1	Original Research Article										
2 3 4	Cytological Features of Fine Needle Aspiration of Breast lesions										
5 6 7 8	ABSTRACT										
	<b>Background:</b> This study aimed at registering the fine needle aspiration cytology (FNAC) of breast lesions cases received by the pathology department in kasr elaini hospital in the last 3 years ( jan 2010 – dec 2012 ). one hundred and three cases were collected.										
	<b>Aims:</b> Revision of all available archival material of Fine Needle Aspiration Cytology of breast lesions in the last 3years (Jan 2010- Dec 2012), collected from the pathology department, faculty of medicine, Cairo University Hospital. Statistical analysis to correlate between clinical and patient data available in the request sheets, in one hand, and the pathological findings of value, on the other hand. Evaluate incidence of different pathological diagnoses for patients, in Cairo University Hospital, during this period.										
	Study design: Cytological and A Retrospective Statistical.										
	<b>Place and Duration of Study:</b> Department of Pathology, Cairo University Hospital Revision of all available archival material of Fine Needle Aspiration Cytology of breast lesions in the last 3 years between Jan 2010- Dec 2012.										
	<b>Methodology:</b> Slides and data will be collected from the archives of the pathology department, Faculty of medicine, Cairo University Hospital during the 3 year period between Jan 2010- Dec 2012.										
	<b>Data required from the pathology sheet is:</b> Age, gender of patients diagnosed to have any breast lesion (neoplastic & non neoplastic lesions), as well as any available mammography and the final cytological diagnosis. Slides will be revised for the cytological features which favored such diagnosis.										
	<b>Results:</b> In the survey of fine needle aspiration cytology (FNAC) of breast lesions in the pathology department of Kasr El-Aini Hospital during the period from January 2010 till December 2012, 201 cytologically documented cases were analyzed. The age range was from 12 to 86 years, the mean age of the sample was 42.85 years. The minimum mass size value was 0.5 cm and the maximum mass size value was 11 cm. The mean of the mass size was 3.8 cm and 199 were females, opposing 2 males.										
	<b>Conclusion:</b> This work may be put as a nidus for a nation wide registery of FNAC diagnosis for different breast lesions in different governorates, and compare between differences in the percentages of each diagnosis category whenever encountered.										
9 0 1	Keywords: Fine Needle Aspiration Cytology										

### 14 **1. INTRODUCTION**

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16 Fine-needle aspiration (FNA) cytology is a popular technique used in the evaluation of breast masses 17 due to its advantages of being sensitive, specific, simple, economical, safe, guick and acceptable to the patients. It is commonly used in addition to clinical examination, mammography, ultra-sonography 18 19 magnetic resonance imaging (MRI) spectroscopy, for the diagnosis of breast lesions 20 [10].Recognizing that the majority of breast lesions are benign (fibro-adenos is, fibrocystic changes, 21 fibro-adenomas, fat necrosis, peri-ductal mastitis, duct-ectasia, granulomatous mastitis, hematoma, 22 abscess ... etc), open biopsy will be inconvenient & costly [10]. Only a small fraction of the patients, 23 who are clinically or radiologically or cytologically suspicious of malignancy, undergo histopathological 24 examination [4]. Nevertheless, in FNAC of breast lesions, there are instances where the differentiation 25 of benign and malignant is not possible. This problem arises when paucity of specimen sampling is 26 encountered or there is a morphological overlap between benign and malignant lesions (e.g., atypical 27 hyperplasia and low-grade carcinoma in situ, or in papillary lesions). As a result and to accommodate 28 these problematic areas, cytological reporting categories are used to objectively describe their 29 features in cytological terms and to incorporate the groups with uncertainties. The most commonly 30 used categorization is a five-tier system, with categories ranging from insufficient materials (C1), 31 benign (C2), atypical (C3), suspicious of malignancy (C4), or frankly malignant (C5) [14]. According to 32 the different Authors , sensitivity of FNAC of breast lumps varies from 87% to 99%, 33 specificity ranges from 56% to 100%, positive predicative value from 76% to 99%, and 34 predicative value from 85% 99% [11]. negative tο [17]and

# 35 2. MATERIAL AND METHODS

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This work included two hundred and one cases of fine needle aspiration cytology smear and
related data for each case obtained through collection of all archived cases of the pathology
department, Faculty of medicine, Cairo University Hospital, during the 3 year period between
January 2010 - December 2012.

i) Data collected from the pathology sheet include age, gender of patients diagnosed to have any
 breast lesion (neoplastic and non-neoplastic lesions), size of the mass, as well as any available
 mammographic data and the final cytological diagnosis.

44 ii) Smears will be revised for the cytological features which favored such diagnosis.

45 iii) the diagnoses will be categorized with categories ranging from insufficient materials (C1), benign
 46 (C2), atypical (C3), suspicious of malignancy (C4), or frankly malignant (C5) [24].

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# 48 Statistical analysis will be conducted:

i) To evaluate incidence of different pathological diagnosis for patients during this timeinterval.

ii) To evaluate a possible relationship between Fine Needle Aspiration diagnoses of the
 different breast lesions and age, gender , sizes of the mass or any available clinical
 pathological data.

54 iii) Statistical analysis will be conducted using SPSS version 15.0 (Statistical Product for55 Services Solutions).

iv) Data will summarized using number and percentages for qualitative variables, while for
 the quantitative variables, the mean; standard deviation; and range will be used and chi
 square test will be used to detect the correlation between the two variable.

# 59 3. RESULTS AND DISCUSSION

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# 64 **3.1** distribution and measures according to sex, age , mass size and diagnosis

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# 66 <u>3.1.1 Sex distribution for all cases:</u>

The majority of cases were females, 199 were females, opposing 2 males (Table 1).

### 68 Table 1.Sex distribution of all cases

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Sex	Frequency	Percent
Male	2	1%
Female	199	99%
Total	201	100%

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## 71 **3.1.2 Age range and distribution for all cases:**

72 We used intervals of 10 years, each starting from age of 10 years. Approximately one-third of the

sample (35%) in the age group 40-50 years. Few individuals are in the age groups; under 20 years

and above 70 years old. In general, the age distribution is fairly symmetric.(Table 2)(Graph 1).

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# 79 Table 2. Age measures

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Measure	Value
Mean	42.85
Median	44.00
Variance	156.041
Std. Deviation	12.492
Minimum Maximum Range	12 86 74

Graph 1. Histogram of age distribution

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#### 83 3.1.3 Mass size range for all cases

84 The majority of individuals have mass size of 3 cm (18.4%). The least mass sizes were 0.5 cm, 1.4 85 cm , 4.2 cm , 4.5 cm , 5.5 cm and 11 cm , each represent 0.5% of individuals. In the same time, most of individuals have mass size between 2 cm and 5 cm , approximately 76% of the individuals. (Table 86 87 3)(graph 2).



### Graph 2. Histogram of the mass size

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#### 93 94

# Table 3. Mass size measures

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Measure	Value
Mean	3.809
Median Variance Std. Deviation Minimum Maximum Range	3.500 3.565 1.8881 0.5 11.0 10.5

#### 96 3.1.4 Categorization of cases in accord to diagnosis:

The majority of the sample is diagnosed as C2 (59.2%). The least percentage 3.0% of the sample is
diagnosed as C1. We can rank the diagnosis in an ascending order of occurrence as C2 (59.2%).
then C5 (17.9%) then C3 (15.4%) then C4 (4.5%) and last C1 (3.0%) (graph3).

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#### Graph (3): Diagnosis frequency for all cases

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# 104 **3.2 Evaluation of clinico-pathological parameters:**

# 105 3.2.1 Evaluation of clinico-pathological parameters with C1 :

106 The number of cases in C1 was 6 cases (3% of total).

i) Relation to age : The age ranged from 42 years old to 60 years old with mean 49.67 years.
 There was no great variation since the standard deviation was a small
 value. The disease was evenly distributed to the two groups of age 40-50 and 50-60 years
 old

ii) Relation to mass size: The mass size for C1 had only three values 1, 2 and 6 cm. The value 1
 was the most common with 50% out of 6 cases. The mean value was 2.167 cm.

113 iii) Relation to sex : All individuals of C1 were females (100%).114

# 115 **<u>3.2.2 Evaluation of clinico-pathological parameters with C2 :</u>**

The number of cases in the C2 group was 119 cases. The distribution with respect to age, mass size and sex was as follows.

i) Relation to age : The age of cases ranges from 12 to 65 years old. The most common age
 group was 40-50 years old with 38 cases out of 119 cases (31.9%). The least common age
 group was 10-20 years old with 3 cases out of 119 cases (2.5%). The mean age was 40.32
 years.

122 ii) Relation to mass size: The mass size ranges from 0.5 cm to 11 cm. The mean mass size
123 was 3.478 cm. The most common mass sizes were 2 cm and 3 cm comprising 21%
124 approximately of the cases. From the graph the distribution of the mass size was positively
125 skewed; few cases with higher values of mass size. On the other hand many cases with
126 smaller values of mass size.

iii) Relation to sex : All the cases were female (100%).

## 128 **3.2.3 Evaluation of clinico-pathological parameters with C3 :**

129 There are 31 cases in the group of C3 (15.4% of total cases).

i) Relation to age: The age of patients ranges from 21 years to 72 years. The most common age category of C3 patients was 40-50 years; 12 out of 31 cases (38.7%). The least common age group was 60-80 years. The mean age was 43.32 years with standard deviation of 11.07 years. The age distribution was skew to the right; many individuals in the young age.

ii) Relation to mass size: The mass size ranges from 1.5 cm to 10.0 cm. The mean mass size
was 4.2 cm with standard deviation of 1.64 cm, which means there was no great variation.
The mass size distribution was almost symmetric. The most common mass size was 4.0 cm

- 138 with 10 cases out of 31 cases (32.3%).
- 139 iii) Relation to sex: All the 31 cases are females (100%).
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# 141 <u>3.2.4 Evaluation of clinico-pathological parameters with C4 :</u>

142 There were 9 cases in this group (4.5% of total cases).

i) Relation to age: The age of patients ranges from 29 years to 61 years. The most common age category of C3 patients was 40-50 years with 3 cases out of 9 cases (33.3%).and the age group 50-60 years with 3 cases out of 9 cases (33.3%). The mean age was 47.78 years with standard deviation of 10.872 years. The age distribution was skew to the left; many individuals in the older ages.

ii) Relation to mass size: The mass size ranges from 2 cm to 6 cm. The mean mass size
was 3.944 cm with standard deviation of 1.38 cm, which means there was no great variation.
The mass size distribution was negatively skewed. There were many small mass size
values. The most common mass size was 5.0 cm with 3 out of 9 cases (33.3%).

iii) Relation to sex: The C4 diagnosis was dominated by females. The females were 8
 patients out of 9 (88.9%). There was only one male out of 9 cases.

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## 155 **3.2.5 Evaluation of clinico-pathological parameters with C5 :**

156 There were 36 cases in this group (17.55 of total cases).

**i) Relation to age:** The age ranges from 27 years to 86 years old. The mean age was 48.42 years with standard deviation 13.31, which means there was great variation. The age distribution was positively skewed; there were few cases of older ages. The most common age was 40-50 years with 15 out of 36 cases (41.7%). The least common ages were the older ones ranging from 70 - 90 years.

ii) Relation to mass size: The mass size ranges from 2 cm to 10.0 cm. The mean mass size was 4.806 cm with standard deviation of 2.13 cm, which means there was no great variation. The mass size distribution was positively skewed; few cases with great mass sizes. The most common mass size was 5.0 cm with 5 out of 36 cases (13.9%) and 6.0 cm with 5 out of 36 cases (13.9%).

iii) Relation to sex: Females dominate this group of patients. The females were 35 out of 36 patients (97.22%). There were only one male out of 36 cases.

# 169 3.3 Clinico-pathological parameters and correlations with FNAC diagnosis

#### 170 **3.3.1 Correlation between age & diagnosis**:

We can rely on Chi-Square test to inspect the correlation between age and diagnosis because
diagnosis was nominal variable. From the results we conclude that there was highly non-significant
relationship between age and diagnosis because p-value = 0.460 which was greater than 0.05 (Table
4).

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#### Table 4. Relation of fine needle diagnosis with age

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	NUMBER	Cases within 10-20	20-30	30-40	40-50	50-60-	02-09	70-80	90-80	MEAN	median	SD	Lowest age	Highest age
C1	6	-	-	3	-	3	-	-		49.67	49.50	6.653	42	60
C2	119	3	30	26	38	18	4	-		40.32	41.00	12.124	12	65
C3	31		5	7	12	5	1	1		43.32	45.00	11.703	21	72
C4	9		1	1	3	3	1	-		47.48	50.00	10.872	29	61
C5	36		3	6	15	7	3	1	1	48.42	47.00	13.315	27	86
Total No.	201	3	39	43	68	36	9	2	1	·		·	-	_

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#### 3.3.2 Correlation between sex & diagnosis: 185

Sex and diagnosis both were nominal variables. Hence, we can use Chi-square test to detect the 186 correlation between the two variables. From the results we see that the P-value was 0.017 which 187 188 is smaller than 0.05. Hence, we can conclude that there was significant relationship between female sex and diagnosis (Table 5). 189

#### 190 Table 5. Relation of fine needle diagnosis with sex

_		NUMBER	М	F	М %	F %
	C1	6	_	6	0 %	100 %
	C2	119	-	119	0 %	100 %
	C3	31	-	31	0 %	100 %
	C4	9	1	8	11.1 %	88.9%
	C5	36	1	35	2.78 %	97.22 %
	Total number	201	2	199		

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#### 192 3.3.3 Correlation between mass size & diagnosis:

193 We use the Chi-Square test. The results were in Table (10). From the table there was non-significant 194 relationship between mass size and diagnosis (Table 6).

195 97	Table 6	Relat	ion of f	ine n	مالم	diadn	neiev	1 with	96 <b>mass</b>	size								
		NUMBER	Cases within 0.5-1	1-2	59 <u>00</u> 7 7	61191 4- 6	4-5	5-6	2-6 7	2-8	8-9	9-10	10-11	MEAN	median	SD	Minimum size	Maximum size
	C1	6	3	2	-	-	-	1	-	-	-	-	-	2.167	1.500	1.9408	1	6
	C2	119	7	29	32	21	18	5	3	2	1	-	1	3.478	3.000	1.7686	0.5	11.0
	C3	31	-	4	4	11	8	2	1	-	-	-	1	4.200	4.000	1.6911	1.5	10
	C4	9	-	1	3	-	4	1	-	-	-	-	-	3.944 4	4.000	1.379	2	6
	C5	36	-	-	5	5	5	7	7	1	4	1	1	4.806	4.000	2.1323	2.6	10.0
	Total number	201		36	44	37	35	16	11	7	5	1	3					

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199 According to this study, The mass size of all cases ranged from 0.5 cm to 11cm, the majority of 200 individuals have mass size of 3 cm (18.4%). The least mass sizes were 0.5 cm, 1.4 cm, 4.2 cm, 4.5 201 cm, 5.5 cm and 11 cm, each represent 0.5% of individuals. In the same time, most of individuals had 202 mass size between 2 cm and 5cm, approximately 76% of the individuals. The mean of the mass 203 size was 3.8 cm means a typical mass index value may be 3.8 cm. The median mass size was 3.5 cm 204 means that 50% of individuals have mass size less than 3.5 cm.our findings were nearly similar to that 205 obtained by [14]. who found that the breast lesions ranged in size from 1 cm to 12 cm, the mean of 206 mass size was 4.4 cm). [17]. stated that primary The tumour size was 1.5 cm to 11 cm with, the mean 207 average of 4.1 cm.

208 So,the mass size of C2 diagnosis in our study ranged from 0.5 cm to 11 cm. The mean mass size was 209 3.478 cm. The most common mass sizes were 2 cm and 3 cm. And in C5 diagnosis cases, the mass 210 size ranges from 2 cm to 10 cm. The mean mass size was 4.806 cm . The most common mass size 211 was 5 cm with 5 out of 36 cases (13.9%) and 6 cm with 5 out of 36 cases (13.9%). So the diagnosis of 212 malignancy increased as tumor size became larger.

in C5 diagnosis cases, the mass size ranged from 2 cm to 10 cm. The mean mass size is 4.806 cm.
 in our findings nearly in agreement with [3]. who reported that the number of positive and suspicious
 aspiration results increased as tumor size became larger.

Female breast cancer incidence is strongly related to age, with the highest incidence rates in older women, supporting a link with hormonal status. By the age of 50 around 10,000 women were diagnosed with breast cancer (in the UK in 2010), but 80% of all diagnoses were in the over 50 and 45% were diagnosed in women aged 65 and over (in the UK between 2008 and 2010 [6].

Age-specific incidence rates rise steeply from around age 35-39, level off for women in their 50s, then rise further to age 65-69 years, drop slightly for women aged 70-74 years, then increase steadily to reach an overall peak in the 85+ age group [4].

223 In this study, the minimum age was 12 years and the maximum age is 86 years. The mean age of the 224 sample was 42.85 years. C2 cases ranged in age from 12 to 65 years old and the mean age was 225 40.32 years. As regards the age in C2 diagnosis[17]. mentioned that in benign conditions C2, the 226 age varied from 16 to 65 years with mean of 34.8 .our results nearly coincide with the results 227 obtained by [30]. in a retrospective study of over 300 referrals in Sheffield they found that the ages of 228 the women ranged from 16 to 85 years with a mean and median age of 45 years of 180 (60%) and 229 were diagnosed as having benign breast disease C2. On the other hand ,our results were not in 230 agreement with that obtained by [18]. who found thate the benign breast lesions C2, was accounting 231 for 556 (17%) of all cases and the mean age at diagnosis was 27 years [18].

In our study, the 36 cases with C5 diagnosis had age range between 27 years to 86 years old. The mean age was 48.42 years. These finding were nearly similar to that obtained by [14]. who mentioned that in malignant condition C5, the patients ranged in age from 28 to 86 years (mean 51 years). which were also supported by [17]. who revealed age range from 24 to 80 years with mean of 42.3 years in malignant breast lesions. Also [18]. in their study of 3279 cases, cancer breast cases constituted 37% with mean age of 49 years. In contrast to these findings, aslightly higher mean age was recored by [33]. which was 54 years.

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Figure 1. Branching sheets of cohesive ductal epithelial cells (staghorn appearance)

surrounding by stromal and myoepithelial cells (C2) H&E Stain px200

# UNDER PEER REVIEW



# **4. CONCLUSION**

253 1-FNAC is a simple , economical , safe , quick and acceptable to patients, and can be performed with

Figure 3. Malignant sheet and individual cell (C5) px200 H&E Stain.

- 254 little complications.
- 255 2-FNAC is a valuable tool in preoperative assessment of breast masses ,to differentiate benign from
- 256 malignant lesions.

3-Classification of FNAC of breast lesions according to five-tier system, with categories ranging from
 insufficient materials; C1, benign; C2, atypical; C3, suspicious of malignancy; C4, or frankly
 malignant; C5. Can serve as acommon dialect amonge all professionals involved in breast
 management.

4-For proper evaluation of breast masses, triple test with assessment of clinical and radiological
 findings has to be established.5-This work may be put as a nidus for a nation wide registery of FNAC
 diagnosis for different breast lesions in different governorates, and compare between differences in
 the percentages of each diagnosis category whenever encountered.

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