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Original Research Article

Analysis of Hormonal Profile in Women with Benign Breast Diseases and Women Without Breast Pathology

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Abstract:

Background: Benign breast diseases (BBDs) represent a heterogeneous group of non-neoplastic conditions affecting women of all ages, often presenting with palpable masses, breast pain, or other clinical symptoms. Despite their prevalence and clinical significance, the underlying hormonal dysregulation in BBDs remains inadequately characterized. Understanding the hormonal profiles associated with BBDs is crucial for elucidating their pathogenesis and informing targeted therapeutic interventions.

Methods: In this cross-sectional study, we enrolled women diagnosed with BBDs (n=106) and age-matched healthy controls (n=97). Hormonal profiling was conducted using automated immunoassay systems to measure serum levels of estrogen, progesterone, prolactin, thyroid-stimulating hormone (TSH), and free thyroxine (T4). Blood samples were collected during the follicular phase of the menstrual cycle or at a consistent time point for postmenopausal women to minimize hormonal variability. Statistical analysis was performed using SPSS version 20.0, using appropriate methods based on the distribution of data.

Results: Our analysis revealed a significant elevation in estrogen levels among women with BBDs compared to healthy controls (mean ± SD: 120.5 ± 65.2 pg/mL vs. 88.3 ± 30.1 pg/mL; $p<0.0001$). Similarly, progesterone levels were markedly higher in the BBD group compared to controls (3.8 ± 3.2 ng/mL vs. 0.9 ± 0.5 ng/mL; $p<0.0001$). However, no statistically significant differences were observed in prolactin (22.3 ± 14.1 ng/mL vs. 26.8 ± 23.9 ng/mL; $p=0.101$), TSH (2.2 ± 1.6 mIU/L vs. 2.4 ± 0.7 mIU/L; $p=0.257$), and free T4 (1.0 ± 0.2 ng/dL vs. 1.1 ± 0.3 ng/dL; $p=1.001$) levels between the two groups.

Conclusion: Our findings suggest a potential role for estrogen and progesterone in the pathogenesis of BBDs, highlighting the importance of hormonal dysregulation in these conditions. Further research is warranted to elucidate the mechanistic underpinnings of hormonal involvement in BBDs and to explore targeted therapeutic strategies aimed at modulating hormonal levels for improved clinical outcomes.

Keywords: Benign breast diseases, Estrogen, Progesterone, Prolactin, Thyroid-stimulating hormone.

Introduction

Benign breast diseases represent a prevalent health concern among women globally, with significant variations in prevalence and incidence rates observed across populations and age groups [1]. Epidemiological studies indicate that up to 50% of women will experience at least one benign breast condition during their lifetime, making these disorders a considerable burden on public health systems [2].

The prevalence of specific benign breast conditions varies, with fibroadenomas, cysts, mastalgia (breast pain), and benign breast masses being among the most commonly encountered entities [3].

The incidence and prevalence of benign breast diseases exhibit distinct patterns across different stages of a woman's life [3]. For instance, fibroadenomas, characterized by the proliferation of glandular and fibrous tissue, are particularly prevalent among women of reproductive age, with peak incidence typically occurring between the ages of 20 and 30 years [4]. In contrast, cysts, fluid-filled sacs within the breast tissue, tend to become more prevalent with advancing age,

particularly during perimenopause and menopause [5].

Hormonal influences play a crucial role in the pathogenesis of benign breast diseases, and epidemiological data support their significant contribution to disease risk and progression [6,7]. Hormonal factors such as estrogen and progesterone levels, menstrual history, reproductive factors, and hormone replacement therapy have been associated with alterations in breast tissue physiology and susceptibility to benign breast conditions [6]. For example, nulliparity, early menarche, late menopause, and the use of exogenous hormones have been linked to an increased risk of benign breast diseases in observational studies [7,8].

Despite the substantial impact of hormonal factors such as prolactin, and thyroid profile on benign breast diseases, the precise mechanisms underlying their association remain incompletely understood [9,10,11].

Given the high prevalence and significant impact of benign breast diseases on women's health, there is a pressing need for further research to elucidate the hormonal underpinnings of these conditions, so present study was conducted with an aim to analyse the hormonal profiles in women with benign breast diseases and healthy controls. By integrating epidemiological data on prevalence and incidence with comprehensive hormonal profiling, researchers can advance our understanding of benign breast diseases and inform strategies for prevention, diagnosis, and management. Ultimately, such efforts hold the promise of improving outcomes and enhancing the quality of life for women affected by these prevalent yet understudied conditions.

Materials and Methods

Study Design: This cross-sectional study was conducted for a period of 2 years among women diagnosed with benign breast diseases and their healthy controls under the department of General Surgery at tertiary care center, Jharkhand.

Study Participants: The study enrolled women aged between 18 and 65 years who presented with symptomatic or incidentally detected benign breast diseases at tertiary care hospital between May 2021 and April 2023. Diagnosis of benign breast diseases was established through a combination of clinical evaluation, imaging studies (mammography, ultrasound), and histopathological confirmation where applicable. Eligible benign breast conditions included, but were not limited to, fibroadenomas, cysts, mastalgia (non-cyclic breast pain), benign breast masses, ductal ectasia, and adenosis. Healthy controls were recruited from the general population residing in the catchment area of tertiary care center during the same study period. Control participants were matched to the patient group based on age (±5 years), reproductive status (premenopausal, perimenopausal, or postmenopausal), and other relevant demographic characteristics (body mass index, parity). Recruitment methods included community advertisements, flyers, and word-of-mouth referrals. Participants with a history of breast cancer, previous breast surgery (lumpectomy, mastectomy), hormone replacement therapy, pregnancy, lactation, or endocrine disorders affecting hormonal levels (polycystic ovary syndrome, thyroid disorders) were excluded from the study. Additionally, individuals with significant comorbidities or medications known to influence hormonal profiles were excluded to minimize confounding effects. So, using convenient sampling technique, a total of 106 patients detected with benign breast diseases and 97 controls were enrolled during defined study period.

Data Collection: Data on demographic characteristics, medical history, reproductive factors, menstrual history, and lifestyle habits were collected through structured interviews and review of electronic medical records. Clinical breast examination was performed by experienced healthcare providers to assess breast symptoms, palpable abnormalities, and disease severity. Imaging studies, including mammography and breast ultrasound, were conducted to confirm the diagnosis of benign breast diseases and characterize the extent and nature of breast lesions.

Hormonal Assays: Prior to blood sample collection, participants were instructed to fast overnight to minimize potential interference from dietary factors on hormonal levels. Blood samples were collected by trained phlebotomists using standard venipuncture techniques. For premenopausal women, blood samples were obtained during the follicular phase of the menstrual cycle, typically within the first 5 days of menses, to minimize variability in hormonal levels due to menstrual cycle fluctuations. Postmenopausal women underwent blood sample collection at a consistent time point to account for stable hormonal status. Serum levels of estrogen, progesterone, prolactin, thyroid-stimulating hormone (TSH), and free thyroxine (T4) were measured using automated immunoassay systems (Siemens Healthineers Advia Centaur XP Series, Germany) [chemiluminescent immunometric assay (CMIA)]. Calibration curves generated from known standards of hormone concentrations were used to quantify the amount of hormone present in the sample. Estrogen levels were quantified in picograms per milliliter (pg/mL), prolactin and progesterone levels in nanograms per milliliter (ng/mL), and thyroid hormones (TSH and T4) in

international units per liter (IU/L) and picograms per milliliter (pg/mL), respectively. Serum samples were processed promptly after collection to prevent degradation of hormones, and aliquots were stored at -80°C until analysis to maintain sample integrity.

Statistical Analysis: Statistical analysis was performed using SPSS version 20.0, using appropriate methods based on the distribution of data. Descriptive statistics were used to summarize demographic and clinical characteristics of the study participants. Continuous variables were compared between groups using independent t-tests. Categorical variables were compared using chi-square tests. Statistical significance was set at $p < 0.05$.

Ethical Considerations: This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and other relevant ethical guidelines. The study protocol was approved by the institutional ethics committee. All participants provided written informed consent before participation in the study, and measures were taken to ensure confidentiality and privacy of their personal information.

Results

In our study a total of 106 patients diagnosed with benign breast diseases and 97 as controls were enrolled. The results revealed comparable demographic and clinical characteristics between women with benign breast diseases and healthy controls. The mean age was 35.2 years (± 6.8) for those with benign breast diseases and 33.6 years (± 7.2) for healthy controls, showing no significant difference between the two groups (p=0.105). In terms of menopausal status, 66.0% of women with benign breast diseases were pre-menopausal compared to 70.1% in the control group (p=0.535). The age at menarche was significantly higher in women with benign breast diseases (13.5 ± 1.1 years) compared to healthy controls (12.3 ± 1.3 years), with a p-value of less than 0.0001. Parity, menstrual history, oral contraceptive use, BMI, family history of breast cancer, breastfeeding history, smoking status, alcohol consumption, and physical activity level showed no significant differences between the two groups (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Participants

Characteristic	Benign Breast Diseases (n=106)	Healthy Controls (n=97)	p-value
	Number (%) / Mean ± SD		
Age (years)	35.2 ± 6.8	33.6 ± 7.2	0.105
Menopausal Status			
Pre-menopausal	70 (66.0)	68 (70.1)	0.535
Post-menopausal/ hysterectomy	36 (34.0)	29 (29.9)	
Reproductive History			
Parous	80 (75.5)	75 (77.3)	0.756
Nulliparous	26 (25.5)	22 (23.7)	
Age at menarche (years)	13.5 ± 1.1	12.3 ± 1.3	<0.0001
Parity	2.5 ± 1.2	2.3 ± 1.1	0.218
Menstrual history			
Regular Menstrual Cycle	89 (84.0)	85 (87.6)	0.455
Irregular Menstrual Cycle	17 (16.0)	12 (12.4)	
Oral Contraceptive Use			
Yes	25 (23.6)	23 (23.7)	0.983
No	81 (76.4)	74 (76.3)	
BMI (in kg/m^2)	25.1 ± 3.4	24.5 ± 3.0	0.265
Family History of Breast Cancer			
Yes	18 (17.0)	15 (15.5)	0.769
No	88 (83.0)	82 (85.5)	
Breastfeeding History			
Yes	44 (41.5)	41 (42.3)	0.912
No	62 (58.5)	56 (57.7)	
Smoking Status			
Current	14 (13.2)	11 (11.3)	0.911
Former	32 (30.2)	29 (29.9)	
Never	60 (56.6)	57 (58.8)	
Alcohol Consumption			
Yes	35 (33.0)	32 (33.0)	0.996
No	71 (67.0)	65 (67.0)	
Physical Activity Level			

Sedentary	42 (39.6)	38 (39.2)	0.995
Moderate	43 (40.6)	40 (41.2)	
Active	21 (19.8)	19 (19.6)	

The distribution of benign breast disease patterns among the study participants revealed a predominant prevalence of fibroadenoma, comprising 64 cases (60.4%). Fibroadenosis followed with 23 cases (21.7%), indicating another significant pattern observed. Breast abscess was identified in 8 cases (7.5%), while mastitis accounted for 7 cases (6.6%). Galactocele was the least common pattern observed, comprising 3 cases (2.8%) (Table 2).

Table 2: Distribution of diseases pattern of benign breast diseases among cases

Pattern	Number	%
Fibroadenoma	64	60.4
Fibroadenosis	23	21.7
Breast abscess	8	7.5
Mastitis	7	6.6
Galactocele	3	2.8

The analysis of symptoms reported by the participants revealed a range of presentations associated with benign breast diseases. The most commonly reported symptom was the presence of a lump, with 74 cases accounting for 69.8% of the study population. Pain was also frequently reported, with 71 cases (67.0%) indicating its prevalence as a symptom. Fever was reported in 19 cases (17.9%), while nodularity was observed in 16 cases (15.1%). Nipple discharge was the least frequently reported symptom, observed in 6 cases (5.7%) (Table 3).

Table 3: Distribution of symptoms among women with of benign breast diseases

Symptoms	Number	%
Lump	74	69.8
Pain	71	67.0
Fever	19	17.9
Nodularity	16	15.1
Nipple discharge	6	5.7

The comparison of hormonal levels between women with benign breast diseases and healthy controls revealed significant differences in estrogen and progesterone levels. Women with benign breast diseases exhibited higher mean estrogen levels (120.5 pg/mL ± 65.2) compared to healthy controls (88.3 pg/mL ± 30.1), with a p-value of <0.0001. Similarly, progesterone levels were also significantly elevated in women with benign breast diseases (3.8 ng/mL ± 3.2) compared to healthy controls (0.9 ng/mL ± 0.5), with a p-value of <0.0001. However, there were no significant differences observed in prolactin, TSH, and free T4 levels between the two groups ($p > 0.05$ for all) (Table 4).

Table 4: Serum Hormone Levels in Women with Benign Breast Diseases and Healthy Controls

Hormones level	Benign Breast Diseases (n=106)	Healthy Controls (n=97)	p-value
	Mean ± SD		
Estrogen (pg/mL)	120.5 ± 65.2	88.3 ± 30.1	<0.0001
Progesterone (ng/mL)	3.8 ± 3.2	0.9 ± 0.5	<0.0001
Prolactin (ng/mL)	22.3 ± 14.1	26.8 ± 23.9	0.101
TSH (mIU/L)	2.2 ± 1.6	2.4 ± 0.7	0.257
Free T4 (ng/dL)	1.0 ± 0.2	1.1 ± 0.3	1.001

Discussion

The present study aimed to investigate the hormonal profile of women with benign breast diseases compared to healthy controls and to explore potential associations between hormonal levels and disease pathology.

Our study provides compelling evidence of significant hormonal dysregulation in women diagnosed with benign breast diseases compared to healthy controls, as evidenced by the markedly elevated levels of estrogen and progesterone observed in the former group. The mean estrogen level among women with benign breast diseases was 120.5 pg/mL (± 65.2), significantly higher than the level observed in healthy controls (88.3 pg/mL ± 30.1), with a p-value of <0.0001. Similarly, the mean progesterone level was substantially elevated among women with benign breast diseases (3.8 ng/mL ± 3.2) compared to healthy controls (0.9

ng/mL ± 0.5), with a p-value of <0.0001. These findings are consistent with numerous studies implicating estrogen and progesterone in breast tissue proliferation and the development of benign lesions [12,13,14]. Estrogen, a potent mitogen, stimulates cell proliferation and differentiation in breast epithelial tissue, thereby fostering the formation of benign breast lesions such as fibroadenomas and fibrocystic changes [15]. Progesterone, acting synergistically with estrogen, further promotes mammary gland development and differentiation, potentially exacerbating the pathological processes underlying benign breast diseases [16].

Interestingly, in our study no significant differences were observed in prolactin, TSH, and free T4 levels between women with benign breast diseases and healthy controls ($p > 0.05$ for all). The mean prolactin level among women with benign breast diseases was 22.3 ng/mL (± 14.1), compared to 26.8 ng/mL (± 23.9) in healthy controls, with a p-value of 0.101. Similarly, the mean TSH level was 2.2 mIU/L (± 1.6) in women with benign breast diseases and 2.4 mIU/L (± 0.7) in healthy controls, with a p-value of 0.257. The mean free T4 level was 1.0 ng/dL (± 0.2) in women with benign breast diseases and 1.1 ng/dL (± 0.3) in healthy controls, with a p-value of 1.001. While previous studies have suggested roles for prolactin and thyroid hormones in breast health, our findings suggest that their contributions to the pathophysiology of benign breast diseases may be less significant as shown in previous studies [17,18,19,20]. Mulani et al., showed that increased serum prolactin levels were observed in 13.3% of patients with benign breast diseases, and the mean serum prolactin level was significantly higher among patients with benign breast disease (16.31±1.72 ng/ml). In a study by Anil et al., benign breast diseases were detected in 54.9% of patients with NTD, in 47.4% of those with HT, and 29.2% of control group in the study. Prolactin, traditionally associated with lactogenic properties, has been implicated in breast tissue growth and differentiation [21]. Similarly, thyroid hormones have been hypothesized to influence breast tissue metabolism and function [22,23].

In our study, the distribution of disease patterns among the study participants revealed fibroadenoma as the predominant pattern, comprising 60.4% of cases, followed by fibroadenosis (21.7%), breast abscess (7.5%), mastitis (6.6%), and galactocele (2.8%). These findings align with previous studies by Kumar et al., Selvakumaran et al., and Giri et al., indicating fibroadenoma as the most common benign breast lesion in young women, while fibroadenosis, characterized by fibrocystic changes, is also prevalent, especially in women of reproductive age [24,25,26].

Symptomatology analysis unveiled a spectrum of presentations associated with benign breast diseases, with the presence of a lump and pain being the most frequently reported symptoms. Specifically, 69.8% of participants reported a lump, while 67.0% reported pain, indicating the significant impact of these symptoms on clinical presentation and patient experience.

Additional symptoms included fever (17.9%), nodularity (15.1%), and nipple discharge (5.7%), albeit less frequently reported. These findings underscore the diverse clinical manifestations of benign breast diseases, necessitating a multifaceted approach to diagnosis and management [27,28].

Limitations

Despite the valuable insights provided by our study, several limitations should be acknowledged. The cross-sectional design precludes causal inference, necessitating longitudinal studies to elucidate the temporal relationships between hormonal levels and benign breast disease development. Moreover, the relatively modest sample size and single-center recruitment may limit the generalizability of our findings, emphasizing the need for larger, multicenter studies to validate our results and explore potential population-specific differences.

Conclusion

In conclusion, our study advances our understanding of the hormonal underpinnings of benign breast diseases, highlighting the pivotal roles of estrogen and progesterone in disease pathogenesis. By elucidating the intricate interplay between hormonal factors and breast health, our findings offer valuable insights into disease mechanisms and potential therapeutic avenues for intervention. Future research endeavors should aim to unravel the complex hormonal dynamics governing benign breast conditions, paving the way for personalized management strategies and improved clinical outcomes.

References

1. Marchant DJ. Benign breast disease. Obstet Gynecol Clin North Am. 2002;29:1-20.
2. Sangma MBM, Panda K, Dasiah S. A clinico-pathological study on benign breast diseases. J Clin Diagn Res. 2013;7:503-6.
3. Galea M. Benign breast disorders. Surgery (Oxford). 2016;34:19-24.
4. Kumar M, Ray K, Harode S, Wagh DD. The pattern of benign breast diseases in rural hospital in India. East Central African J Surg. 2010:15:59-64.
5. Kaur N, Agarwal N, Panwar P, Mishra K. Clinicopathologic profile of benign breast

conditions in Indian women: prospective study based on aberrations of normal development and involution classification. World J Surg. 2012;36:2252-8.
6. Rohan TE, Negassa A, Chlebowski RT, et al. Estrogen plus progestin and risk of benign proliferative breast disease. Cancer Epidemiol Biomarkers Prev. 2008;17:2337-43.
7. Dyrstad SW, Yan Y, Fowler AM, Colditz GA. Breast cancer risk associated with benign breast disease: systematic review and meta-analysis. Breast Cancer Res Treat. 2015; 149: 569-75.
8. Samoli E, Trichopoulos D, Lagiou A, et al. The hormonal profile of benign breast disease. Br J Cancer. 2013;108:199-204.
9. Courtillot C, Chakhtoura Z, Bogorad R, et al. Characterization of two constitutively active prolactin receptor variants in a cohort of 95 women with multiple breast fibroadenomas. J Clin Endocrinol Metab. 2010;95:271-9.
10. Bhargav PR, Mishra A, Agarwal G, Agarwal A, Verma AK, Mishra SK. Prevalence of hypothyroidism in benign breast disorders and effect of thyroxine replacement on the clinical outcome. World J Surg. 2009;33:2087-93.
11. Giustarini E, Pinchera A, Fierabracci P, et al. Thyroid autoimmunity in patients with malignant and benign breast diseases before surgery. Eur J Endocrinol. 2006;154:645–9.
12. Brkić M, Vujović S, Ivović M, et al. THE role of E2/P ratio in the etiology of fibrocystic breast disease, mastalgia and mastodynia. Acta Clin Croat. 2018;57:756-61.
13. Bansal C, Pujani M, Misra S, Srivastava AN, Singh US. Circulating tumor cells in breast cancer: correlation with clinicopathological parameters, hormone profile and microrna polymorphisms. Turk Patoloji Derg. 2016; 32:148-57.
14. Chopra A, Thomas S, Sharma K, Yadav A, Jain M, Anand R. Clinical spectrum and hormonal profile of patients with non-inflammatory benign breast disorders: a cross-sectional study. Int Surg J. 2023;10:1599-605.
15. Johansson A, Christakou AE, Iftimi A, et al. Characterization of benign breast diseases and association with age, hormonal factors, and family history of breast cancer among women in Sweden. JAMA Netw Open. 2021;4:e2114716.
16. Gorins A, Denis C. Effects of progesterone and progestational hormones on the mammary gland. Arch Anat Cytol Pathol. 1995;43:28–35.
17. Nicol M, Willis C, Yiangou C, Sinnett D, Shousha S. Relationship between serum prolactin levels and histology of benign and malignant breast lesions: a detailed study of 153 consecutive cases. Breast J. 2002;8:281–5.
18. Mulani J, Murhar B, Jambhulkar R, Mishra G. Serum Prolactin: A clue to breast malignancy. Med J Lab. 2022;16:13-9.
19. Anil C, Guney T, Gursoy A. The prevalence of benign breast diseases in patients with nodular goiter and Hashimoto's thyroiditis. J Endocrinol Invest. 2015;38:971-5.
20. Tanwar P, Gupta S, Bharti D et al. Magnitude of hypothyroidism in benign breast disorders and effect of thyroxin replacement on clinical outcome of benign breast disorders with hypothyroidism as co morbidity. Int J Health Sci Res. 2016; 6:61-70.
21. Kolomiiets O, Yazykov O, Piddubnyi A, et al. The Expression of Prolactin Receptors in Benign Breast Tumors Is Not Associated with Serum Prolactin Level. J Clin Med. 2021;10:5866.
22. Han M, Wang Y, Jin Y, et al. Benign thyroid disease and the risk of breast cancer: an updated systematic review and meta-analysis. Front Endocrinol. 2022;13:984593.
23. Zheng Y, Tang H, Wu J, Guan D, Mo Q, Zheng Q. The crosstalk between benign thyroid disease and breast cancer: A single center study. Medicine (Baltimore). 2024; 103: e37298.
24. Kumar N, Prasad J. Epidemiology of benign breast lumps, is it changing: A prospective study. Int Surg J. 2019;6:465-9.
25. Selvakumaran S, Sangma MB. Study of benign breast disease. Int Surg J. 2017;4:339-43.
26. Giri R, Bhandari R, Mahato I, Poudel M, Kumari S, Yadav A. Breast problems in women. Health Renaissance. 2013;11:33-7.
27. Geethamala K, Vani BR, Srinivasa MV, Radha M. Fibroadenoma: A harbor for various histopathological changes. Clin Cancer Investig J. 2015;4:183-7.
28. Khanzada TW, Samad A, Sushel C. Spectrum of benign breast diseases. Pak J Med Sci. 2009;25:265-8.