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Original Article

Surgery Section

Analysis of Hormonal Profile in Women with Benign Breast Diseases and Women without Breast Pathology at a Tertiary Care Hospital in Lucknow, India: A Cross-sectional Study

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ABSTRACT

Introduction: Disruptions in normal hormonal pathways contribute to the development of various benign breast conditions. Having a general understanding of specific hormonal interactions, such as estradiol, progesterone, and prolactin, among breast tissue, the hypothalamus, the pituitary, and the gonads, can enhance understanding of the causes and manifestations of benign breast conditions such as fibroadenoma, fibroadenosis, breast cyst, abscess, mastitis, galactocele, and phyllodestumour. However, there is limited available information regarding the hormonal environment associated with Benign Breast Disease (BBD).

Aim: To compare serum levels of estradiol, progesterone, and prolactin between women with BBD and those without breast pathology.

Materials and Methods: This cross-sectional study was conducted in the Department of General Surgery, Era Lucknow Medical College and Hospital (ELMC and H), Lucknow, Uttar Pradesh, India, from January 2021 to January 2023. A total of 80 female subjects were enrolled and divided into two groups: Group A (40 subjects diagnosed with BBD by triple assessment) and Group B (40 subjects with no breast pathology). Serum levels of estradiol, progesterone, and prolactin were tested during the follicular phase and compared between the two groups. Student t-test and Spearman's correlation with a 95% confidence interval were used for mean comparison between the groups. Receiver Operating Characteristic (ROC) analysis was performed to determine cut-off values, sensitivity, and specificity for the hormones. A p-value of <0.05 was considered as significant.

Results: The mean age showed no statistical differences between Group A (26.5 years) and Group B (28.8 years). The mean levels of estradiol and progesterone hormones were significantly higher in Group A (188.38±96.06 pg/mL; 4.34±5.05 ng/mL) than in Group B (103.21±39.52 pg/mL; 0.38±0.30 ng/mL) with a p-value of 0.001. The sensitivity of estradiol was found to be 80% with a specificity of 75% based on ROC analysis when the cut-off was set to <139.5. Furthermore, progesterone showed a sensitivity of 92.50% and specificity of 80% at a cut-off <0.8560. Prolactin showed a sensitivity of 52.50% and specificity of 62.50% at a cut-off <18.96.

Conclusion: Authors concluded that steroidal harmones have a significant effect on the development of BBD. The present study had demonstrated that women with BBD exhibit higher levels of estradiol and progesterone compared to women without breast pathology.

Keywords: Endocrine milieu, Hormone dependency of breast diseases, Non malignant breast disease

INTRODUCTION

During the fifth or sixth week of development, the ectoderm transforms into a modified sweat gland that gives rise to the mammary gland. It is the secondary female sexual organ. It is primitive in men. Multiple hormonal cues, including estrogen, progesterone, prolactin, oxytocin, and growth hormone, stimulate breast growth and function [1]. The production of neurotrophic hormones from the brain controls the secretion of hormones that influence the breast tissues. The breast experiences ongoing structural and physiological changes. When these typical changes (pubertal, cyclical, pregnancy, lactational, and menopausal) become excessive and cause concern for women, they are labeled as benign breast illnesses [2]. Benign breast illnesses are the most prevalent diseases affecting females, causing significant morbidity and concern. Women before menopause are the most affected. The breast has historically represented femininity and maximum fertility [3]. Therefore, both sickness and breast surgery induce a dread of mutilation and loss of femininity.

Benign Breast Diseases (BBD) encompass all benign breast problems, such as benign tumours, trauma, mastalgia, mastitis, and nipple discharge. Benign tumours comprise pathological abnormalities that do not enhance a patient's risk of having cancer, lesions that confer a slightly increased risk, and lesions that are associated with a risk of developing breast cancer of up to 50%. BBD can manifest as a palpable mass, discomfort, or even discharge from the nipple [4]. Pain and swelling are the most prevalent symptoms. Non proliferative breast lesions, proliferative breast lesions without atypia, and proliferative breast lesions with atypia are comprised of benign breast disorders [5]. Compared to malignant tumours of the breast, BBD is a largely overlooked feature of breast disorders that has received stepmotherly treatment.

While the majority of breast lesions are non cancerous, research has demonstrated that benign breast lesions are much more prevalent than malignant ones [6]. The author had suggested that human prolactin may impact Deoxyribonucleic Acid (DNA) synthesis in organ cultures of benign breast tumours, leading to the possibility of elevated hormone levels in individuals with non cancerous breast conditions [7]. However, a study had not discovered any connection between increased prolactin levels and breast fibrocystic disorders [8]. Therefore, authors aimed to evaluate differences in serum estradiol, progesterone, and prolactin levels between women with BBD and those without breast pathology.

MATERIALS AND METHODS

The present cross-sectional study was conducted in the Department of General Surgery Era Lucknow Medical College and Hospital

(ELMC and H), Lucknow, Uttar Pradesh, India, from January 2021 to January 2023. Institutional Ethical Committee approval was obtained (IEC Number-RCell IEC/2021/20). Informed consent was obtained from each subject enrolled.

Inclusion criteria: Women who had reached menarche and were diagnosed with BBD through triple assessment were included. Additionally, women who visited the hospital but were diagnosed as healthy and did not require a breast biopsy were also included.

Exclusion criteria:

- Pregnant women.
- Women who were on hormonal contraception and other hormonal therapies.
- Women who were diagnosed with malignant pathology before or during the study.

Study Procedure

Prior to the study, informed consent was obtained from all subjects. Each patient underwent a comprehensive triple assessment, which involved a thorough clinical examination, radiological evaluation through high resolution ultrasonography, and Fine Needle Aspiration Cytology (FNAC) for palpable lumps. Furthermore, histopathological assessment of excised lumps or drained cysts was conducted. For patients diagnosed with BBD using the aforementioned triple assessment method, blood samples were taken during the follicular phase of their menstrual cycle to test the levels of estradiol, progesterone, and prolactin. This testing was carried out in both outpatient and inpatient settings.

A total of 80 female subjects who visited the hospital during the study period were enrolled and divided into two groups: Group A (40) and Group B (40). Group A consisted of subjects diagnosed with BBD by triple assessment, and Group B consisted of subjects with no breast pathology.

STATISTICAL ANALYSIS

The data were entered into Microsoft Excel and analysed using the statistical software Statistical Package for the Social Sciences (SPSS) version 26.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were evaluated using mean (standard deviation) or range values when necessary. Dichotomous variables were presented as number/frequency and analysed using the Chi-square test. For comparison of means between the two groups, analysis by student t-test and Spearman's correlation with a 95% confidence interval was used. ROC analysis was conducted to determine the cut-off, sensitivity, specificity, and other parameters for the hormones. A p-value of <0.05 was considered as significant.

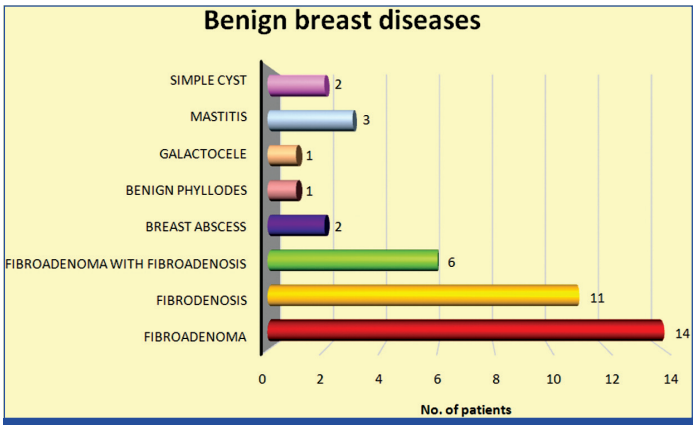
RESULTS

The mean age in Group A was 26.5 years, while in Group B it was 28.8 years. The majority of patients in Group A belonged to the upper class (47.50%), whereas in Group B they belonged to the upper middle class (55%) [Table/Fig-1]. Symptoms of fibroadenoma were seen in 14 (35%) of patients [Table/Fig-2]. The mean levels of estradiol and progesterone hormones were significantly higher in Group A (188.38±96.06 pg/mL; 4.34±5.05 ng/mL) compared to Group B (103.21±39.52 pg/mL; 0.38±0.30 ng/mL). On the contrary, the mean prolactin hormone level in Group B was higher (27.24±27.7 ng/mL) compared to Group A (24.34±13.88 ng/mL) [Table/Fig-3].

ROC analysis showed that the sensitivity of estradiol was found to be 80% and the specificity to be 75% at a cut-off <0.8560. Prolactin showed a sensitivity of 52.50% and a specificity of 62.50% at a cut-off <18.96 [Table/Fig-4-7].

Parameters	Group A N (%)	Group B N (%)	p-value
Age (years)			
11-20	12 (30%)	5 (12.50%)	χ^2=4.205 p=0.2402
21-30	16 (40%)	17 (42.50%)	
31-40	8 (20%)	11 (27.50%)	
41-50	4 (10%)	7 (17.50%)	
Socio-economic status			
Upper class	19 (47.50%)	5 (12.50%)	χ^2=14.97 p=0.0018*
Upper middle class	18 (45%)	22 (55%)	
Lower middle class	3 (7.50%)	12 (30%)	
Upper lower class	0	1 (2.50%)	
Lower class	0	0	
Body Mass Index (BMI) (kg/m^2)			
Underweight (<18.5)	8 (20%)	2 (5%)	χ^2=17.78 p=0.0005*
Normal (18.5-24.9)	20 (50%)	26 (65%)	
Overweight (25.0-29.9)	12 (30%)	10 (25%)	
Obese (≥30.0)	0	2 (5%)	
Menopausal status			
Menopausal	4 (10%)	3 (7.50%)	χ^2=0.1566 p=0.6923
Non menopausal	36 (90%)	37 (92.50%)	
Parity			
Parous	18 (45%)	23 (57.50%)	χ^2=1.251 p=0.2634

[Table/Fig-1]: Demographic parameters of enrolled patients (N=80).



[Table/Fig-2]: Incidence of of BBD cases.

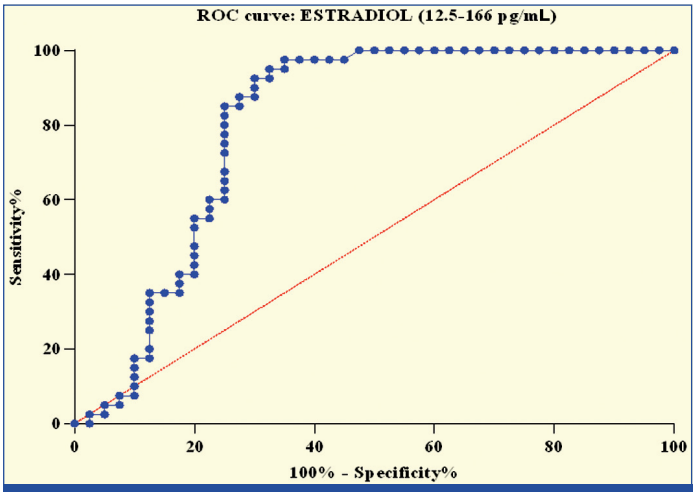
Hormonal profile	Group A Mean±SD	Group B Mean±SD	p-value
Estradiol (12.5-166 pg/mL)	188.38±96.06	103.21±39.52	t=5.186 p<0.0001*
Progesterone (0.057-0.893 ng/mL)	4.34±5.05	0.38±0.30	t=4.951 p<0.0001*
Prolactin (3-18 ng/mL)	24.34±13.88	27.24±27.71	t=0.6005 p=0.5499

[Table/Fig-3]: Hormonal profile of enrolled patients (N=80).
SD: Standard deviation

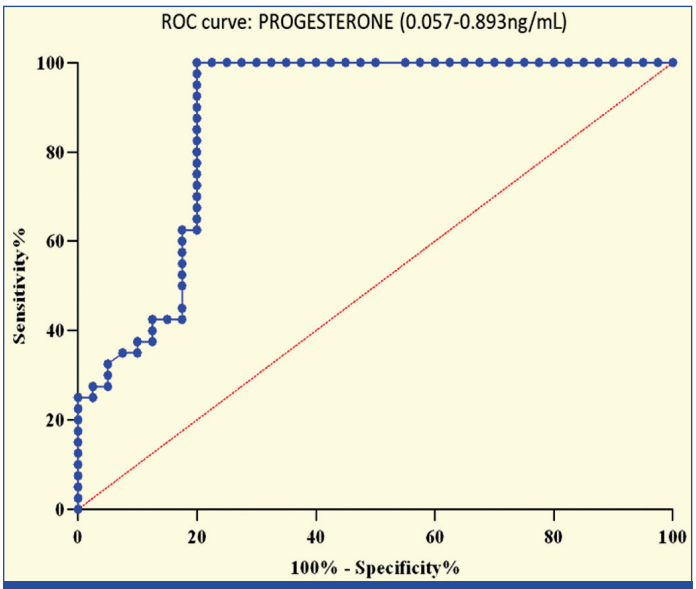
ROC analysis			
Area under the ROC curve {Estradiol (12.5-166 pg/mL)}			
Area	0.8016	Cut-off	<139.5
Standard error	0.05466	Sensitivity%	80.00
95% confidence interval	0.6944 to 0.9087	Specificity%	75.00
p-value	<0.0001*	Likelihood ratio	3.200
Area under the ROC curve {Progesterone (0.057-0.893 ng/mL)}			
Area	0.8766	Cut-off	<0.8560
Standard error	0.04225	Sensitivity%	92.50

95% confidence interval	0.7937 to 0.9594	Specificity%	80.00
p-value	<0.0001*	Likelihood ratio	4.625
Area under the ROC curve {Prolactin (3-18 ng/mL)}			
Area	0.5428	Cut-off	<18.96
Standard error	0.06565	Sensitivity%	52.50
95% confidence interval	0.4141 to 0.6715	Specificity%	62.50
p-value	0.5098	Likelihood ratio	1.400

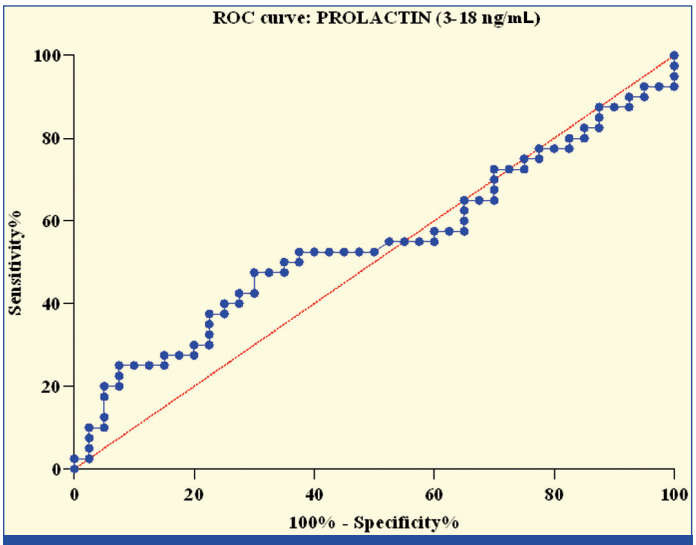
[Table/Fig-4]: Area under ROC curve of the measured hormones.



[Table/Fig-5]: Area under ROC curve of the estradiol hormone.



[Table/Fig-6]: Area under ROC curve of the progesterone hormone.



[Table/Fig-7]: Area under ROC curve of the prolactin hormone.

DISCUSSION

In the present study, the majority of patients were enrolled in the age group of 21-30 years, accounting for 40% in Group A and 42.50% in Group B. These findings align with a study by Goss PE et al., which also enrolled patients in the age range of 20-35 years on average [9]. Similarly, Gudur H and Basa SD discovered that the majority of their patients (54.2%) were between the ages of 21 and 30 [10]. In present study, there were slightly more patients with a left breast mass (n=31) compared to those with a right breast mass (n=29). Another study by Datey A et al., examined the mode of presentation, clinical characteristics, therapeutic options, and demographic factors associated with BBD [11]. They found that fibroadenoma was the most prevalent benign lesion, accounting for 65.9% of cases. In present study, authors observed a lower occurrence of fibroadenoma at 35%. In a study by Khanna S et al., BBD patients underwent evaluation of their blood estradiol levels, serum lipid profiles, and Oestrogen Receptor (ER) status [12]. They found that BBD patients had significantly higher serum levels of estradiol and triglycerides compared to the control group. In present study, authors also observed higher estradiol levels in the BBD group (188.38 pg/mL) compared to the control group (103.21 pg/mL).

Regarding socio-economic status, in present research, the majority of patients belonged to the upper class (47.50%) and upper middle class (45%), and most of them had a normal weight (65%). This contrasts with a study by Freedman AN et al., which suggested that the use of chemoprevention agents for breast cancer prevention may be hampered by racial, ethnic, and socio-economic disparities [13]. However, it is worth noting that the majority of enrolled women in present study fell within the normal weight range. Recent evidence suggests that race should be considered when analysing risk-benefit profiles, age, and comorbidities. Additionally, Arthur R et al., reported that there was no observed correlation between the risk of breast cancer and factors such as smoking, BMI, early menarche, multiparity, oophorectomy history, or lobular involution [14].

In the current study, the area under the ROC curve for estradiol was 0.8016 pg/mL, while for progesterone, it was 0.8766 ng/mL, and for prolactin, it was 0.5428. In a study by Patrício M et al., the ROC curve for estradiol was 0.7852 pg/mL, for progesterone it was 0.8598 ng/mL, and for prolactin it was 0.4989 ng/mL [15]. The present study found that the mean level of estradiol hormone in Group A was 188.38±96.06 pg/mL and in Group B it was 103.21±39.52 pg/mL. The mean level of progesterone hormone in Group A was 4.34±5.05 ng/mL and in Group B it was 0.38±0.30 ng/mL. The mean level of prolactin hormone in Group A was 24.34±13.88 ng/mL and in Group B it was 27.24±27.71 ng/mL. Similarly, in a study conducted by Henderson BE et al., patients had higher 22-day estradiol-plus-oestrone levels compared to controls [16]. Sixth day prolactin levels were also elevated. About half of the patients could be distinguished from the controls based on the sixth day levels of oestrogens and prolactin.

Similarly, Samoli E et al., compared blood levels of oestrogens, testosterone, and Insulin-like Growth Factor-1 (IGF-1) between BBD patients by histological subtype and women without breast malignancy [17]. They concluded that elevated levels of steroid hormones, particularly oestrogens, promote the development of BBD, especially the proliferative subtype. Although not directly associated with endogenous hormones, these findings suggest a role for hormones in the pathogenesis of BBD.

In addition, Khanna S et al., conducted a prospective study to determine the serum estradiol levels, serum lipid profile, and tissue ER status of patients with BBD [12]. They found higher serum triglyceride and estradiol levels in BBD patients compared to controls, suggesting a potential aetiopathological role. It is possible that elevated lipid levels increase peripheral estrogen production. They also observed that fibroadenomas were more likely to be positive for ER compared to fibroadenosis or fibrocystic disease.

Additionally, they found that ER positivity decreased with age. These findings align with the results of present study. Overall, present study serves as a baseline document for BBD, providing insights into the hormonal profile, types of BBD, distribution, and frequency of BBD.

Limitation(s)

Due to the limited sample size of 80, drawing definitive conclusions about the relationship between oestrogen, progesterone, prolactin, and BBD is challenging. However, present study can serve as a foundational reference for documenting aspects such as the hormonal profile, types, distribution, and frequency of BBD.

CONCLUSION(S)

The present research has demonstrated that women with BBD exhibit higher levels of estradiol and progesterone compared to women without breast pathology. These findings have potential therapeutic implications as understanding the hormonal factors associated with BBD can inform treatment strategies. Additionally, identifying individuals with specific hormonal profiles may aid in assessing their risk of developing breast diseases and guide preventive measures. Overall, investigating estrogen, progesterone, and prolactin tests in females with BBD enhances understanding of the condition, assists in making diagnosis and treatment decisions, and opens possibilities for further research and intervention.

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