing in 1940, medullary carcinoma is said to account for 5% to 7% of breast cancers. Strict application of all the morphologic criteria for diagnosis of medullary carcinoma is of paramount importance for identification of patients likely to benefit from the better prognosis of this tumour type. Medullary carcinoma of the breast was found in 7.7% of the subjects taken for pathological examination in the present investigation. Patients with medullary carcinoma tend to be younger than those with other types of breast cancer and a prominent lymphocyte infiltrate is the hallmark of the disease. The prognosis is generally better than for invasive ductal cancer. The median size of medullary carcinoma is 2 to 3 cm, not significantly different from ordinary ductal carcinomas reported concurrently. The importance of strict histological criteria for diagnosis is stressed by most authors (Bloom *et al.,* 1970 ; Maier *et al.,* 1977; Rapin *et al.,* 1988; Elston and Ellis, 1991; Gaffey *et al.,* 1995; Wargotz Silverberg, 1988; and Ridolfi *et al.,* 1999). The tumour is grossly well circumscribed, nodular or lobular and soft or only moderately firm, and it may exhibit area of hemorrhage, necrosis, or cystic degeneration. The characteristic histologic features are a round and pushing tumour border and a sheet like growth pattern with indistinctly delineated cells, referred to as a syncytial growth pattern. The sheets of tumour cells are sharply defined at the perimeter of the tumour where they are separated from adjacent breast tissue by fibrous tissue and a lymphocytic and plasma cell infiltrate. A similar infiltrate is found within the tumor. The varied growth patterns of usual ductal carcinoma, such as trabecular, glandular, alveolar, and papillary patterns, are absent or minimal. Medullary carcinoma cells are large and highly pleomorphic and show frequent mitosis and frequent necrosis and there may be squamous metaplasia as well. A sparse *in situ* component with similar histology may be found in ducts and lobules at the periphery of the tumor. In the majority of cases, an *in situ* component is not seen. Inflammatory carcinoma of breast is defined by its clinical features and its mode of spread within the breast, and not by architectural pattern or cytology (Lee and Tannenbaum, 1924). Inflammatory breast cancer is a rare and aggressive form of breast cancer, accounting for 1-4% of breast cancers. This cancer is not necessarily a histological subtype but rather a type of clinical change that occurs as a result of breast cancer cells blocking lymph channels in the breast (Watson, 2001). An exceptional series from Tunisia recorded a 28% incidence (Costa *et al.,* 1982). This form of the disease is characterized by diffuse skin oedema, skin and breast redness, and firmness of the underlying tissue without a palpable mass. The clinical manifestation is primarily due to the tumour forming emboli in the dermal lymph channels, with associated engorgement of superficial capillaries. Inflammatory breast cancer carries a poor prognosis. Inflammatory carcinoma and mucinous carcinoma of the breast were found to have equal incidence, that is, 8.25% each of the total population (180) taken for the present study. The breast tissue involved in mucinous carcinoma is usually a small cluster of epithelial cells, constituting mucinous or colloid carcinoma. It is a less common variant of breast carcinoma. Most probably, this type of tumour occurs in older age group. Paget's disease of the nipple is a rare form of breast cancer that is characterized clinically by eczematous changes of the nipple. It is believed that Paget's disease represents the migration of malignant cells from adjacent mammary ducts in the nipple. The prognosis for patients with paget's disease appears to be similar to that of women with other types of breast carcinoma. The reasons behind these different patterns of spread are unclear, however, they appear to be unrelated to histological characteristics or pathological grade of the primary tumour (Harri, 2000). In the present investigation, Pagets disease of the breast was found to be least occurring of just 5.5% in the population of breast carcinoma subjects. In order to assess the prognostic value of family history (FH) of malignancies in patients afflicted with breast cancer, Atri *et al.,* (2002) examined FH and histopathologic characteristics of 542 Iranian primary breast cancer. Accordingly the younger the age of the relatives diagnosed with cancer, the higher the stage of the probands themselves. The family history of breast cancer does not have any significant correlation with proven prognostic factors but a history of breast cancer among relatives at or before the age of 36 is associated with more aggressive tumour. Evidently the current investigation also reveals that the none of the subjects (180) with breast carcinoma had a family history of breast cancer.

CONCLUSION

In order to assess the prognostic value of family history (FH) of malignancies in patients afflicted with breast cancer. Accordingly the younger the age of the relatives diagnosed

with cancer, the higher the stage of the probands themselves. The family history of breast cancer does not have any significant correlation with proven prognostic factors but a history of breast cancer among relatives at or before the age of 36 is associated with more aggressive tumour. Evidently the current investigation also reveals that the none of the subjects (180) with breast carcinoma had a family history of breast cancer.

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