



THE BREAST MOUSE: AN OBSERVATIONAL STUDY OF BREAST FIBROADENOMAS IN THE PAKISTANI POPULATION

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ABSTRACT

OBJECTIVE: To assess the characteristics of fibroadenomas and demographics of women presenting with breast masses in order to differentiate such masses from malignant breast masses.

METHODS: This cross-sectional survey was conducted at Khyber Teaching Hospital, Pakistan. Women with breast masses presenting to surgical outpatient department were assessed by taking a thorough history and breast examination, followed by imaging (ultrasound/mammography). Diagnosis was confirmed by fine needle aspiration cytology/core biopsy. Only diagnosed cases of fibroadenomas were included in this study.

RESULTS: Majority (n=93; 70.5%) of fibroadenoma patients were aging from 16-30 years. Seventy (n=70; 53.0%) patients belonged to urban areas. Menstrual cycle was regular in 123 (93.2%) cases. Sixty-four (48.5%) patients were using oral contraceptive pills. Majority (n=79; 59.8%) of patients were nulliparous. Most (38.6%) women presented with a duration of the lump in 1-6 months. Approximately half (n=51; 53%) of patient reported no increase in size. Lump was painful in 77 (58.3%) cases and 34 (74.2%) stated that the pain was acyclical. Lumps were mainly located on left side (n=64; 48.5%) and in upper outer quadrants (n=54; 40.9%) of breast. Mean lump size was 4.05 cm. Only 9 (6.8%) patients reported nipple discharge. Almost all of the patients (n=128; 97%) chose to undergo excision of the fibroadenoma.

CONCLUSION: Fibroadenomas are a common presentation in women presenting with breast masses in the surgical outpatient department, most frequent in women aging 16-30 years and nulliparous. There is a strong predominance in the left breast in the upper outer quadrant.

KEYWORDS: Fibroadenoma (MeSH); Breast Neoplasms (MeSH); Benign Breast Diseases (Non-MeSH); Pakistan (MeSH)

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INTRODUCTION

Breast masses are a frequent presentation in the Surgical OPD, of which most are found to be benign. The most common of these masses, fibroadenomas, were first acknowledged as being benign by Sir Astley Cooper.¹ Fibroadenomas are a proliferation of stromal and epithelial cells and the most common cause of breast mass in women below the age of thirty years, followed by cystosarcoma phyllodes and fibrocystic disease of the breast.²

A study in India has shown that fibroadenomas are the most common cause of breast masses followed by

adenosis and inflammatory diseases.³ The incidence of benign breast disorders is 1.5/1000 hospital admissions; however, no accurate data is available regarding fibroadenomas in Pakistan. Although, a lot of work has been done on malignant breast masses in Pakistan, there are no studies that map out characteristics of fibroadenomas of the breast.

Though rare to see a fibroadenoma convert into a malignancy, it is seen in the past that there is a small chance of this occurring (0.0002 to 0.0125%).⁴ The risk of missing carcinoma breast under the age of 25 in young females having been diagnosed with fibroadenomas ranges from 1 in 229 to 1

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in 700.⁵ This further emphasizes the need to properly diagnose a breast mass as fibroadenoma, and differentiate it from a malignancy, so the management can be planned out accordingly and the patient's anxiousness regarding a breast mass may be addressed appropriately. However, for this to be implemented, accurate data in relation to fibroadenomas must be present.

All around the world, awareness regarding breast masses is increasing and is necessary to differentiate between benign and malignant masses for which a better understanding of the presentation of such masses is needed particularly, locally in the Southeast-Asian region. The importance of this lies in the fact that the ethnicity, socioeconomic status, healthcare, education and awareness vary drastically, not only from the Western countries but within rural and urban areas of Pakistan itself. Large amounts of studies have been carried out on malignant breast masses, albeit not many descriptive studies are present regarding benign breast masses, particularly fibroadenomas.⁶ Although, some local data is available stating that the left sided breast and upper outer quadrant is the common site of the fibroadenoma of the breast,⁷ no work has been done defining the demographics of women and further characteristics of a breast fibroadenoma. In this study we aim to identify the demographics and patient history associated with breast fibroadenomas presenting in a surgical

TABLE I: DEMOGRAPHICS OF PATIENTS AND THEIR RELATIVE PREVALENCE

Fibroadenoma Features	Diagnosis	No. of Patients (n=132)	Percentage (%)
Age (years)	0-15	6	4.5
	16-30	93	70.5
	31-45	24	18.2
	46-60	5	3.8
	61-75	4	3
Address	Urban	70	53
	Rural	62	47
Marital Status	Married	66	50
	Unmarried	66	50
Family History of Breast Disease	History of Carcinoma Breast	7	5.3
	Not significant	121	91.7
	History of Breast lumps	4	3
Menstrual History	Regular Cycles	123	93.2
	Irregular Cycles	4	3
	Menopausal	5	3.8
Past History	Excision/Lumpectomy Same Side	1	0.8
	Excision/Lumpectomy Opposite Side	1	0.8
	Other surgeries	13	9.8
	None	117	88.6
Oral Contraceptive Use	Absent	68	51.5
	Present	64	48.5

outpatient department in a tertiary care hospital along with the characteristics of these fibroadenomas.

METHODS

This observational, cross-sectional study was carried out from January 2015 to January 2016, in the outpatient department of Surgical D unit, Khyber Teaching Hospital, Peshawar, Pakistan. Khyber Teaching Hospital is a Tertiary Care Hospital in the urban city of Peshawar, Pakistan, where a large number of patients are received from both the urban as well as rural population.

Female patients, aging 13 years and above who had a palpable lump for a duration of at least one month, presenting to Surgical OPD were selected in this study through nonprobability, consecutive sampling technique. Patients with a past history of carcinoma breast were excluded. Informed consent was taken from all participants of the study.

All patients with breast masses were

assessed following the principles of Triple Assessment which comprises of a thorough history, breast examination, followed by imaging (ultrasound/mammography) and confirmation of the diagnosis by fine needle aspiration cytology (FNAC)/Core biopsy.

Subjects were evaluated using proformas after taking a verbal informed consent (patients who did not feel comfortable were excluded from the study). Proformas consisted of sections assessing the patients age, marital status, parity, use of oral contraceptives, rural or urban background, duration of symptoms, site and size of lump, number of lumps, nipple discharge, past surgical history, and family history. Menstrual history was also recorded and pre-menstrual and post-menstrual symptoms were also inquired about. Proformas were handed out to all surgical trainees on call in the outpatient departments where each of these were filled by a trainee medical officer. It was emphasized that marital history was taken into account not only because it affects the

socioeconomic status but also because Pakistan being an Islamic state parity can mostly only be linked to the married.

Examination was carried out to confirm the site, size, mobility, tenderness and number of breast lumps. Special care was taken to note any nipple discharge, inversion, or retraction. This was accompanied by a full examination of the axillary lymph nodes. Patients were then advised imaging as needed. Confirmatory diagnosis was made on obtaining the report of FNAC, core biopsy or excision biopsy. Of the various cases of breast masses that presented to the outpatient department, only those diagnosed as fibroadenomas by FNAC, core needle biopsy or excision biopsy were finally included in this study.

Evaluation of the clinical and pathological features of fibroadenomas was done in all recruited patients. Patients were followed up after surgery at an interval of one and two weeks afterwards (two follow-up visits). Patients who opted for conservative treatment were not followed.

In order to measure the objectives, the collected data was subjected to analysis. Frequency of fibroadenomas was determined amongst all the presenting breast masses. Characteristics such as age, size and duration were determined within ranges. Percentages of the side and quadrant of breasts affected and their features such as mobility, associated lymph node enlargement, pain, and nipple discharge were calculated. Final diagnosis and method of diagnosis were also determined. Results were analyzed using SPSS version 22.

RESULTS

A total of 132 cases were confirmed as fibroadenomas and were finally included in this study. The majority of the patients diagnosed with fibroadenoma were in the age group of 16-30 years (n=93; 70.5%). Approximately half (n=70; 53.0%) of the women belonged to the urban area. A small number (n=7; 5.3 %) of patients had a family history of carcinoma of the breast. Menstrual cycles were normal in the majority (n=123; 93.2 %) of the patients with 3.8 % of the patients being menopausal.

TABLE II: CHARACTERISTICS OF FIBROADENOMAS

Fibroadenoma Features	Diagnosis	No. of Patients (n=132)	Percentage (%)
No. of Lumps	1	119	90.2
	2	9	6.8
	4	4	3
Duration of Lump (months)	< 1	5	3.8
	1-6	51	38.6
	7-12	23	17.4
	13-36	22	16.7
	37-60	9	6.8
	61-71	7	5.3
	>72	15	11.4
Increase in Size	Present	62	47
	Absent	70	53
Pain	Present	77	58.3
	Absent	55	41.7
Cyclical Pain	Present	34	25.8
	Absent	98	74.2
Tenderness	Present	29	22
	Absent	103	78
Side	Right	51	38.6
	Left	64	48.5
	Bilateral	17	12.9
Location	Upper Outer	54	40.9
	Upper Inner	18	13.6
	Lower Outer	19	14.4
	Lower Inner	15	11.4
	Central	8	6.1
	Multiple Sites	14	10.6
	All quadrants	4	3
Size (cm)	<2	40	30.3
	2-5	59	44.7
	6-10	15	11.4
	11-20	9	6.8
	>20	9	6.8
Mobility	Present	124	93.9
	Absent	8	6.1
Nipple Discharge	Present	9	6.8
	Absent	123	93.2
Palpable axillary lymph nodes	Present	6	4.5
	Absent	126	95.5
Diagnosis	FNAC	70	53
	Core Biopsy	29	22
	Excision Biopsy	33	25
Imaging	Ultrasound/Mammogram	86	65.2
Treatment	Conservative	4	3
	Excision	128	97

Around half the women (n=68; 51.5 %) had no history of use of oral contraceptive pills use (Table I).

Out of 132 patients, 119 (90.2%) presented with a single breast lump

(Table II). Most women presented to the outpatient department with a duration of the lump being 1-6 months (n=51; 38.6%). No increase in size was reported by seventy patients (53

%), whereas 77 (58.3 %) patients found the lump painful, of which 74.2 % stated that the pain was acyclical and had no relation to the menstrual cycle. Of these painful masses, only 28 (21.2 %) were tender on examination. A predominance (n=64; 48.5 %) was found on the left sided breast. Majority (n=54; 40.9%) of breast lumps lied in the upper outer quadrant followed by lower outer quadrant (n=19; 14.4 %). The sizes of the fibroadenoma were mainly in the range of 2-5 cm (n=59; 44.7%) followed by 30.3% (n=40) having a size less than 2 cm. Mean size of the lump was 4.05 cm. Most (n=124; 93.9%) of these lumps were mobile. Majority (n=123; 93.2 %) of the women had no nipple discharge or axillary lymph nodes palpable (n=126; 95.5%).

Almost half the patients (53%) were diagnosed via FNAC whereas 22 % were diagnosed through core biopsy (as malignancy was suspected in these cases), rest being diagnosed through excision biopsy. Of these patients 65.2 % had undergone imaging prior to invasive investigations. Almost all the patients (n=128; 97 %) chose to undergo excision of the fibroadenoma (Table II). Nulliparity was seen as a common factor (n=79; 59.8 %) amongst the subjects (Table III).

DISCUSSION

Fibroadenomas are a frequent cause of breast masses both internationally and in the national population.^{8,9} Being the most common cause of a benign breast mass, fibroadenomas are seen to be frequent amongst women of ages 16-30 years as corroborated by Kalim et al (15.5 years to 31 years for Pakistani population).⁷ A large Pakistani study, however, comprising of over three thousand patients found fibroadenomas to be the second largest benign breast disorder.⁹ The age range of 16-30 years for fibroadenomas may be linked to the dependency of these tumors on hormones, as one of the key factors to the development of fibroadenomas is considered an excess of estrogen.¹⁰

According to previous studies by Hanna and Ashebu and Gogo-Abite, giant fibroadenomas are a common finding in puberty and a greater incidence is seen

TABLE III: PARITY AMONGST STUDY SUBJECTS

Parity	Frequency (n=132)	Percentage (%)
0	79	59.8
1	18	13.6
2	6	4.5
3	6	4.5
4	6	4.5
5	8	6.1
6	4	3.0
7	2	1.5
8	2	1.5
10	1	.8

amongst married women and multiparous women in their second and third decades of life.^{11,12} Fibroadenomas are more frequently seen in women living in urban areas and women of higher socioeconomic status,¹³ as they are more likely to have a broader knowledge of the diseases due to greater exposure to media and literacy and thus are more likely to present to the clinics.

Although Canny, et al have briefly mentioned oral contraceptives to possibly contribute to the pathogenesis of Fibroadenoma formation; there is no definite evidence.⁴ Results from our study can neither confirm nor deny these as approximately half of the patients did have a history of use of oral contraceptives. Predominance was seen in the left sided breast which is in accordance with Rimstein's study.¹⁵ Local data also supported this finding.⁷ Data from a recently conducted study in Saudi Arabia however indicated a predominance of fibroadenomas detected in the right breast.¹⁶ The majority of the fibroadenomas were found in the upper outer quadrant. This finding is supported by Oluwule G. Ajao in his study of benign breast lesions in 1979.¹⁷ The results of our study also reiterate these findings.

Fibroadenomas are most commonly discovered via self-examination or medical examination, and are usually about 1-2 cm in size.¹⁶ They range from 1 cm to over 20 cm. Fibroadenomas over 5 cm are usually considered giant fibroadenomas however this is not universally accepted. Giant fibroadenomas are usually said to be found in pregnant or lactating mothers due to an increased surge of estrogen.

Giant juvenile fibroadenomas are more common in the African American ethnicity and are attributed to the sudden surge in estrogen at this stage. These are uncommon in the Asian population with the first of its kind being reported recently in a teenage girl in Pakistan.¹⁸ According to Pike et al, these are rarely seen to undergo malignant transformation.¹⁹

Alamri et al in their study of the Middle Eastern population determined that the majority (95%) of the women diagnosed with fibroadenomas present with the complaint of a breast mass with pain in only one third of the patients, nipple discharge in 3.9 %, palpable axillary lymph nodes in one-third, and size less than 2 cm in 37.5 % of the females. More than two thirds of the females were married and only one third were multiparous.¹⁶ This is in contrast with the Pakistani population we studied in which approximately two thirds of the patients had pain as a presenting complaint and more than ninety percent women had no nipple discharge or palpable lymph nodes.

Fibroadenomas may undergo variable changes over time, including regression, increase in size and progression to malignancy or may remain the same size.²⁰ Conservative treatment has been tried in which progesterone and danazol have been employed to cause regression as it is thought the estrogen surge leads to fibroadenoma formation, however it is seen that fibroadenomas fail to respond to these.²¹ Greenblatt et al limits excision to patients who fail to respond to conservative treatment of wait and watch (which means waiting until there is a gross change in the size, shape or growth of the mass) as most

fibroadenomas will regress after menopause.²² In patients who did not benefit from long term conservative treatments, thereby leading to anxiety, were treated surgically with excision as surgical treatment is the definite treatment. Most fibroadenomas were excised through simple excision whereas simple mastectomy was employed for giant fibroadenomas.

Fibroadenoma excision through circumareolar incision was the preferred method in our study which offers a much better result cosmetically and aesthetically.²³ This allows the scar to be hidden by the darker area of areola. FNAC was used to distinguish between benign, malignant, solid and cystic masses as it is a fast, accurate and inexpensive method.²⁴ FNAC comprises 50 % of all breast biopsies and about 75 % of all biopsies in women under the age of 20 years. About 22 % of patients were diagnosed via excision biopsy which is considered the gold standard. The risk of a fibroadenoma converting to malignancy is 3.1 annual incidence per thousand, person-year rate and the relative cancer risk is at 7.0.²⁵

A study carried out to delineate the features of a Fibroadenoma and its relation to conversion to a malignancy lead to the coining of the term 'complex Fibroadenoma'.²⁶ A complex fibroadenomas is one with a diameter > 3 mm in diameter, or with elements of sclerosing adenosis, epithelial calcifications, or papillary apocrine metaplasia,²⁷ which were associated with an elevated risk of 3.1 for developing breast cancer. Adjacent parenchyma showing proliferative changes increases the risk to 3.88, whereas a family history of carcinoma breast and complex Fibroadenoma increases the relative risk to 3.72 compared to women with a family history of breast cancer with no fibroadenomas. Women with no family history and no complex fibroadenomas were not found to have a higher risk of developing carcinoma breast.

The overall risk of developing a malignancy remains low in women below 35 years and thus it is advised that regular assessment be done until this age after which excision can be done.

Some other studies indicate that excision should be done at the age of 25 years to avoid complications.²⁸ Presence of data specific to the population in Pakistan can help formulate guidelines particular to the region. Developing guidelines will mainstream the management of fibroadenomas not only in Pakistan but in the whole South Asian region as no data specific to the region is available currently.

CONCLUSION

Fibroadenomas are a common presentation in women presenting with breast masses in the surgical outpatient department most frequently presenting in the ages 16-30 years and an average age of 27 years. There is a strong predominance in the left breast in the upper outer quadrant. Fibroadenomas have a higher incidence in married women of urban areas. FNAC is the most accurate and timely method to diagnose fibroadenomas however excisional biopsy remains the gold standard. Although conservative treatment may be given, surgical excision is the preferred method of treatment particularly in older women to avoid missing a possible malignancy. Early detection and identification of fibroadenomas with the help of characteristics indigenous to the Pakistani population can help differentiate it from malignant and premalignant conditions of the breast in the region. This will improve clinical detection of fibroadenomas in the outpatient department and alleviate patients' concern regarding a breast mass

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

TH: Concept and acquisition of data, drafting the manuscript, approval of the final version to be published.

MMK: Concept and study design, analysis and interpretation of data, critical review, approval of the final version to be published.

RH: Analysis and interpretation of data, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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