

# Finding the Correlation of Thyroid Disorders and Menopausal Relationship with Benign Breast Diseases

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**Abstract:** *Benign breast diseases can occur at any time, during the life span of women. Thyroid hormones play an important role in regulating the growth and metabolism. This study aims at identifying the correlation of Thyroid disorders and relationship of menopausal status with benign breast diseases. This study also describes the risk factor and their clinical presentation. It is a prospective study. A total 202 patients screened & grouped into case group (n=102) which consists subjects with BBD and control group (n=100). Statistical analysis done using chi square test in graph pad prism. A total of 202 patients were taken them as average mean age in controls found to be 41 and 39 in BBD cases. The BMI status was found to be clinically significance (p value-0.0525) between 2 groups. According to our study the age of menarche found at less than 13 years. A total no of premenopausal women in controls is 38 and in BBD is 20 and no of postmenopausal women in controls is 62 and in BBD is 82. The accelerated risk of thyroid disorders in breast diseases as evidence suggests can attributed as a risk factor, but actual relation and possible researches in field of breast cancer prevention, treatment change are to be explored.*

**Keywords:** Thyroid hormones, Benign breast diseases, Menopause status

## 1. Introduction

In human beings thyroid hormones play an important role in regulating the growth, differentiation and metabolism. They maintain normal development of breast by stimulating alveolar budding and ductal branching<sup>[1-4]</sup>.

Together with the thyroid, breast tissue shares the ability to take up circulated iodide and sodium /iodide symporter is expressed in lactation and in mammary tumors<sup>[5-7]</sup>. The mammary glands have a trapping system for iodine similar to that of thyroid gland<sup>[8]</sup>.

Menopause does not cause cancer, but the risk of developing cancer increases as women ages. A women who has no menstrual flow since 12 months are considered as post menopausal women and the rest are pre menopausal<sup>[9]</sup>. Breast symptoms are more common in post menopausal period, Especially when taking hormonal therapy<sup>[10]</sup>. Benign breast diseases can occur at any time, during the life span of women<sup>[11]</sup>. Hormones and growth factors acting on epithelial and stromal elements right from onset of puberty to menopause cause many morphological changes leading to aberration in normal development and involution (ANDI) Inflicting majority of benign breast illnesses<sup>[12]</sup>.

This study aims at identifying the correlation of Thyroid disorders and relationship of menopausal status with benign breast diseases. This study also describes the risk factor and their clinical presentation.

## 2. Literature Survey

Mitra I, et al, 1976 conducted study on “An epidemiological study of breast carcinoma” and the study is to conclude most cases of breast lumps are benign but most of these patients are in a state of heightened anxiety until they have undergone specialist assessment, the necessary investigations and eventual reassurance

Cochrane RA, et al, 1997 conducted study on “Evaluation of general practitioner referrals to a specialist breast” and the study concluded that Most cases of breast lumps are benign but most of these patients are in a state of heightened anxiety until they have undergone specialist assessment, the necessary investigations and eventual reassurance

Lai L, et al, 2002 Conducted study on “Role of steroid hormones and growth factors in breast carcinoma.” and the study concluded that Growing and developing breasts require the coordinated action of several hormones such as Estrogen, Progesterone, Thyroid hormones, Adrenal steroids, Insulin and Prolactin.

## 3. Methodology

This study was conducted after having permission from institutional ethics committee, Balaji Institute of pharmaceutical sciences, Warangal India. It is a prospective study conducted at Sai Shree Hospitals, Warangal, Telangana, India for a period of 8 months.

Female subjects bearing age group >14yrs are included in the study and their menopausal status is recorded. Subjects who are newly diagnosed with Benign breast diseases

(BBD) are also included in this study. Females who are <14yrs of age, Men and subjects who are already undergoing breast tumour treatment are excluded from this study.

A total 202 patients were screened and grouped into case group (n=102) which consists of subjects with BBD and control group (n=100). Depending upon their pre and post menopausal status their classified and complete thyroid profile was studied to find the association between them with benign breast diseases. Statistical analysis was done using chi square test in graph pad prism.

**4. Results**

A total of 202 patients were taken in them the average mean age in controls was found to be 41 and 39 in benign breast disease cases. The BMI status was found to be clinically significance(p value-0.0525) between the 2 groups. According to our study the age of menarche was found at less than 13 years.The total no of premenopausal women in controls is 38 and in Benign breast disease is 20 and number of postmenopausal women in controls is 62 and in BBD is 82.All the details were enlisted in table 1.

**Table 1:** Demographic Details and Risk Factors In Benign Breast Diseases

Groups/Data	Controls	Benign breast Diseases	P-value
Total number	100	102	N.D
Age (mean)	41	39	N.D
BMI			
<25	36	24	0.0525
>25	64	78	
Age of menarche			
<13	45	65	0.0258
14-15	38	24	
>15	17	13	
Menopausal status			
Pre menopausal	38	20	0.0039
Post menopausal	62	82	
Marital status			
Yes	74	87	0.046
No	26	15	
History of pregnancy			
Yes	63	77	0.0543
No	37	25	
Age of 1 <sup>st</sup> birth			
<20	47	69	0.0122
20-25	36	22	
>25	17	11	
Use of OCPs			
Yes	56	56	0.8753
No	44	46	

**Table 2:** Frequency of Thyroid Disorders in Control and Benign Breast Diseases Cases

Thyroid Disorder	Benign Breast Diseases Cases (n=102)	Control (n=100)	P-Value
Hyperthyroidism	20	15	<0.0001
Hypothyroidism	60	25	
Hashimotos thyroiditis	10	2	
Goiter	4	0	
Normal	8	58	

The number of people suffering with hyperthyroidism in BBD are 20 and in controls are 15, The patients suffering with hypothyroidism in benign breast diseases are 60 and in controls are 25, The patients suffering with hashimotos thyroiditid in BBD are 10 and controls are 2, The patients suffering with goiter in BBD are 4 and the controls are 0, The normal patients in BBD are 8, and controls are 58.

**Table 3:** Comparison of Serum Thyroid Hormones (T3, T4, TSH) in Benign Breast Diseases Cases and Controls

	Benign breast diseases cases (mean)	Controls (mean)	P-value
T <sub>3</sub> (80-200ng/dl)	48.22	72.82	0.1854
T <sub>4</sub> (5.1-14.1mcg/dl)	4.89	5.26	
TSH(0.27-4.2IU/ml)	15.20	10.80	

The mean values of T3 in BBD are 48.22 and in controls are 72.82, the mean values of T4 in BBD are 4.89 and in controls are 5.26, The mean values of TSH in BBD are 15.20 and in controls are 10.80.

**5. Discussion**

Some previous studies stated that benign breast diseases occurs in an older women and its incidence increases with age, and it is rare below the age of 20 years<sup>[13, 14, 15]</sup> In this study mostly benign breast diseases were occurs between the third and fifth decade of their life.

However the Thyroid hormone profile may be altered in various disorders which include hypothyroidism, hyperthyroidism. Our findings stated that hypothyroidism is one of the risk factors similar to the reports of Mitra et al., whose reports were hypothyroidism is the one suspected to be a risk factor in breast cancer.<sup>[16]</sup>

Thyroid hormones are important regulators of growth, development and metabolism in higher animals and humans.<sup>[2]</sup>The possible interaction between thyroid gland and breast tissue are based on the common property of the mammary and thyroid epithelial cell to concentrate iodine by a membrane active transport mechanism as well as on the presence of TSH receptors in mammary gland.<sup>[17]</sup>

In our study we found the low levels T4 and T3 further substantiates that there is no association between hypothyroidism and breast diseases but the association was seen in Goldman et al, who found frequently observed finding when thyroid disease and breast disease<sup>[18]</sup>

Most of the patients, both pre-and post-menopausal patients had dense breast tissue. Dense breast tissue means there is more gland tissue and less fatty tissue that is associated with epithelial proliferation and stromal fibrosis<sup>[19, 20]</sup> The relation between these histological features and risk of breast cancer may be explained by the known actions of growth factors that play an important role in breast development and carcinogenesis. Breast cancers originate in epithelial cells, so greater areas of fibroglandular tissue may reflect a greater number of cells that are at risk of carcinogenesis and/or an increased rate of epithelial proliferation.<sup>[19, 20]</sup> Unfortunately, dense breast tissue can also make it harder for doctors to spot problems on mammograms.<sup>[21, 22]</sup>

S.mahar and S. Chandanwale et al, studies reported that age of patients ranged from 1-76 years, with a median age of 39 and 66. but the median age was lower when compared to studies by Burch et al (1996). Our study reported that age of patients ranged from 13-80 with the median age of 35-55 years which is similar to that of S.mahar et al reports<sup>[23]</sup>

Some of the studies showed higher incidence of breast cancer in patients with thyroid dysfunction compared to healthy controls. Significantly some studies stated that higher levels of T3 and T4 were present in breast cancer patients in comparison to women with benign breast tumors and healthy controls. Thus our work is showing that hypothyroidism (low T3 and T4 levels) is most trigger factor for benign breast diseases which was contradictory to the Nina ditsch et al reports and similar to the reports of Kujipens et al<sup>[24]</sup> showed significantly lower levels of T4 levels in breast cancer patients compared to women without breast cancer.

However, Limanova et al and Jiskra et al showed increased TSH serum levels which is similar to our reports<sup>[25, 26]</sup>

Thyroid nodules are very common occurring in 4% of the population aged between 30 and 60.<sup>[27]</sup> Therefore, surgery as the initial intervention or investigation will have a very low yield. Very few diagnostic tests help differentiate between benign and malignant nodules. Thyroid ultrasound can distinguish solid from cystic lesions but not all cystic lesions are benign.<sup>[28]</sup> Thyroid isotope scans using technetium-99 classify nodules as hot or cold. Hot nodules are functioning and should be benign whereas cold nodules are nonfunctioning and might be malignant. However, fewer than 20% of cold nodules are malignant leading to a high false positive rate. The addition of thallium scans is a newer development but again has high false positive rates. The poor accuracy and high cost of nuclear imaging plus the significant radiation burden it places on patients has led some to suggest that its routine use in investigating the solitary thyroid nodules should be abandoned, while recognizing its value in follow up after a thyroid malignancy.<sup>[29, 30]</sup>

The one area in which thyroid and breast functions overlap is in the uptake and utilization of dietary iodide and there is strong evidence that lack of iodine predisposes to cancer. One of the causes of this geographical variation in the incidence of breast cancer was attributed to iodine intake in diet<sup>[16]</sup> Many studies showed association of thyroid disease with breast cancer<sup>[31]</sup>. Few studies showed prevalence of hypothyroidism in breast cancer patients<sup>[32]</sup> But some other studies failed to get any significant correlation.

The possible correlation between thyroid diseases and breast cancer was based on the existence of common pathophysiological mechanisms in both glands. Thyroid hyperoxidase and lactoperoxidase are immunologically similar enzymes that have been identified in both thyroid and breast tissue<sup>[33, 34]</sup> The incidence of breast diseases in this study was found slightly more in postmenopausal women than in premenopausal women.

Some studies reported that younger age at menarche increased breast cancer risk only in premenopausal women, while some reported increased risk only for postmenopausal women<sup>[35, 36, 37]</sup> In some studies done previously, age at menarche was found to be associated with both pre- and post-menopausal breast cancer while in another studies, it had no association with either pre- or post-menopausal breast cancer<sup>[35, 36, 37]</sup> In this study, early onset of menarche was found to be associated with both pre- and post-menopausal patients. The median age of menarche with a range from 14 to 15 years. Some studies done on Indian women showed that the risk of both premenopausal and postmenopausal breast cancer decreased with delay in the onset of menarche<sup>[38]</sup>

## 6. Conclusion

The accelerated risk of thyroid disorders in breast diseases as the evidence suggests it can be attributed as a risk factor, since most of the patients belonged to low iodine consumption area. But the actual relation and the possible researches in field of breast cancer prevention and treatment change are yet to be explored.

In this work a set of benign breast diseases were examined in pre and postmenopausal women. Our findings showed that a history of thyroid disease was not associated with risk of Breast cancer. However, a history of thyroid disease was associated with a significantly lower frequency of lymph node metastases.

This study shows that menopause does not cause cancer, but the risk of developing cancer increases as a women ages. The risk is greater if a women also began menstruating before age 12.

## 7. Future Scope

Thyroid hormones play an important role in development of breast by stimulating the ductal branching and alveolar budding. Numerous studies in medical literature have reported the evaluation of thyroid hormone importance by indirect methodology-epidemiology, pharmacology etc.. This study is to evaluate the difference between pre- and post-menopausal breast disease women regarding risk factors, nature of disease presentation and management. The study also aims to find out the prevalence of breast diseases, to identify the clinical correlation and thyroid hormone levels. This study explores the assessment of clinical relation of thyroid hormone levels in pre and postmenopausal women with benign breast diseases.

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