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**Tumor Markers and Their relation to Structure of
Normal and Pathological
Breast Tissue**

Thesis

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of M.D. in Anatomy*

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Arabic Summary

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INTRODUCTION AND AIM OF THE WORK

Pathological lesions of the breast, namely fibroadenoma and cancer breast are widely prevalent world wide. Histological examination of these conditions is the most reliable method for diagnosis. However tumor markers, although not diagnostic, provide information that may contribute to the diagnostic process, and the management of cancer patients "both monitoring and prognosis" (*Agentis , 2003*).

Trials to correlate between fine needle aspiration (FNA) cytology and tumor marker levels in benign breast disease were also reported (*Swiatatecka , 2004*).

Moreover, (*Anderson, 2002*) found a relatively small number of cells in the human mammary gland that express receptors for estrogen and progesterone which are considered as valuable tumor markers. He suggested that, in these cases the risk of breast cancer was significant.

The identification of prognostic tumor markers is a main strategy for planning treatment and predicting outcome of patients with various malignancies (***Tobias et al., 1985***)

And in general, presence of hormone receptor as estrogen and progesterone predicts the likelihood of response to hormone based therapy (***Carton et al., 2006***)

Nowadays a large number of serum markers exist for breast cancer, of these markers CEA, CA15-3 are most commonly used (***Molina et al ., 1999***)

A tumor marker HER-2/neu, is known to be the most useful molecular prognostic factor in aggressive breast cancer cases (***Eissa et al .,2002***)

Ki-67 is a marker of proliferation, absent only in resting cells, it gives idea about the rate at which the cells within a tumor are growing (***Fabian et al .,2003***)

Each tumor marker has a variable profile of usefulness for screening, determining diagnosis and prognosis, response to therapy and monitoring for cancer recurrence (***Malakasian et al ., 1988***)

Aim of work:

So The aim of the present study was to correlate the structure of the normal, fibroadenomatous and cancerous breast tissues with the expression of some tumor markers e.g. CEA, CA 15-3, estrogen receptors, progesterone receptors, HER-2\neu, and Ki-67, in an attempt to confirm the value of each marker in relation to pathological conditions of the tumor, and also to compare its prevalence in breast diseases within the normal and non malignant condition.

Chapter I

Normal Breast

Histological Structure of Breast “Mammary gland”:

In general the female mammary gland is formed of connective tissue stroma and a parenchyma of alveoli and ducts (*Alan and James, 1992*).

The parenchyma or glandular system is formed of about 20 compound alveolar glands, which open individually on a surface elevation known as the nipple; the gland system is formed of 15-25 lobule of compound tubuloalveolar type of glandular epithelium. Its function is to secrete milk that differs in composition from blood and intracellular fluid. Glands always arise from covering epithelia by means of cell proliferation, compound glands have ducts that branch repeatedly (*Junqueira et al.,1995*).

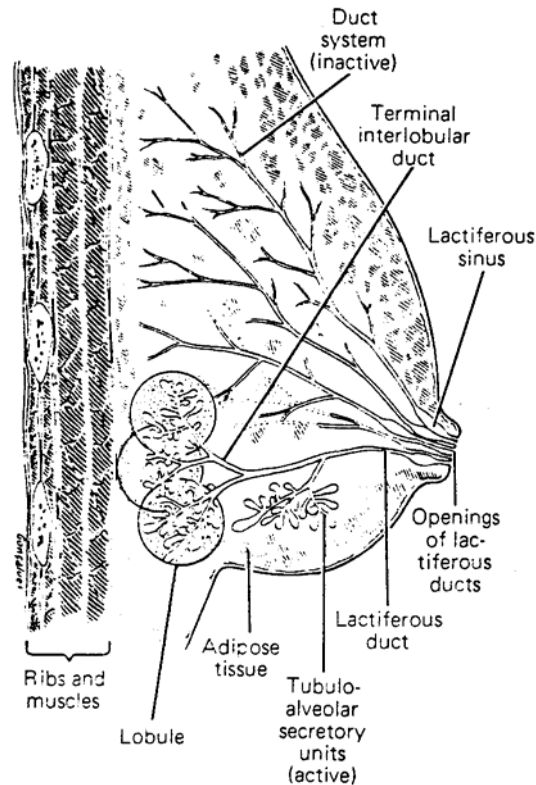


Diagram (1). : Schematic drawing of female breast showing the mammary glands with ducts that open into the nipple. The outlines of the lobules do not exist in vivo but are shown for instructional purposes. The stippling indicates the loose intralobular connective tissue (Junqueira et al.,1995).

The lobe of glandular tissue is formed of varying number of ducts and lobules. Each lobule connects to a lactiferous duct that converges to form a lactiferous sinus or milk chamber. These sinuses empty into the nipple

which is surrounded by a pigmented area, the areola. The latter is lubricated by the secretion of sebaceous glands (*Osborne et al., 2000*).

Each lobe is a system of branching ducts which penetrates deep into fibroadipose tissue of the breast. Each duct is lined by columnar or cuboidal epithelium, which is a continuous surface layer of epithelial cells. These cells have oval nuclei. Another outer discontinuous layer of myoepithelial cells is seen which have clear cytoplasm. Each duct is surrounded by loose fibrocollagenous support tissue containing rich capillary network. Elastic fibers are present. The duct system terminates in clusters of blind-ending terminal ducts, each cluster and its feeding duct comprises a mammary lobule which is ovoid in shape. The terminal ducts are embedded into loose fibrous support tissue which is rich in capillaries and also contains few lymphocytes. This tissue is surrounded by a more dense fibrocollagenous support tissue intermingled with adipose tissue (*Hartmann, 2002*).

Breast Development and Age Changes:

In fetal life from the fifth to seventh week of the pregnancy the fetus develops a mammary ridge, which runs from the axilla to the inguinal region (**Black et al., 1998**).

In sixth gestational week, the ridge becomes depressed into the pectoral region, forming the primary breast buds.

At birth, the main lactiferous ducts are present as well as the nipple and areola (**Hartmann, 2002**).

The anatomical description of the breast is not fully developed at birth (**Moore, 1993**).

During **puberty** each menstrual cycle stimulates proliferation and active growth of breast tissue. The breast development is concerned with growth of the ductile system and the formation of ductile buds (**Black et al., 1998**).

The surrounding fat pad, also development, giving the breast size and shape but this is not related to the functional capacity of the breast (**Riordan and Auerback, 1999**).

Humans appear to be the only mammals that experience breast growth during puberty (**Hartmann, 2002**).

However - small alternation in histological structure of these mammary glands occur during the **menstrual cycles**, this is proliferation of cells of the ducts at about the time of ovulation. These changes coincide with the time at which circulating estrogen is at its peak. Greater hydration of connective tissue in premenstrual phase produces breast enlargement. The lactiferous sinuses are lined by stratified squamous epithelium at their external openings.(*Junqueira et al., 1995*).

This epithelium very quickly changes to stratified columnar or cuboidal epithelium at the time of beginning of the activity of breast tissue “**pregnancy and lactation**”. The intralobular connective tissue surrounding the alveoli contains lymphocytes and plasma cells the plasma cell population increases significantly toward the end of pregnancy;confer passive immunity to the newborn(*Junqueira et al., 1995*).

Breast changes in size and shape, during and after lactation, this involves two distinct processes: organogenesis (ducts and lobular growth) and lactogenesis (milk production) .
(*Black et al., 1998*).