Efficacy of Fine-Needle Aspiration Cytology in Diagnosis of Breast Tumors and Correlation with Histopathological Findings: An Al Galaa Teaching Hospital Experience

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Abstract: Background: In many countries, fine-needle aspiration cytology (FNAC) is the most common useful tool for breast lump diagnosis. In Egypt, however, breast FNAC plays an important role in breast mass assessment. In this retrospective study, we tried to evaluate the validity of its performance in Al Galaa teaching hospital, by comparing the FNAC with the corresponding definitive histological examination results. **Material and Methods:** This study included a total of 375 consecutive breast masses. Each FNAC was classified into one of four categories: inadequate 1.3%, benign 56%, atypical/suspicious 25.3% (indeterminate), and malignant 17.3%. Sensitivity, specificity, positive predictive values, and negative predictive values were 94.4%, 84.6%, 98.8%, and 91.7%, respectively. **Conclusion:** Breast FNACs compare very well with excisional biopsies histology and are extremely useful in managing breast lumps in experienced hands. Therefore, we concluded that FNAC in our hospital is a reliable breast lump diagnostic tool. We advise that clinicians should continue to promote this diagnostic approach in the surgical management of breast lumps as a fast and cheap diagnostic tool, as highlighted by previous studies.

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Introduction

Breast cancer is the most common type of cancer among women worldwide, and the second most common type recorded. There were about 1.7 million recent cases discovered in 2012 (Mane *et al.*, 2017). The most frequent breast disease presentation is a breast lump. Although most cases of breast lumps are benign, they cause concern about achievable malignancy. Preoperative diagnosis helps to plan the correct surgery and therapeutic treatment (Ferlay *et al.*, 2014). In Egypt, breast FNAC continues to thrive and plays a significant role in the evaluation of breast masses as it's a cost-efficient and an effective diagnostic procedure. According to (NCI) guidance in 1996 (Abdel-Hadi *et al.*, 2010). Though histopathological diagnosis is universally accepted confirmatory method to the identification and follow up, FNAC of breast lumps is a valuable part of triple assessment (Clinical examination, radiologic, and FNAC) of detectable breast lumps (Garber and Cure, 2013).

Additionally, FNAC offers advantages such as less invasiveness, minimal discomfort, and quickness of results when compared with core biopsy (Daramola *et al.*, 2015). FNAC is, therefore, an especially very important tool in the diagnosis of detectable breast lumps in resource-limited settings (Ahmed *et al.*, 2007). Although histopathological diagnoses are universally accepted as a confirmatory method for identification and follow-up, FNAC is a valuable part of the evaluation for detecting breast lumps with clinical and radiological assessments (Garber and Cure, 2013).

The purpose of this study is identifying the value of FNAC in breast mass and to compare its result with a histological diagnosis to assess its accuracy.

Patients and Methods

The material of this work consists of 375 cases of fine needle aspiration of breast masses which were retrieved from Al Galaa Teaching Hospital. This study includes cases from 2014-2018.

A pathologist used a 10-ml syringe and 23 G needle to make fine needle aspirations under aseptic precautions. The needle had been placed inside the lesion and tenderly pulled back the syringe device connected to a vacuum. The needle was moved backward and forward within the lesion and the needle was removed after negative pressure was created.

The sample was smeared on glass slides, for 15 minutes, fixed in 95% ethyl alcohol solution and stained with H&E. All fine needle specimens have been classified into five classes from C1-C5. At least 6 sheets of ductal cells on each smear comprised of 10 cells per sheets were criteria for adequacy.

Cytological diagnoses were then categorized according to the UK National Health Services Breast Screening Program (NHSBSP) recommendations (Guideline 2001) (Table 1).

Category	Cytomorphological findings				
Unsatisfactory(C1)	Scant cellularity, smearing artifacts,				
	obscuring blood, or inflammation				
Benign (C2)	No evidence of abnormalities				
Atypical/ indeterminate (C3)	Cellular findings are not diagnostic, and				
	should be correlated with clinical and				
	mammographic data				
Suspicious/probably malignant (C4)	Findings are suggestive but not				
	unequivocally diagnostic of cancer				
Malignant/ positive (C5)	Conclusive evidence of cancer				

Table 1. Categories of cytological diagnosis according to the modification of the National Health Breast (NHB) reporting criteria

The biopsy specimens were fixed for twenty-four hours in 10 percent formalin for histopathology. Then grossly examined by histopathology consultant in the pathology department. The findings of the gross and cut section have been noted. Few bits were processed and paraffin embedded from suitable sites.

From each block, serial sections were taken at a thickness of 4-5 μ m and stained with H&E. Relating microscopic findings from excisional biopsy (lumpectomy) or mastectomy specimens were associated with FNAC findings.

The results were determined to be either true-positive (TP), true negative (TN), false-positive (FP), or false-negative (FN). When both FNAC and the final histological examination identified the case as malignant, it was considered true-positive. If it was identified, by both, as benign, then it was considered true-negative.

However, when the FNAC determined the case malignant but it was histologically nonmalignant, then it was considered false-positive. Lastly, when the FNAC determined the case to be benign but it is histologically malignant, then it is considered false-negative. Histopathological slides of relating cytological cases were correlated.

According to these finding, The statistical parameters for the sensitivity $[(TP/TP + FN) \times 100)]$, the specificity $[(TN(TN/FP) \times 100]]$, the positive predictive values (PPV) $[(TP/TP + FP) \times 100]$ and the negative predictive values (NPV) $[(TN/TN + FN) \times 100]$ have been calculated. The study excluded all cases with missing data. Furthermore, both absolute sensitivity and complete sensitivity were calculated.

The absolute sensitivity is the count of the malignant cases diagnosed, presented as the percentage out of the total number of carcinomas sampled. The complete sensitivity is the number of malignant cases, presented as the percentage out of the total number of carcinomas that are not negative or inadequate.

Results

Total of 375 FNAC cases was retrieved over the study period. Most of them were obtained from 370(98.7%) females and 5(1.3%) males, who were treated on early cancer breast detection unit, with a male to female ratio of 1:75. Tissue biopsies were done.

The assessment of the FNAC for all the cases included in this study follows the NHSBSP guideline (Table 1). All breast masses were examined using FNAC, and were assessed of which 5(1.3%) as inadequate (C1) (these five FNA repeated, showing three benign and two malignant cases).

There were 210 (56%) cases of C2 lesions. Classified as C3 was 50 (13.3%) and C4 was 45 cases (12%). There were 65 (17.3%) cases of malignant FNA C5.

(Table 2) Among the C2 cases, in histological sections, nine cases diagnosed with FNAC as benign showed malignant foci (4.3% of C2 cases). Regarding C3, 9(18%) revealed malignant findings and 4(8.9%) of C4 revealed benign histological evaluation features (Table 2).

All C5 group cases showed malignancy in histology (100 %). The absolute sensitivity was determined to be 96.4% and the complete sensitivity 98.2%.

Only the lesions diagnosed conclusively as benign or malignant were considered. The predominant malignant diagnosis was infiltrating duct carcinoma (69.84%), followed by invasive lobular carcinoma. The frequent benign lesion was fibroadenoma followed by fibrocystic and finally fibrocystic with atypia (Figure 2).

FNAC results that matched the ultimate histological diagnosis will be positive while variance with the final histological diagnosis will be negative. For an appropriate statistical analysis, cases evaluated as C4 and C5 were stratified together as malignant, while C2 and C3 were designated benign.

Sensitivity, specificity, positive predictive values, and negative predictive values were 94.4%, 84.6%, 98.8%, and 91.7%, respectively, as a diagnostic method for breast mass statistical parameters.

Cytology grade	Number of	Histological diagnosis					
	cases	Benign		Malignant			
		No	%	No	%		
C1	5	3	60	2	40		
C2	210	201	95.5	9	4.5		
C3	50	41	82	9	18		
C4	45	4	8.9	41	91.1		
C5	65	0	0	65	100		

Table 2.	Comparison	of FNAC and	histologic	findings
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Table 3.	Correlation	of specific	cvtologic a	and histologic	diagnosis of	breast lumps

Cytolo	Benign Lesions				Malignant Lesions			
gy								
grade		r						
	Fibro	Fibrocystic	Fibrocystic	Total	Ductal	Lobular	Another	Total
	adenoma		with atypia				type	
C1	2	1	-	3	1	1	-	2
C2	103	89	9	201	2	6	1	9
C3	21	10	10	41	3	5	1	9
C4	1	1	2	4	32	6	3	41
C5	-	-	-	-	50	10	5	65
Total	127	101	21	249	88	28	10	126



Figure 1. False positive case (C3)-Atypical, probably benign turned out to be malignancy. (a) smear showing discohesive ductal cells with mild to moderate atypia (H&E, X

(a) showing disconcerve ductate cens with find to inductate drypta (freez, if 100)(b) follow-up histopathologically showing invasive lobular carcinoma (H&E, X)

(b) follow-up histopathologically showing invasive lobular carcinoma (H&E, X 400)



Figure 2. A false negative case-suspicious, probably malignant (C4) turned out to be benign.

(c) smear showing slight cohesive ductal cells with moderate nuclear atypia (H&E, X 100)

(d) follow up histopathologically showing nodular sclerosis (H&E,X 100)

Discussion

Breast carcinoma is a major health problem in Egypt, as shown by the high incidence rate among the screened population according to the implemented Women's Health and Development breast screening program. Therefore, a cost-effective method must be applied (Abdel-Hadi *et al.*, 2010). Breast FNAC is commonly a one of the diagnostic triad that includes a clinical examination and radiological assessment (mammography and ultrasonography). The accuracy of the diagnosis is nearly 100% if all three procedures indicate a benign or malignant diagnosis (Obaseki *et al.*, 2010, Ibikunle *et al.*, 2017).

The "gold standard" diagnostic procedure with a sensitivity of almost 100% is open surgical excisional biopsy when to be compared with other methods. A disadvantage of excisional biopsy is the expensive consequences compared to FNAC and CNB, associated with a higher rate of patient mortality, cosmetically leave a visible unwanted scar and may complicate mammographic follow up. Furthermore, open biopsy is associated with a much longer "turnaround" time compared to the one that accompanies FNAC.

(Tham *et al.*, 2009, Ibikunle *et al.*, 2017) Both, the lump's physical characteristics and the unit's expertise are important factors for the ideal methods for breast cancer assessment (Ibikunle *et al.*, 2017). Fortunately, our country's clinicians continue to rely extensively on FNAC and consider it an invaluable diagnostic tool for evaluating and diagnosing many subsets of breast lesions. In addition, nearly all histopathologists are trained in cytology as well. Therefore, the role of FNAC is prevailing in Egypt (Abdel-Hadi *et al.*, 2010).

In addition, FNAC is a helpful tool in breast mass preoperative assessment. Precise preoperative evaluation is important because it enables the rapid reference of malignant cases for treatment and discharges from the clinic of benign cases and their return to routine follow-up (Garber and Cure, 2013; Daramola *et al.*, 2015). The sensitivity and specificity of the results made it easier for the surgeon to manage the breast lumps better for the patients.

The sensitivity ranges from 80% to 98% and the specificity can be as high as 100% (Gukas *et al.*, 2000; Ibikunle *et al.*, 2017). It is necessary to mention some difficulties and limitations about FNAC. There may be both false-negative and false-positive outcomes (Georgieva *et al.*, 2013). The overlapping characteristics of different lesions are the most significant difficulties in determining a diagnosis (Bakhos *et al.*, 2000, Abdel-Hadi *et al.*, 2010).

The most frequent cause of a false-negative cytological diagnosis is missing one of the sampling lesion during aspiration (Ellis *et al.*, 2001; Daramola *et al.*, 2015). Such a result may be produced by certain carcinomas such a result as mucinous, medullary, scirrhous or tubular, including lobular carcinoma (responsible for one of the false-negative findings in this study). (Ibikunle *et al.*, 2017), (Figure 1).

Indeed, the rate of false-negative and confusing diagnosis in FNAC increases with invasive lobular carcinoma (Hwang *et al.*, 2004; Abdel-Hadi *et al.*, 2010) which is likely to produce a paucicellular smear with minimal pleomorphism and rare sporadic intact small epithelial cells (Abdel-Hadi *et al.*, 2010). In this study, the false-positive cases diagnosed in FNAC was fibroadenoma with proliferative change foci.

This is due to the occasional intact isolated cells with dissociation, nuclear epithelial atypia, and high cellularity, frequently present (Tse *et al.*, 2013; Daramola *et al.*, 2015). Additional pitfalls are hyalinized fibroadenomas, apocrine metaplasia, multinucleation, and paucicellularity (Tse *et al.*, 2013). However, many studies found the FNAC has an accuracy of over 90% for a breast mass in their study, when triple assessments are performed and concordant for the benign or malignant lesion. However, the cytological results are not matching in 40% of their cases.

The sensitivity for carcinomas various from 35% to 95% and 48% to 100% specificity. Also, their procedure false positive rate is low (about 1%) (Garg *et al.*, 2007; Rakha *et al.*, 2007; Barra *et al.*, 2008; Hakkinen *et al.*, 2008; Willems *et al.*, 2012) Garg *et al.*, (2007) calculated sensitivity as 78% and specificity as 94% in 50 patients when conducted both core biopsy and FNAC.

Whereas, Kocaay *et al.*, determined FNAC's sensitivity and specificity as 95% and 100%, respectively, a mentioned in their literature. While, we determined sensitivity and specificity of FNAC in our study as 94.4% and 84.6%, respectively. Kocaay *et al.*, (2016) Studies from other Egyptian centers also agree with this findings.

The study was implemented in Alexandria, during a program that was held at the Suzanne Mubarak Regional Center for Women's Health and Development (SMRC). They conducted a study to evaluate the efficacy of FNACs guided by ultrasound, by comparing the results with the corresponding histological examination results, similar to our study. But, they also explored the role that core needle biopsy can play in specific cases as a complementary procedure for breast cancer diagnosis (Abdel-Hadi *et al.*, 2010).

In regard to our study results, sensitivity, specificity, positive predictive values, and negative predictive values were 94.4%, 84.6%, 98.8%, and 91.7%, respectively, as a diagnostic procedure for breast mass statistical parameters. Using nearly a similar methodology, Abdel-Hadi *et al.*, (2010) found FNAC's specificity and sensitivity was 99.3%, and 96.7% respectively. The overall positive predictive values and negative predictive values were respectively 99.3% and 96.7%.

Therefore, to maximize preoperative cancer diagnosis, they concluded that using FNAC as a first-line investigation would be cost-effective and time-saving, as to take advantage of the wealth of cytological information provided, followed by CNB in selected cases (Abdel-Hadi *et al.*, 2010; Ibikunle *et al.*, 2017). Finally, we agree with the opinion that to reach good sensitivity, specificity and optimal diagnostic accuracy of FNAC results, a framework must be implemented to decrease sample defects by repeating and multidirectional aspirates, evaluation of the adequacy of the sample immediately by cytopathologist and lastly ultrasound guidance and multidisciplinary approach.

Conclusion

The advantages of FNAC are minimal invasiveness, cost-effectiveness, fast, painless, and high-positive predictive diagnosis. Furthermore, it has a few complications that can be done in the outpatient clinic. In our experience at the Al Galaa Teaching Hospital, those benefits were highly prevalent. It facilitated the work between the pathologist and the surgeon.

Therefore, the procedure should continue to be used by the surgeons and pathologists for early detection of breast cancer. This will also minimize the waiting time for the incision/excision biopsy of the patient significantly.

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