

# Study of Cytomorphology Patterns of Breast Lesions and their Correlation with Thyroid Profile Over a Period of One and Half Years in a Tertiary Care Centre of Malwa Region

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## ABSTRACT

**Introduction:** Fine needle aspiration cytology (FNAC) has become an increasingly popular technique for assessment and initial diagnosis of breast lumps as it is the least invasive technique for obtaining a cytological diagnosis and is of high accuracy if done by experienced personnel. Thyroid hormone receptors affect both the normal breast cell differentiation and breast cancer cell proliferation, with effects of thyroid hormones similar to those caused by estrogens. Relationship between thyroid disease, such as nodular hyperplasia, hyperthyroidism and thyroid cancer, with breast cancer was demonstrated in several studies. In the present study, we have evaluated the correlation of cytomorphological diagnosis of breast lesions with thyroid profile.

**Material and Methods:** Total of 80 cases were included in the study and all necessary statistical analysis was done including the percentages, means, standard deviations, ranges and p values.

**Results:** Triiodothyronine (T3) and Tetraiodothyronine (T4) levels were statically significantly lower among participants with malignant breast lesions as compared to benign breast lesions. ( $p < 0.01$ ). However mean values of both were normal in both these groups. Thyroid stimulating hormone (TSH) levels among study participants with malignant breast lesions were statistically higher than those of benign breast lesions. However mean in both these groups was within normal range.

**Conclusion:** No significant correlation between thyroid profile and breast lesions was established. But the effect of thyroid hormone on breast cancer clearly requires further research.

**Keywords:** Benign, Malignant, Cancer, Hyperthyroidism

Growth and development of breast requires the coordinated action of several hormones such as prolactin, estrogen, progesterone, adrenal steroids, insulin, growth and thyroid hormones. Estrogen is considered to be potent mitogen for normal mammary gland, whereas thyroid hormone stimulates lobular development. Almost every form of thyroid disease including hyperthyroidism has been identified in association with breast cancer.<sup>6</sup>

Thyroid hormone receptors also affect both the normal breast cell differentiation and breast cancer cell proliferation, with effects of thyroid hormones similar to those caused by estrogens. Relationship between thyroid disease, such as nodular hyperplasia, hyperthyroidism and thyroid cancer, with breast cancer was demonstrated in several studies. In contrast hypothyroidism due to Hashimoto's thyroiditis was documented as a protective factor against breast cancer.<sup>7</sup>

A study conducted by P.P Saravia et al concluded that hyperthyroidism was the only statistically significant thyroid alteration found in our breast cancer population. This, together with the fact that the majority of patients with subclinical hyperthyroidism were postmenopausal, showed that the normal ratio between thyroid hormones and estrogen concentration was enhanced in these patients due to increase in serum thyroid hormone and reduced estrogen concentration. So they speculated that subclinical hyperthyroidism in post menopausal patients contributed to breast tumor growth.<sup>7</sup> Still further studies in this field are warranted to find a correlation of thyroid profile in benign and malignant breast lesions. This will enable the identification of the high risk women who could benefit from heightened vigilance and, ultimately, clear diagnosis and early treatment.

## INTRODUCTION

Breast lumps are very common, most of the lumps are benign, and prevalence of malignant lumps increases with age.<sup>1</sup> Breast cancer is one of the commonest cancers amongst women in India<sup>3</sup> with approximately 75,000 new cases estimated to occur every year.<sup>2</sup>

In patients presenting with a breast lump, the diagnosis should be made by clinical assessment, radiological imaging and tissue sample taken either for cytology or histology analysis: the so called TRIPLE TEST.<sup>3</sup> There are several competing approaches to breast biopsy such as surgical excision biopsy, core needle biopsy and biopsy by aspiration or Fine-needle aspiration (FNA).<sup>4</sup> FNAC has become an increasingly popular technique for assessment of breast lumps as it is the least invasive technique for obtaining a cytological diagnosis and is of high accuracy if done by experienced personnel.<sup>5</sup>

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So in the present study have evaluated the correlation of cytomorphological diagnosis of breast lesions with thyroid profile in Adesh Institute of Medical Sciences and Research, Bathinda.

## MATERIAL AND METHODS

The study was done in the Department of Pathology, AIMSR Bathinda, over a period of one and a half year, i.e. 1<sup>st</sup> January 2017 to 30<sup>th</sup> June 2018, on the cases of breast lumps on which Fine Needle Aspiration Cytology was done.

**Time frame:** All the Fine Needle Aspiration Cytology cases received during the period of 1 year and 6 months, i.e. 1<sup>st</sup> January 2017 to 30<sup>th</sup> June 2018, were considered, satisfying the inclusion and exclusion criteria for prospective cases.

**Inclusions:** All females with breast lump undergoing Fine Needle Aspiration Cytology for cytomorphological diagnosis irrespective of their age, in whom thyroid profile was done.

### Exclusions

- Male patients with breast lumps undergoing FNAC for diagnosis.
- All female patients who had undergone Fine Needle Aspiration Cytology for breast lump but didn't give consent for thyroid profile.

**Population/Participants:** Members of the study group were selected when they presented to Department of Pathology with breast lump for cytomorphological studies applying inclusion and exclusion criteria and after obtaining their informed consent.

**Sample Size:** All the female patients reported as breast lump to cytology section of AIMSR for cytomorphological studies.

### Method

Female patients presenting to the Department of Pathology for FNAC of palpable breast lesions of all age groups were taken for the study. Detailed history and clinical examination was done. The Fine Needle Aspiration Cytology was done in the Department of Pathology and final diagnosis was made with the observations of two pathologists. Then the blood sample of patient was collected in the plain vial and thyroid hormonal assay (T3, T4, and TSH) was done by immunofluorescent technique by Tosoh –Japan Automated analyser (AIA-360). Normal reference ranges of T3, T4 and TSH according to manual of Tosoh- Japan Automated Analyzer (AIA-360).

- T3 - 0.60-1.80 ng/dl
- T4 - 4.5-10.9 µh/dl
- TSH - 0.39-4.30 µIU/mL

All the relevant data was recorded on Microsoft excel sheet including age, cytological diagnosis, BMI, T3, T4 and TSH values.

## STATISTICAL ANALYSIS

All necessary statistical analysis was done including the percentages, means, standard deviations, ranges and p values.

## RESULTS

Various observations and results are described as following:

## Cytological diagnosis

Out of total 80 cases studied, 65 were cytologically benign

<b>Benign lesions – 65 (81.25%)</b>	
<b>Benign epithelial lesions - 36 (45%)</b>	
Fibroadenoma	22
Phyllodes	01
Other Proliferative lesions	13
<b>Benign proliferative lesions with atypia – 01 (1.25%)</b>	
<b>Benign non proliferative lesions – 22 (27.5%)</b>	
Fibrocystic disease	20
Galactocele	01
Lactating breast	01
<b>Benign inflammatory lesions - 06 (7.5%)</b>	
Breast Abscess	02
Granulomatous lesions	02
Duct Ectasia	01
Resolving Acute Mastitis	01
<b>Carcinomas - 15 (18.75%)</b>	

**Table-1:** Details of cytological diagnosis

<b>T3</b>	<b>Benign</b>		<b>Malignant</b>	
	<b>No of cases</b>	<b>% of cases</b>	<b>No of cases</b>	<b>% of cases</b>
< 0.6	03	4.6%	05	33.3%
0.6-1.2	19	29.2%	05	33.3%
1.2-1.8	26	40%	04	26.7%
>1.8	17	26.2%	01	6.7%
Total	65	100%	15	100%

**Table-2:** Showing T3 levels of benign and malignant cases

<b>T4</b>	<b>Benign</b>		<b>Malignant</b>	
	<b>No of cases</b>	<b>% of cases</b>	<b>No of cases</b>	<b>% of cases</b>
< 4.5	05	7.7%	09	60.0%
4.5 -7	25	38.5%	04	26.7%
7-10.9	19	29.2%	02	13.3%
>10.9	16	24.6%	00	0.0%
Total	65	100%	15	100%

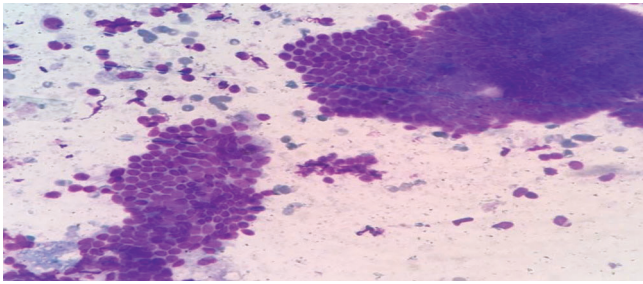
**Table-3:** Showing T4 levels of benign and malignant cases

<b>TSH</b>	<b>Benign</b>		<b>Malignant</b>	
	<b>No of cases</b>	<b>% of cases</b>	<b>No of cases</b>	<b>% of cases</b>
< 0.39	16	24.6%	01	6.7%
0.39 – 2.5	18	27.7%	03	20.0%
2.5 – 4.3	27	41.5%	02	13.3%
>4.3	04	6.2%	09	60%
Total	65	100%	15	100%

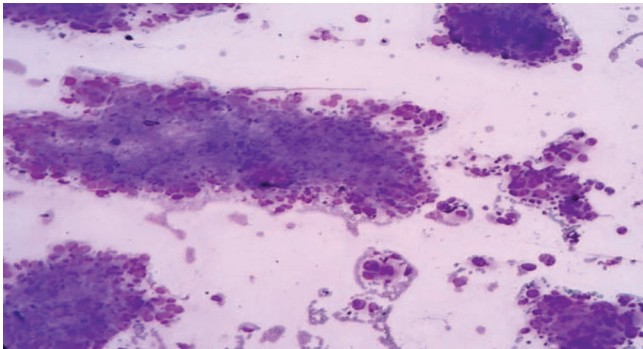
**Table-4:** Showing TSH levels of benign and malignant cases

	<b>Benign</b>		<b>Malignant</b>		<b>p-value</b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>	
T3	1.36	0.51	0.89	0.32	0.003
T4	7.91	3.27	5.13	2.04	0.006
TSH	2.34	1.64	3.83	1.70	0.005

**Table-5:** Statistical correlation of thyroid profile with respect to benign and malignant lesions



**Figure-1:** Fibroadenoma-Photomicrograph showing tightly cohesive clusters of benign ductal epithelial and myoepithelial cells along benign bare bipolar nuclei



**Figure-2:** Carcinoma breast- Smears studied show highly cellular smear comprising of loosely cohesive clusters of malignant cells.

with or without focal atypia and 15 were outrightly malignant (carcinomas) (table-1).

Out of total 65 benign lesions, most common were benign epithelial lesions (36/65), followed by benign non proliferative epithelial lesions (22/65), benign inflammatory lesions (6/65) and 1 benign proliferative lesion with atypia. Fibroadenoma was the most common lesion (27.5%) of total followed by fibrocystic disease 25% (figure-1,2).

**Correlation of T3 levels with benign and malignant lesions**  
The normal range of T3 levels is from 0.60 – 1.80ng/dl. Maximum number of benign cases had T3 levels in the range of 1.2 -1.8 ng/dl, i.e, 26 (40%) followed by 17 cases (26.2%) having T3- 0.6 -1.8 ng/dl. The maximum number of malignant cases had T3 levels in the range of < 0.6 and 0.6-1.2 ng/dl (5 cases each -33.3%) (table-2). The mean of T3 levels of benign lesions was 1.36 ng/dl and mean of T3 levels of malignant lesions was 0.89 ng/dl, both having mean in the euthyroid range.

**Correlation of T4 levels with benign and malignant lesions**  
The normal range of T4 levels is from 7.1 – 10.9 µg/dl. Maximum number of benign cases had T4 levels in the range of 4.5 - 7 µg/dl, i.e., 25 (38.5%) followed by 19 cases (29.2%) having T4 levels - 7 -10.9 µg/dl. The maximum number of malignant cases had T4 levels in the range of < 4.5 µg/dl i.e. 9 cases (60%). The mean of T4 levels of benign lesions was 7.91µg/dl and mean of T4 levels of malignant lesions was 5.13µg/dl, both having mean in the euthyroid range (table-3).

#### **Co-relation of TSH levels with benign and malignant lesions**

The normal range of TSH levels is from 0.39 – 4.30 µIU/

mL. Maximum number of benign cases had TSH levels in the range of 2.5 – 4.3 µIU/mL, i.e., 27 (41.5%) followed by 18 cases (29.2%) having TSH- 0.39 -2.5 µIU/mL. The maximum number of malignant cases had TSH levels in the range of > 4.3 µIU/mL i.e. 9 cases (60%). The mean of TSH levels of benign lesions was 2.34 µIU/mL and mean of TSH levels of malignant lesions was 3.83 µIU/mL., both in normal range (table-4).

T3 and T4 levels were statically significantly lower among participants with malignant breast lesions as compared to benign breast lesions ( $p < 0.01$ ). However mean values of T3 and T4 levels were normal in both these groups (table-5). TSH levels among study participants with malignant breast lesions were statically higher than those of benign breast lesions. However mean of TSH levels in both these groups was within normal range.

#### **DISCUSSION**

In our study 65 out of 80 cases were benign and 15 were malignant. Out of benign lesions majority were benign epithelial lesions (36 out of 65), fibroadenoma (33.8%) being the commonest benign lesion. Fibrocystic disease was second most common benign lesion (30.7%).

Shirish S et al<sup>8</sup> did a similar study on 902 cases and concluded that maximum cases were of fibroadenoma (43%) and fibrocystic disease (19.6%).

Prakash H Muddegowda et al<sup>9</sup>, categorized lesions on FNAC as benign, atypical, suspicious and malignant in total of 225 cases. Maximum number of cases were falling in benign (146 cases,64%) category followed by malignant (63 cases,28%). In our study also maximum number of cases fall into benign category (81%).

In some theories, it has been stated that in development of breast lobules, thyroid hormone plays important role. So in our study we have attempted to find the correlation between breast lesions and thyroid profile.

In a study profile of thyroid hormone in breast cancer patients by P.P Saraiva et al<sup>7</sup>, it is mentioned that the hyperthyroidism was present in breast cancer patients. So they also stated that there is subclinical link between breast cancer and subclinical hyperthyroidism. But in our study T3 and T4 levels were in lower range of normal in malignant breast lesions.

Chien Hsiang Weng et al<sup>10</sup> evaluated whether hyperthyroidism or hypothyroidism was associated with breast lesions. They took women with breast lesions with mean of 53years. They concluded that Asian women under the age of 55 years of age with history of hyperthyroidism have significant increased risk of breast cancer regardless of treatment but they also mentioned that hypothyroidism is also associated with increased risk of breast lesions. In this study correlation of breast lesions with hyperthyroidism or hypothyroidism was not clear. In our study also, correlation of thyroid profile with breast lesions has null hypothesis, neither hyperthyroidism or hypothyroidism was associated with breast lesions. Rather patients with malignant lesions had T3, T4 levels on lower side but in normal range.

Similar results were stated in a study of “The thyroid, iodine



and breast cancer by” Peter PA Smyth<sup>11</sup>, in which there was no significant correlation between thyroid hormone profile and development of breast lesions.

Thus in our study, no significant correlation between thyroid profile and breast lesions was established. Both benign and malignant lesions had mean T3, T4 and TSH in normal range. However contrary to various studies, our study had T3 and T4 in low normal range which may be due to sedentary lifestyle and other confounding factors like obesity.

Thus it is concluded that even though in this present study results of thyroid profile on breast lesions is non contributory, effect of thyroid hormone on breast cancer clearly requires further research. However since some studies suggest a correlation between hyperthyroidism and breast cancer it is advised that women with an overactive thyroid should stay cautious and follow routine breast cancer screening programmes.

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