



TO STUDY THE CLINICOPATHOLOGICAL PROFILE OF BENIGN BREAST DISEASE BASED ON ABERRATION IN NORMAL DEVELOPMENT AND INVOLUTION (ANDI)

General Surgery

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ABSTRACT

Benign breast disease encompasses various non-cancerous conditions characterized by changes in breast tissue. The Aberration of Normal Development and Involution (ANDI) framework serves as a valuable tool in classifying these conditions, focusing on natural tissue variations rather than categorizing all changes as pathological. This approach reduces patient anxiety and facilitates personalized evaluations based on the severity of the aberrations. This descriptive cross-sectional study, conducted over 12 months involved 63 patients with symptoms indicative of benign breast disorders. The mean patient age was 25.63 years, predominantly within the 15 to 30 age range. The primary symptom reported was a breast lump (66.6%). The study emphasizes the significance of early detection and structured classification in managing benign breast diseases, highlighting the predictable clinical and pathological patterns associated with ANDI, influenced by hormonal factors. Integrating clinical, imaging, and histopathological findings enhances patient care and minimizes unnecessary interventions.

KEYWORDS

Benign breast disease (BBD), Aberration of normal Development and Involution (ANDI), Hormonal Factors, Triple assessment

INTRODUCTION

Benign breast disease is a group of conditions marked by changes in breast tissue that are benign (not cancer). There are different types of benign breast disease, which are caused either by an increase in the number of cells or by the growth of abnormal cells in the breast ducts or lobes.¹

Benign breast disease (BBD) is a neglected entity despite the fact that it constitutes the majority of breast complaints.² They are most common cause of breast problems in females and are more frequent than malignancy.³

Understanding the underlying biological mechanisms and the clinicopathological spectrum of BBD is essential for accurate diagnosis, risk stratification, and the development of tailored management strategies.⁴

Breasts or mammary glands in the females can be considered as a distinguishing and unique feature of mammals.³ Hormones and growth factors acting on the epithelial and stromal elements right from the onset of puberty till menopause cause significant morphological changes which can lead to Aberration in Normal Development and Involution (ANDI) causing majority of benign breast diseases.³

Among all the diseases related to breast, benign diseases (60.1%) were the commonest followed by malignant (28.4%) and inflammatory lesions (11.5%) in India.⁵

BBD are at least 10 times more common than breast cancer in the west.³ Up to 30% of the women who suffer from BBD will require treatment at some time in their lives.³ Globally, BBD account for approximately 90% of the clinical presentations related to the breast.³

The incidence of BBD begins to rise during the second decade of life and peaks in the fourth and fifth decade.⁶

Leslie E. Hughes, Robert E. Mansel, and David J. Webster coined the term "aberrations of normal development and involution" in their

study in 1987.¹²

The concept of ANDI provides a novel framework for understanding the pathogenesis and classification of benign breast disorders. This perspective seeks to elucidate the physiological deviations that result in a spectrum of non-cancerous breast conditions.⁷

ANDI encompasses a variety of factors-hormonal, genetic, and environmental-that impact the natural development and involution of breast tissue. By examining these deviations through the lens of ANDI, researchers aim to enhance diagnostic accuracy and improve the management of benign breast diseases.⁷

The majority of benign breast disorders can be categorized within the ANDI framework, highlighting distinct patterns of development and involution. Several specific types of benign conditions, such as fibroadenomas, cysts, and hyperplastic lesions, are identified which demonstrated unique histopathological characteristics linked to aberrant developmental processes.⁷

The study's data also illustrate a significant correlation between hormonal fluctuations and the prevalence of these benign conditions, suggesting that understanding these relationships is crucial for effective clinical management.⁷

The exploration of ANDI offers a comprehensive perspective on benign breast disorders, emphasizing their multifactorial nature. By integrating the principles of normal breast development and involution, this study underscores the significance of recognizing and classifying benign conditions appropriately. The insights gained are anticipated to facilitate improved diagnostic tools and therapeutic strategies, ultimately leading to better patient outcomes for those affected by benign breast diseases.⁷

ANDI CLASSIFICATION⁸

By being a framework of pathogenesis and emphasizing the normal changes, ANDI avoids labelling every breast change as a disease thus alleviating anxiety and reassuring the patients. It allows for a more

tailored assessment of each individuals concerns based on the severity of the aberration.

Stage	Main clinical presentation		
	Normal Process	Aberration	Diseases
Early reproductive (15-25 years)	Lobular Development	Fibroadenoma	Giant Fibroadenoma
	Stromal development	Adolescent hypertrophy	Gigantomastia
	Nipple eversion	Nipple inversion	Subareolar Abscess/mammary duct fistula
Mature reproductive (25-40 years)	Cyclical changes of menstruation	Cyclical mastalgia	Incapacitating mastalgia
	Epithelial hyperplasia of pregnancy	Nodularity	
Involution (35-55 years)	Lobular involution	Bloody nipple discharge	
	Duct involution -dilation -sclerosis	Macrocystis	Periductal mastitis
	Epithelial turnover	Sclerosing lesions	
		-Duct ectasia -Nipple retraction -Simple epithelial hyperplasia	With atypia

Recent research has highlighted that deviations from the normal processes of breast development and involution can lead to the pathological changes observed in BBD. Persistent estrogenic stimulation, especially when unopposed by progesterone can cause excessive ductal proliferation and hyperplasia.⁹ Aberrant expression of growth factors and their receptors has been documented in benign lesions, suggesting that disruptions in cell signalling pathways are central to lesion formation.¹⁰

The diagnostic workup of BBD poses unique challenges because of the overlapping clinical and imaging features with malignant lesions, while majority of them prove to be benign. Patients often present with palpable masses, cyclical breast pain, or nipple discharge, prompting further evaluation through imaging modalities such as mammography and ultrasonography.¹¹

Triple assessment consists of a detailed personal and family history and a clinical breast examination (CBE), radiological investigations and histopathological examination. A standardised universal grading system is used for clinical, radiological, and pathological scoring of each breast according to the most suspicious lesion. If there is no concordance between clinical and radiological assessment, a clinical core biopsy is performed.¹²

Clinical exam	Radiology	Biopsy pathology
S1 — Normal	R1 — Negative	B1 — Inadequate sample
S2 — Benign	R2 — Normal/benign	B2 — Normal/benign
S3 — Indeterminate, probably benign	R3 — Indeterminate/ probably benign	B3 — Uncertain
S4 — Suspicious, probably malignant	R4 — Suspicious	B4 — Suspicious
S5 — Malignant	R5 — Highly Suspicious	B5a — Malignant (non-invasive) B5b — Malignant (invasive)

While histopathological examination remains the gold standard for diagnosis, subtle differences among benign conditions often complicate tissue interpretation. A deeper understanding of the aberrations in normal breast development and involution could improve diagnostic precision by correlating specific histological features with distinct molecular profiles.¹³

The integration of these methodologies holds promise for refining diagnostic criteria and developing targeted therapeutic interventions.¹⁴

MATERIAL AND METHOD

This descriptive cross-sectional study was conducted at the Department of General Surgery, Hind Institute of Medical Sciences, Barabanki, from January 2024 to December 2024, encompassing 63 female patients aged 15 to 43 years who exhibited symptoms related to benign breast conditions. Inclusion criteria consisted of patients with clinical features of benign breast disease, while those with malignant disease or breast abscess were excluded.

Data were collected through detailed patient history, clinical examination, radiological evaluations (ultrasonography for patients under 40 and mammography for those over 40), and cytological or histological examinations. Follow-ups were conducted at one week, one month, and three months post-consultation to assess symptom resolution.

RESULTS

Table 1: Age Distribution Of Patients (n - 63)

Age group (years)	Number of patients (n)	Mean
15 – 20	15	18.2
21 – 25	19	22.47
26 – 30	15	28.6
31 – 35	10	32.9
36 – 40	03	38
41 – 45	01	43

The study encompassed 63 patients, with a mean age of 25.63 years.

The most commonly affected age group was 15-30 years with 49 cases (77.7%) comprising the majority of cases.

Younger patients (15-30 years, 49 cases, 77.7%) primarily presented with fibroadenomas, while older patients (31-43 years, 14 cases, 22.2%) were more likely to have duct ectasia and mastalgia.

Table 2: Distribution Of Symptoms Among Patients With Clinical Diagnosis

Chief complaints	Frequency (n)	Side		Percentage (%)	Category
		U/L	B/L		
Breast Lump	42	36	6	66.6%	Fibroadenoma
Nodularity	3	1	2	4.7%	Duct ectasia
Breast pain	8	2	6	12.6%	Mastalgia
Nipple Discharge	9	4	5	14.2%	Fibroadenosis
Other Complaints	1	-	1	1.5%	Physiologic inverted nipple

The most common presenting symptom was a breast lump (66.6%), followed by nipple discharge (14.2%), mastalgia (12.6%), nodularity (4.7%), and other complaints (1.5%).

Fibroadenoma was the most frequent clinical diagnosis (42 cases), followed by duct ectasia (9 cases), mastalgia (8 cases), fibroadenosis (3 cases), and physiologic inverted nipple (1 case).

Table 3:

Category	Age (years)	n	Symptoms	Signs	HR-USG Findings	Other Findings	Treatment
Fibroadenoma	< 20	9	Breast lump	Palpable lump	Wider than taller heterogeneously hypochoic lesion	Size < 3 cm (5 patients)	conservative
						Size > 3 cm (4 patients)	surgical
	20-40	33	Breast lump	Palpable lump	Wider than taller heterogeneously hypochoic lesion	Size < 3 cm (14 patients)	conservative
						Size > 3 cm (19 patients)	surgical
Duct Ectasia	< 20	1	Blood mixed discharge with breast lump	Sero sanguinous discharge with palpable lump	Dilated ducts with minimal intraductal collections	Single duct	Conservative for nipple discharge, surgical for lump
	20-40	8	Blood mixed discharge	Sero sanguinous discharge	Dilated ducts with minimal intraductal collections	Single duct (5 patients)	conservative
						Multiple ducts (3 patients)	surgical
Mastalgia	20-40	7	Breast pain	Breast tenderness (cyclical only)	Prominent fibroglandular parenchyma	-	Conservative

	> 40	1	Breast pain	Non-tender	Prominent fibroglandular parenchyma	BIRADS 1 b/l breast	Conservative
Fibroadenosis	20-40	3	Breast lump	Breast lumpiness	Prominent fibroglandular parenchyma	-	Conservative
Physiologic Inverted Nipple	20-40	1	Inverted nipple	Bilateral indrawing nipple	No significant abnormality	-	Conservative

Out of 63 cases, FNAC was done in 46 cases (73.01%). Biopsy was not done as FNAC was conclusive in making diagnosis.

Histopathological analysis in this study revealed that fibroadenomas (42 cases, 66.6%) were the most common pathological finding, followed by duct ectasia (3 cases, 4.76%) and fibrocystic lesions (1 case, 1.58%).

Treatment Modalities

In our study out of 63, total of 37 cases (58.7%) were managed conservatively, mainly for benign lesion (fibrocystic disease with or without fibroadenoma/ other) and mild duct ectasia and 26 cases (41.2%) required surgical intervention, mostly for larger fibroadenomas and symptomatic duct ectasia.

Of 42 out of 63 cases (66.6%) of fibroadenoma, 19 cases (45.2%) were treated conservatively as the size of lump was < 3cm and 23 (54.7%) were treated surgically as the size of lump was > 3cm.

Of 9 out of 63 cases (14.2%) of duct ectasia, 6 cases (66.66%) were treated conservatively as these cases consisted involvement of a single duct and 3 (33.33%) were treated surgically as these cases had multiple ducts involved.

8 cases of mastalgia (12.6%), 3 cases of fibroadenosis (4.76%) and 1 case of physiologic inverted nipple (1.58%) out of 63 respectively, all were treated conservatively.

Follow-up And Outcomes

Out of 63, 42 cases (66.6%) were of fibroadenoma of which 19 cases (45.2%) were managed conservatively (as the size of palpable lump was < 3cm) showed partial resolution of symptoms and considerable reduction in size of lump till 12 weeks and 23 cases (36.5%) were managed surgically (as the size of palpable lump was > 3cm) showing no recurrence till 12 weeks.

Out of 63, 9 cases (14.2%) were of duct ectasia of which 6 cases (66.66%) were managed conservatively (involving single duct) showed partial resolution till 1st week and resolution till 4th week and 3 cases (33.33%) were managed surgically as conservative management yielded no results till 4th week (involved multiple ducts) showed considerable resolution after surgical management in 1st week. Of all cases of duct ectasia, no patient had any comorbidity or deranged serum prolactin.

Out of 63, 8 cases (12.6%) were of mastalgia all of which were treated conservatively of which 7 cases (87.5%) were non-cyclical that showed partial resolution till 4th week with significant resolution of symptoms till 12th week and 1 case (12.5%) exhibited symptoms of cyclical mastalgia showed partial resolution till 1st week and significant resolution till 4th week.

Out of 63, 3 cases (4.76%) were of fibroadenosis all of which were treated conservatively showed partial resolution till 4th week and significant resolution till 12th week.

Out of 63, 1 patient (1.58%) presented with physiologic inverted nipple and was managed conservatively showed considerable reduction of symptoms till 12th week.

No major complications were observed in either treatment group.

Key Clinical Findings:

- Fibroadenoma was commonly seen in younger patients, with surgical management in cases where the lump exceeded 3 cm.
- Duct ectasia cases with single duct involvement were treated conservatively, while those with multiple ducts required surgery.
- Mastalgia was mostly cyclical and managed conservatively.
- Fibroadenosis and physiologic inverted nipple were managed conservatively.

Conservative management was effective for most cases, while surgical intervention was necessary for larger fibroadenomas and symptomatic duct ectasia.

Regular follow-up and patient education on self-examination were crucial in preventing recurrence. Integration of clinical, radiological, and pathological findings ensured accurate diagnosis and effective treatment.

Table 4: Treatment Modalities And Follow Up

Category	Frequency (n)	Treatment	Follow up (weeks)			
			1 st	4 th	12 th	
Fibroadenoma	42	Cx	19	N.R	P.R	P.R
		Sx	23	R	-	-
Duct ectasia	9	Cx	6	v	R	-
		Sx	3	R	-	-
Mastalgia	8	Cx	7	N.R	P.R	R
		NCy	1	P.R	R	-
		Cy	1	-	-	-
Fibroadenosis	3	Cx	3	N.R	P.R	R
		Sx	-	-	-	-
Physiologic inverted nipple	1	Cx	1	N.R	P.R	P.R
		Sx	-	-	-	-

Table 5: Comparison Of ANDI With Research Data

Age group in this study	Age group in ANDI	Category of ANDI	Aberration in ANDI	Finding according to this study
< 20 years	15-25 years	Early reproductive	Fibroadenoma	Fibroadenoma
			Adolescent hypertrophy	Fibroadenosis (nodularity)
			Nipple inversion	Nipple inversion
20-40 years	25-40 years	Mature reproductive	Cyclical mastalgia	Mastalgia (NCy > Cy)
			Nodularity	
			Bloody nipple discharge	
>40 years	35-55 years	Involution	Macrocyts	Duct ectasia
			Sclerosing lesions	
			Duct ectasia	
			Nipple retraction	
			Simple epithelial hyperplasia	

DISCUSSION:

This study highlights the critical role of understanding benign breast diseases in the context of ANDI classification. The findings reveal that BBDs predominantly affect younger women, correlating with hormonal influences during their reproductive years. The consistency in clinical presentations such as palpable lumps and nipple discharge aligns with existing literature, affirming the importance of thorough clinical evaluations to distinguish between benign and malignant conditions.

Furthermore, the significance of ultrasonography and histopathological evaluations in guiding diagnosis was substantiated. The study's results advocate for individualized treatment approaches, emphasizing that a well-structured diagnosis and management plan can enhance patient outcomes.

CONCLUSION

Benign Breast Disease represents a significant component of breast health, contributing to both morbidity and anxiety among affected individuals. This study reaffirms the necessity of utilizing the ANDI framework to guide diagnosis and management strategies effectively. By focusing on clinical presentation, diagnostic methodologies, and treatment outcomes, healthcare providers can better address the complexities associated with benign breast diseases, ultimately

improving patient care and health outcomes. The continued exploration of molecular profiles and advancements in diagnostic techniques will further enhance understanding and management of these conditions. The study highlights the importance of early diagnosis and structured management of benign breast diseases.

Summary

Benign breast disease (BBD) includes various non-cancerous conditions that can significantly affect women's health, yet it is often disregarded despite its prevalence. This study utilizes the Aberration in Normal Development and Involution (ANDI) framework to explore BBD's clinicopathological spectrum, biological mechanisms, and implications for diagnosis and treatment. BBD accounts for about 90% of breast-related clinical presentations, with hormonal factors such as estrogen playing a crucial role in its pathogenesis. The study involved 63 female patients, primarily aged 15-30, with fibroadenomas being the most common diagnosis. A triple assessment approach combining clinical evaluation, imaging, and histopathology was essential for accurate diagnosis. Results showed a favorable 85% symptom resolution rate in follow-ups. The study emphasizes the need for accurate classification and tailored management strategies to optimize patient outcomes and reduce unnecessary interventions, while future research should focus on molecular profiling and the potential progression of high-risk BBD subtypes.

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