



doi: <https://doi.org/10.20546/ijcrar.2018.606.013>

Clinical Evaluation of Breast Mass - Fine Needle Aspiration Cytology versus Histopathology - A Comparison Study

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Abstract

This was a prospective clinical and pathological study included 24 Iraqi women patients complaining of breast lump managed in Alsader teaching hospital in Najaf. It is aimed to evaluate the benefit of fine needle aspiration (F.N.A.C.) cytology in comparison to histopathology examination in diagnosis of breast lump. Out of the 48 cases of breast lump to which F.N.A.C. was applied, the material aspirated by fine needle was found to be of benign cytology in 37 cases and malignant cells were diagnosed in 11 cases. The final histopathological examination of these 48 cases showed 34 cases benign and 14 were malignant. We have no false positive result in this study, specificity rate was (100%) and 2 false negative result giving sensitivity rate of (78.6%). Conclusion: Fine needle aspiration was highly specific and good sensitive compared to histopathology and can assist the diagnosis of breast lumps.

Article Info

Accepted: 30 June 2018

Available Online: 20 July 2018

Keywords

Breast mass; fine needle aspiration; histopathology

Introduction

Diagnosis and assessment of a lump in the breast is very important issue worldwide, the type of the breast lumps may be long or small and may feel hard or spongy. Some lumps cause pain, while others go unnoticed until they are identified during an imaging examination. A lump can be discovered by a woman doing a breast self-exam, or by her doctor during a physical examination. Suspicious lumps can also be detected during annual mammograms for early detection (Tikku and Umap, 2016; Kumar *et al.*, 1999; Haas *et al.*, 2005). There is increasing awareness with associated anxiety and stress among women, who perceive every symptom in breast as cancer, compelling them to seek medical advice. It is sometimes difficult to determine whether a suspicious

lump is benign or malignant simply from clinical assessment (Ibikunle *et al.*, 2017).

Although not very common, breast lumps can also appear in men. Breast cancer is the most frequent malignancy in women in Western countries, mainly in the United States 1 and is currently the second leading cause of death behind lung cancer. In Mexico it ranks second among cancers in the female population and its incidence has been increasing.

Early diagnosis has been recognized as the cornerstone to improve the prognosis of this group of patients, reliable and accurate studies are essential with a low cost and high margin of safety. (Haas *et al.*, 2005; Ridge *et al.*, 2016)

Epidemiology

For several decades, breast cancer has increased to a remarkable degree around the world, especially in Western countries. 8 and this growth remains, despite the fact that there are better diagnostic tools, different early detection programs, better treatments and greater knowledge of risk factors.

Breast cancer is the most common malignancy in Western women and the leading cause of death from cancer in women in Europe, the United States, Australia and some Latin American countries (The Economist Intelligence Unit, 2016).

As of 2006, this condition occupies the first place of mortality due to neoplasia in women older than 25 years, displacing cervical cancer, causing about 500,000 deaths each year, of which 70% occurs in developing countries, although the risk of dying is greater among women who live in poor countries, due to less access to health services for early detection, treatment and control. In 2010, the standardized mortality rate was 18.7 per one hundred thousand women aged 25 and over, which represents an increase of 49.5% in the last 20 years (The Economist Intelligence Unit, 2016; Schneider *et al.*, 2014).

Breast cancer represents 31% of all cancers of women in the world. Approximately 43% of all the cases registered in the world in 1997 correspond to the developing countries. 11 The incidence is increasing in Latin America and in other regions where the risk is intermediate (Uruguay, Canada, Brazil, Argentina, Puerto Rico and Colombia) and low (Ecuador, Costa Rica and Peru) (Lukong, 2017; Curado, 2011; Bray *et al.*, 2004).

Fine needle aspiration biopsy (FNAC)

Although open surgical biopsy is the 'gold standard' for diagnosis of palpable breast lesions, in recent years two types of minimally invasive breast biopsy techniques, core needle biopsy (CNB) and fine needle aspiration cytology (FNAC), have become established for the diagnostic evaluation of palpable breast lesions. A triple test consisting of clinical examination, mammography and FNAC is considered the gold standard in making a definitive assessment of breast lumps. FNAC is a method that emerged in the 1930s, described by Martin and Ellis (Tikku and Umap, 2016; Sujith *et al.*, 2015), which is used to obtain a sample for cytological analysis of

various lesions, including those located in the breast. Currently, it is considered a safe and economical procedure that can avoid unnecessary surgeries by differentiating benign and malignant lesions with great certainty. 3 Since its origin and mainly during the last decade, studies from different countries have analyzed the diagnostic effectiveness of this technique. (Sujith *et al.*, 2015; Saraf *et al.*, 2016; Aly *et al.*, 2014; Kumar and Kothari, 2014). In these studies, the diagnostic accuracy was between 88.5 and 94.8%. This method has been included in multiple diagnostic protocols in which the diagnostic triad of breast stands out, where clinical examination and mammography are added with a sensitivity of this triad of 100% and a specificity of 57%. Recently, the emergence of new techniques, mainly trucut biopsy, as well as Mammotome-guided biopsy, promoted the disuse of FNAC as the method of choice, mainly due to the fear of lack of diagnostic accuracy and the impossibility of distinguishing between invasive and non-invasive cancers. Those that are not. In this study we analyze the recent experience of our institution with breast FNAC, identifying its diagnostic accuracy, complications and factors associated with the diagnosis of malignant lesions by this method of study. FNAC comes readily useful for its obvious advantages. It is a cheap, fast, and reliable diagnostic method. It also reduces the frequency of open biopsies.⁵ Some of the setback of FNAC include pain and haematoma formation. It has also been found to have the potential to mask radiological assessment when done prior to mammography. It is also possible that the smears may be a cellular (no cells are harvested) making cytological analysis impossible. These are described as inadequate aspirates and rates vary markedly, being particularly operator dependent and cases have to be converted to CNB which is able to solve the problem (Tikku and Umap, 2016; Ibikunle *et al.*, 2017; Aly *et al.*, 2014; Kumar and Kothari, 2014; Ige *et al.*, 2014)

Materials and Methods

A total of 48 patients presented with breast lump were admitted to the surgical unit in the teaching hospital in Najaf during a period of 8 months (November. 2014 - July 2015).

Data collection

Data of the studied group were collected using a pre-constructed data collection sheet for each participant woman. Through direct interview with the participant patients. Demographic data and anthropometric

measurements of the studied group were reported. Full history and complete clinical examination were performed and the baseline clinical evaluation of the patients depend on the clinical presentation that made the patients seeking surgical management, complete physical examination of the patient was done in addition to local examination regarding the site size and shape of breast lump, the relationship to skin and underlying tissue, axillary and other lymph nodes were examined.

A sample of venous blood was taken from each participant woman under aseptic venipuncture technique. Blood samples send to the laboratory for analysis for complete blood picture, hemoglobin level and ESR, lipid profile and hormonal assay were also requested. Radiology, ultrasonography and other investigations were done.

Procedures

The method of FNAC utilized a gauge of 21 or 22 thin needle attached to disposable (5cc or 10cc) syringe. The mass was firmly fixed between finger and thumb after sterilization of skin by antiseptic solution then the needle was introduced directly in the mass and aspiration was done under negative pressure with moving of the needle around. Prior to withdrawing of the needle the plunger was allowed to return and aspirated material was immediately processed in the cytology lab of the same hospital. It was smeared between the two surfaces of glass slide. The slides were immediately fixed in 95% ethyl alcohol for at least 15 minutes.

The smear then stained by haematoxylin-Eosin stain. Surgical specimen of the 48 patient were studied, biopsies were fixed in 10% formalin solution embedded and later on stained by Haematoxylin-Eosin stain.

Statistical analysis

Data of the studied group were transformed into computerized database, checked for errors or inconsistency, entered and analyzed using the statistical package for social sciences version 22. Descriptive statistics were expressed as mean, standard deviation (SD), frequencies and simple percentages.

Chi square test used to assess the significance of differences in categorical variables, Fisher's exact test was used as an alternative when chi square was inapplicable. Level of significance was ≤ 0.05 considered as significant.

Results and Discussion

There were 48 patients enrolled in this study, they were 47 female and one male, the mean age of the studied group was 44.2 ± 8.9 (range: 18 – 70) years, more than half (54.2%) of the patients aged between 21 and 40 years, 27.1% aged 41 – 60 and only one patient (2.1%) aged more than 60 years while 16.7% aged 20 years or less, (Table 1)

Table 2 shows the main sign and symptoms at presentation of the patients; all were presented with breast lumps, 45.8% with pain and discomfort, 29.2% with enlarged axillary lymph nodes, 16.7% with skin involvement and pseudorange and the least frequent, 8.3%, with nipple retraction (all were females), The duration of lump ranged less than one month to more than one year and almost 84% had their lumps since 6 months or less (Table 3). Cytological findings are shown in (Table 4); where 62.5% of the patients had benign looking cytological features, including inflammatory, Fibroadenomas, and not otherwise specified. Unfortunately, 10 female patients, (20.8%), had malignant lumps, and 2 patients (4.2%) ad cells with some atypia. On the other hand, in 6 patients, (12.5%), were inadequate.

Regarding the histopathological findings; fibroadenoma, ca. breast, chronic abscess, fibro adenosis and gynaecomastia were documented in 29.2%, 29.2%, 25.0%, 12.5% and 4.2%, respectively, (Table 5).

According to the FNAC and histopathological findings patients were classified to have malignant or benign lesions. Histopathology revealed malignancy in 14 patients and benign in 34 while FNAC revealed malignant lesions in 11 and benign in 37, the cross-tabulation between FNAC against Histopathology revealed that FNAC had sensitivity of 78.6%, specificity of 100%, Accuracy of 93.8%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 93.8%, in detection of malignancy (Table 6).

All of the patients in this study were complaining of breast lump, the rate of carcinoma were (29.2%), of these cancers patients, (66.5%) of these cancer were aged 30-40 years, (33.5%) aged 41-50 years. Fibroadenoma diagnosed in 29.2% of the patients, 85.7% of them were below 30 years of age.

In this study the age incidence of cancer was relatively early and high in comparison with other study which has

been done on 286 patients in Iran; they found the incidence of cancer was higher in older age women age (Account *et al.*, 2002) and other study from Canada (Nguyen *et al.*, 2014).

In our study all of the 48 patients were subjected to FNAC which was used for completion of clinical and other investigation data during their presence in the hospital and all the patients subjected later on to definitive surgery and subsequent histopathological biopsy study.

FNAC can be safely used as an outpatient procedure to reassure patients and save them if unnecessary rapid surgical intervention in clinicallyy benign lesion, however in highly suspicions cases of malignant breast neoplasm it can help to confirm the clinical and radiological suspicion and facilitate other definitive steps of management. This method found to be painless devoid of any announce and# show a high degree of patient acceptance (Ige *et al.*, 2014; Sujith *et al.*, 2015).

In contrast to surgical biopsy intake, in this study we divide the FNAC into 2 major groups according to malignant cells; Those with definite malignant cells and those with no malignant cells. Out of the 48 patients in

this study 11 were cytologically diagnosed as being inflammatory cells, occasional necrotic debris and benign epithelial element on subsequent surgery, the inflammatory nature was confirmed, of the remaining cases with the benign cytological diagnosis further sub typing of cases was possible depend on the quantitative and qualitative assessment.

Variable cytologicai feature such as epithial clusters, stromal fragments, bare nuclei, foamy maviophages and apocrine metaplasia. Interestingly there was no false positive result in our study. This could be easily explained by small number of our cases and to the clinco-pathological correlation. The cells show some anisocytisis, prominent nuclei and fragment of high cellularity however these feature were not sufficient to label cases as malignant, histological examination confirm that this is malignant disease.

The 11 cases of malignant cytologicai diagnosis further surgery and biopsy examination confirm the malignant nature of the lesion (there was no false positive diagnosis of malignancy in our study). These findings agreed that reported in previous studies where the false positive rate did not exceeded zero to 0.5%, (Ige *et al.*, 2014; Kumar and Kothari, 2014; Aly *et al.*, 2014)

Table.1 Demographic characteristics of the studied group (N = 48)

Variable		Number of patients	%
Age (years)	≤ 20	8	16.7
	21 - 40	26	54.2
	41 - 60	13	27.1
	> 60	1	2.1
Residence	Urban	40	83.3
	Rural	8	16.7
Marital status	Married	32	66.7
	Unmarried	16	33.3
Parity (out of 32 married)	Nulliparous	13	40.6
	Multiparous	19	59.4
Lactating (out of 32 married)		4	12.5

Table.2 Signs and symptoms at presentation of the patients

Feature	Number of patients	%
Breast lump	48	100
Pain and discomfort	22	45.8%
Axillary lymph node enlargement	14	29.2%
skin involvement and pseudorange	8	16.7%
Nipple retraction	4	8.3%

Table.3 Duration of breast lumps at the time of presentation of the patients

Duration of lump (month)	Number of patients	%
< one	20	41.7
1- 6	20	41.7
6- 12	6	12.5
> 12	2	4.2
Total	48	100.0

Table.4 Cytological findings of the patients (N = 48)

Finding	Number of patients	%
1. Benign looking	30	62.5%
a. Inflammatory	12	25.0%
b. Fibroadenoma	14	29.2%
c. Not otherwise specified	4	8.3%
2. Malignant	10	20.8%
3. Cells with some atypia	2	4.2%
4. Inadequate	6	12.5%

Table.5 Histopathological findings of the patients (N = 48)

Diagnosis	Number of patients	%
Fibroadenoma	14	29.2%
Ca. breast	14	29.2%
Chronic abscess	12	25.0%
Fibro adenosis	6	12.5%
Gynaecomastia	2	4.2%
Total	48	100.0%

Table.6 Comparison of FNAC and Histopathological findings of the patients (N = 48)

		Histopathology		Total
		Malignant	Benign	
FNAC	Malignant	11	0	11
	Benign	3	34	37
Total		14	34	48

Sensitivity	78.6%
Specificity	100.0%
Accuracy	93.8%
PPV	100.0%
NPV	91.9%

Our result of sensitivity and specificity were (78.6%) and (100%) respectively, these are comparable to the result obtained by Kumar and Kothari (India, 2014), Kumar *et al.*, (India, 2015), Silas *et al.*, (Nigeria, 2015) and Ibikunle (Nigeria, 2017) (Ige *et al.*, 2014; Sujith *et al.*, 2015; Kumar and Kothari, 2014; Ibikunle *et al.*, 2017) the high specificity allows for the early diagnosis and treatment and management of breast cancer.

An earlier study was done by Saraf *et al.*, on 321 patients with solid tumor of breast showed very high diagnostic accuracy rate of more than 98%, and the sensitivity and specificity of FNAC for detecting malignancy was 98.27% and 99.49% respectively (Saraf *et al.*, 2016).

Most of the cases with breast lump in this study ranging from 21-40 years and most of cases of malignant

pathology were from 30-40 years which is early age and relatively with a high incidence which was 29%.

There is no strong relationship between carcinoma and family history or smoking or ingestion of contraception pill.

The FNAC is a rapid method, easy to perform of little cost, easily accepted by the patient.

It can be applied for a palpable masses of breast as well as im-palpable or diffuse swelling or enlargement of breast.

The technique provide a high specificity rate and quite reasonable sensitivity rate that can be used for rapid diagnosis and screening.

Acknowledgments

Author would like to thank all who supported the study, particularly the staff of the department of surgery and department of gynecology and obstetrics, Operation Theater and the laboratory staff in both hospitals. Also I'd like to register my great thanks to all participants of the study for their time and cooperation hoping have good health and life.

Conflict of interest: None

Source of Funding: Self-funded

Ethical clearance

Data of participants were collected according to the Declaration of Helsinki, Informed written signed consent was obtained from each participant, and all official agreements were obtained prior to initiation of the study

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How to cite this article:

Mohammed Hassen AI-Dabbagh and Aeman Yaakob Kezar Almasoudi. 2018. Clinical Evaluation of Breast Mass - Fine Needle Aspiration Cytology versus Histopathology - A Comparison Study. *Int.J.Curr.Res.Aca.Rev.* 6(6), 93-99. doi: <https://doi.org/10.20546/ijcrar.2018.607.013>