

Diagnosis of breast lesions on frozen section and its cyto-histopathological correlation**Shabina Naznin Haqiqullah^{1*}, Nadeem Ahmad², Malik Atiur Rehman³**¹*Senior Resident, Department of Pathology, Rajiv Gandhi Medical College & Chhatrapati Shivaji Maharaj Hospital, Kalwa, Thane, Mumbai, Maharashtra, India*²*Assistant Professor, Department of General Surgery, Integral Institute of Medical Sciences & Research, Dasauli, Kursi Road, Lucknow, U.P, India*³*Assistant Professor, Department of General Surgery, Integral Institute of Medical Sciences & Research, Dasauli, Kursi Road, Lucknow, U.P., India***Received: 02-11-2021 / Revised: 15-12-2021 / Accepted: 07-01-2022****Abstract**

Aim: To compare the finding of frozen section with findings of FNAC and histopathology & study the sensitivity, specificity and predictive value of frozen section biopsy. **Methods:** A hospital based cross sectional study was done to compare the finding of frozen section with findings of FNAC and histopathology. This research included total 70 female patients of age group 11-80 years clinically presenting with palpable breast lesions referred to the Department of Pathology, for FNAC, frozen section and histopathological evaluation and a prospective study was conducted. FNAC procedure was performed according to the standard protocol. Only diagnosed cases were included in the study. Cases did not undergo surgery were excluded from the study. **Results:** Following FNAC, out of the total 70 cases, 35 (50%) patients had benign breast lesions while 35 (50%) patients had malignant breast lesions. Following Frozen Section, out of the total 70 cases, 33 cases (47.1%) were benign lesions and 37 cases (52.9%) were malignant. According to The histopathological diagnosis of breast lesions noted that 32 (45.7%) patients had benign breast lesions while 38 (54.3%) patients had malignant breast lesions. Frozen section findings correlated with the histopathological findings in 69 of 70 cases (98.6%), which included 32 of 32 (100%) of the benign lesions and 37 of 38 (97.4%) of the malignant lesions. 1 case of malignant lesion was wrongly diagnosed as benign on frozen section findings. The correlation of frozen section and histopathological findings was found to be statistically significant as per Chi-Square test ($p < 0.05$). FNAC findings correlated with the histopathological findings in 65 of 70 cases (92.9%), which included 31 of 32 (96.9%) of the benign lesions and 34 of 38 (89.5%) of the malignant lesions. 1 case was wrongly diagnosed as malignant on FNAC findings while 4 cases were wrongly diagnosed as benign. The correlation of FNAC and histopathological findings was found to be statistically significant as per Chi-Square test ($p < 0.05$). The Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of Frozen section were 97.37%, 100%, 100% and 96.97% respectively. Accuracy of Frozen section was 98.57%. It was observed that frozen section was more accurate than FNAC with higher sensitivity (97.37% vs. 89.47%), specificity (100% vs. 96.88%), PPV (100% vs. 97.14%), NPV (96.97% vs. 88.57%) and accuracy (98.57% vs. 92.86%). **Conclusion:** Despite increasing popularity and undisputed utility of FNAC, there are cases where frozen section still stands out as the method of choice for rapid diagnosis mainly for determining the resection margins of the lesion and the extent of metastasis in case of malignant lesion to ensure no residual tumour mass thus helping in further treatment and follow-up of patients. Final histopathological study is required to accurately arrive at a definitive diagnosis along with IHC marker study which is considered as a gold standard for patient care.

Keywords: Palpable breast lesions; FNAC; Frozen section; Histopathology.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

The incidence of cancer has been on the rise worldwide. As per the WHO cancer control and prevention programme for breast cancer, it is the most common cancer in women worldwide, comprising 16% of all female cancers. It is estimated that approximately 519, 000 women succumbed to this cancer.

Although breast cancer is thought to be a disease of the developed world, a majority (69%) of all breast cancer deaths occurs in developing countries[1]. Breast cancer survival rates vary greatly worldwide, ranging from 80% or over in North America, Sweden and Japan to around 60% in middle-income countries and below 40% in low-income countries[2]. The lower survival rates in less developed countries can be explained mainly by the lack of early detection programme, resulting in a high proportion of women presenting with

late-stage disease, as well as by the lack of adequate diagnosis and treatment facilities.

During the past few decades, across the world, breast cancer has emerged as one of the major cancers resulting in mortality among women. In the year 2010, one million new cases were diagnosed and more than five hundred thousand lives were claimed by breast cancer globally. For a long time, USA had the worst breast cancer mortality statistic in the world but for the first time, last year in 2008, India surpassed USA with more than fifty thousand deaths due to breast cancer. WHO forecasts that by 2020, 70% of all breast-cancer cases worldwide will be in developing countries[3].

Most concerning is the spread of breast cancer in Asian world including India and China, where breast cancer is rapidly emerging in younger, premenopausal women, as featured in an article in TIMES 2007 with inputs from WHO cancer prevention and control programmes[4].

In India, the average age of breast cancer patients range from 44.2 years to 49.6 years of age. Breast cancer occurs a decade earlier in Indian women when compared to the western countries[5].

FNAC though not entirely specific, is an important source of information in patients with breast lumps. In particular; it confidently

*Correspondence

Dr. Shabina Naznin Haqiqullah

Senior Resident, Department of Pathology, Rajiv Gandhi Medical College & Chhatrapati Shivaji Maharaj Hospital, Kalwa, Thane, Mumbai, Maharashtra, India

E-mail: nazneenkhan5199@gmail.com

allows exclusion of breast cancer and other more common disease and is useful in planning a surgical approach to the lesion[6]. It is the most common diagnostic modality for palpable breast lumps[7]. FNAC is simple, safe and quick procedure with high sensitivity and specificity. The accuracy rate of FNAC in diagnosing breast cancer is up to 96%. The frozen section technique for intra-operative pathologic diagnosis has been used for more than 100 years. The introduction of the cryostat in 1960 established intraoperative frozen section examination as a highly reliable procedure for the rapid histological evaluation of tissue specimen during surgery[8].

Although the recent decades have seen immense development in cytological methods and more core needle biopsies are performed before operation, frozen sections are still widely used in some countries[9].

As for breast oncology, intra-operative frozen section diagnosis has been playing a vital role in making appropriate therapeutic decisions. The most important indications for frozen section are 1) to confirm the diagnosis of carcinoma in case of inconclusive reports in fine needle aspiration cytology (FNAC), or core needle biopsies prior to major radical surgery, and 2) to provide an assessment of resection margins and completeness of excision in carcinoma[10].

The aim of this study was to compare the finding of frozen section with findings of FNAC and histopathology and to study the sensitivity, specificity and predictive value of frozen section biopsy.

Materials and methods

A hospital based cross sectional study was done among 70 patients to compare the finding of frozen section with findings of FNAC and histopathology.

Study design

A hospital based cross sectional study

Study area

The study was done at a tertiary care centre in department of pathology.

Study population

All cases clinically presenting with breast lesions referred to the department of pathology who fulfilled the inclusion criteria.

Sample size

70 patients

Inclusion Criteria

1. FNAC diagnosed cases included in the study.
2. FNAC diagnosed cases undergoing for surgery.

Exclusion criteria

1. Cases did not undergo surgery were excluded from the study

Statistical analysis

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of Fisher test, student 't' test and Chi-Square test. 'p' value less than 0.05 is taken as significant.

Methodology

The study was done at a tertiary care centre in department of pathology, after due permission from the Institutional Ethics Committee and Review Board and after taking written informed consent from the patients.

This research included total 70 female patients of age group 11-80 years clinically presenting with palpable breast lesions referred to the Department of Pathology, for FNAC, frozen section and histopathological evaluation and a prospective study was conducted. FNAC procedure was performed according to the standard protocol[11]. Only diagnosed cases were included in the study. Cases did not undergo surgery were excluded from the study. The interpretation of the slides was done by the cytopathologist and treatment is decided by the surgeon from the cytological diagnosis. All the breast specimens received in normal saline (0.9%) solution immediately from the operation theatre without fixation in formalin were subjected for frozen section. Following this they were fixed in 10% formalin for 24 hrs and processed for H&E staining for histopathological examination.

Results

In our study, all the cases in present study were female patients and no case of male patient was found. In the present study, the age group ranged from 11-80 years. The maximum number of breast lesions that is 18 cases (25.7%) were found in the age group of 31-40 years. The left and right breast were equally affected in our study. Considering the quadrant of breast involved Upper outer quadrant was most commonly affected with (47.2%) cases while the least was the lower inner quadrant with (10%) cases only.

Following FNAC, out of the total 70 cases, 35 (50%) patients had benign breast lesions while 35 (50%) patients had malignant breast lesions. The most common benign breast lesion was fibroadenoma (28.7%) followed by fibrocystic disease (11.4%), epithelial hyperplasia (7.1%) and benign phyllodes (2.8%). The most common malignant breast lesion was invasive ductal carcinoma (48.6%) followed by medullary carcinoma (1.4%).

Table I: FNAC Diagnosis of Breast Lesions of patients

FNAC Diagnosis	N	%
Benign (n=35)		
Fibroadenoma	20	28.7%
Fibrocystic disease	8	11.4%
Epithelial hyperplasia	5	7.1%
Benign phyllodes	2	2.8%
Malignant (n=35)		
Invasive ductal carcinoma	34	48.6%
Medullary carcinoma	1	1.4%
Total	70	100%

Following Frozen Section, out of the total 70 cases, 33 cases (47.1%) were benign lesions and 37 cases (52.9%) were malignant. The most common benign breast lesion was fibroadenoma (25.7%) followed by fibrocystic disease (12.8%), epithelial hyperplasia (5.7%) and benign phyllodes (2.8%). The most common malignant breast lesion was invasive ductal carcinoma (48.8%) followed by ductal ca in situ (1.4%), invasive lobular carcinoma (1.4%) and medullary carcinoma (1.4%).

Table II: Findings of Frozen section of breast lesions of patients

Findings of Frozen section	N	%
Benign (n=33)		
Fibroadenoma	18	25.7%
Fibrocystic disease	9	12.8%
Epithelial hyperplasia	4	5.7%
Benign phyllodes	2	2.8%
Malignant (n=37)		
Invasive ductal carcinoma	34	48.8%
Ductal Ca in situ	1	1.4%
Invasive lobular carcinoma	1	1.4%
Medullary carcinoma	1	1.4%
Total	70	100%

According to The histopathological diagnosis of breast lesions noted that 32 (45.7%) patients had benign breast lesions while 38 (54.3%) patients had malignant breast lesions. The most common benign breast lesion was fibroadenoma (25.7%) followed by fibrocystic disease (12.8%), epithelial hyperplasia (4.3%) and benign phyllodes (2.8%). The most common malignant breast lesion was invasive ductal carcinoma (48.6%) followed by Ductal Ca in situ (2.8%), invasive lobular carcinoma (1.4%) and medullary carcinoma (1.4%).

Table III: Histopathological Diagnosis of Breast Lesions of patients

Histopathological Diagnosis	N	%
Benign (n=32)		
Fibroadenoma	18	25.7%
Fibrocystic disease	9	12.8%
Epithelial hyperplasia	3	4.3%
Benign phyllodes	2	2.8%
Malignant (n=38)		
Invasive ductal carcinoma	34	48.6%
Ductal Ca in situ	2	2.8%
Invasive lobular carcinoma	1	1.4%
Medullary carcinoma	1	1.4%
Total	70	100%

Frozen section findings correlated with the histopathological findings in 69 of 70 cases (98.6%), which included 32 of 32 (100%) of the benign lesions and 37 of 38 (97.4%) of the malignant lesions. 1 case of malignant lesion was wrongly diagnosed as benign on frozen section findings. The correlation of frozen section and histopathological findings was found to be statistically significant as per Chi-Square test ($p < 0.05$).

FNAC findings correlated with the histopathological findings in 65 of 70 cases (92.9%), which included 31 of 32 (96.9%) of the benign lesions and 34 of 38 (89.5%) of the malignant lesions. 1 case was wrongly diagnosed as malignant on FNAC findings while 4 cases were wrongly diagnosed as benign. The correlation of FNAC and histopathological findings was found to be statistically significant as per Chi-Square test ($p < 0.05$).

The Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of Frozen section were 97.37%, 100%, 100% and 96.97% respectively. Accuracy of Frozen section was 98.57%.

Table IV: Sensitivity, Specificity, PPV, NPV and Accuracy of Frozen Section

Frozen Section Findings	Histopathological Findings	
	Malignancy Absent	Malignancy Present
Malignancy Absent	32	1
Malignancy Present	0	37
Total	32	38

Parameter	Value	95% CI
Sensitivity	97.37%	86.19% to 99.93%
Specificity	100%	89.11% to 100%
Positive Predictive Value	100%	89.11% to 100%
Negative Predictive Value	96.97%	82.23% to 99.55%
Accuracy	98.57%	92.30% to 99.96%

The Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of FNAC were 89.47%, 96.88%, 97.14% and 88.57% respectively. Accuracy of FNAC was 92.86%.

Table V: Sensitivity, Specificity, PPV, NPV and Accuracy of FNAC

FNAC Findings	Histopathological Findings	
	Malignancy Absent	Malignancy Present
Malignancy Absent	31	4
Malignancy Present	1	34
Total	32	38

Parameter	Value	95% CI
Sensitivity	89.47%	75.20% to 97.06%
Specificity	96.88%	83.78% to 99.92%
Positive Predictive Value	97.14%	83.12% to 99.58%
Negative Predictive Value	88.57%	75.37% to 95.15%
Accuracy	92.86%	84.11% to 97.64%

It was observed that frozen section was more accurate than FNAC with higher sensitivity (97.37% vs. 89.47%), specificity (100% vs. 96.88%), PPV (100% vs. 97.14%), NPV (96.97% vs. 88.57%) and accuracy (98.57% vs. 92.86%).

Table VI: Comparison of Frozen section and FNAC findings

		Histopathological Findings	
		Malignancy Absent	Malignancy Present
Frozen Section Findings	Malignancy Absent	32	1
	Malignancy Present	0	37
	Total	32	38
FNAC Findings	Malignancy Absent	31	4
	Malignancy Present	1	34
	Total	32	38

Parameter	Sensitivity	Specificity	PPV	NPV	Accuracy
Frozen Section	97.37%	100%	100%	96.97%	98.57%
FNAC	89.47%	96.88%	97.14%	88.57%	92.86%

Discussion

Breast carcinoma is one of the commonest cancer among females in India preceded only by cervical cancer[12,13]. Early screening and diagnosis of breast lesions can aid in prevention as well as accurate management of the patients thus alleviating discomfort and anxiety in the process[14,15].

In the present study, majority of the patients (25.7%) were in the age group of 31-40 years followed by 18.6% in the age groups of 11-20 years and 51-60 years. This is similar to the studies of Sheikh SA et al[16], Sultana N et al[17], Das M et al[18], Mahadevappa A et al[19] and Siddegowda MS et al[20].

Sheikh SA et al[16] cross-sectional validation study comparing the diagnostic accuracy cytology and frozen section with histopathology malignant breast lumps keeping found 76 patients with a mean age of 49±15.14 years (range: 26-87 years).

Sultana N et al[17] study on validity of frozen section in the diagnosis of breast lumps found out of the 319 breast cancer patients age ranged from 24 and 90 years with a mean age of 53.3 years.

In our study, maximum number of lumps was located in Upper Outer Quadrant (UOQ) (47.2%) followed by Upper Inner Quadrant (UIQ) (7.1%), Lower Outer Quadrant (LOQ) (15.7%) and Lower Inner Quadrant (LIQ) (10%). Evaluation of lump size showed that in 33 (47.2%) and 19 (27.1%) cases the lump measured between <5 cms and 5-10 cms respectively. In 10 (14.3%) and 8 (11.4%) cases, the lump measured between 10-15 cms and >15 cms respectively. This is comparable to the study of Mahadevappa A et al[19].

The findings of frozen section of breast lesions in our study noted that 33 (47.1%) patients had benign breast lesions while 37 (52.9%) patients had malignant breast lesions. The most common benign breast lesion was fibroadenoma (25.7%) followed by fibrocystic disease (12.8%), epithelial hyperplasia (5.7%) and benign phyllodes (2.8%). The most common malignant breast lesion was invasive ductal carcinoma (48.8%) followed by ductal ca in situ (1.4%), invasive lobular carcinoma (1.4%) and medullary carcinoma (1.4%). This is concordant to the studies of Mahadevappa A et al[19] and Sheikh SA et al[16].

Mahadevappa A et al[19] descriptive cross-sectional study found out of 28(45.16%) cases of benign lesions, eight (12.9%) were non-neoplastic and 20 (32.26%) were benign neoplastic. Benign looking epithelial cells arranged in acinar pattern with intervening stroma; inflammatory cells in stroma either neutrophils, lymphocytes, plasma cells or macrophages especially in non neoplastic lesions. Malignant tumour cells arranged in various patterns infiltrating the stroma. The main histologic feature of invasion was total disorganized

arrangement of the neoplastic cells in the stroma. Compression artifacts, ice crystals ("bubbles") in stroma and nuclei.

Sheikh SA et al[16] cross-sectional study found 61(80%) were diagnosed with malignant breast disease and 15(20%) had benign breast disease. Among the 61 patients with malignant breast lesions, 53(86%) were diagnosed with invasive ductal carcinoma, 5(8%) invasive lobular carcinoma, 1(2%) patient each for medullary, metaplastic carcinoma and invasive cribriform carcinoma.

The FNAC diagnosis of breast lesions in the present study noted that 35 (50%) patients had benign breast lesions while 35 (50%) patients had malignant breast lesions. The most common benign breast lesion was fibroadenoma (28.7%) followed by fibrocystic disease (11.4%), epithelial hyperplasia (7.1%) and benign phyllodes (2.8%). The most common malignant breast lesion was invasive ductal carcinoma (48.6%) followed by medullary carcinoma (1.4%). This is consistent with the studies of Das M et al[18] and Siddegowda MS et al[20].

Das M et al[18] study evaluating of diagnostic accuracy of FNAC in diagnosis of breast lesions found out of 1088 cases diagnosed on FNAC, 703 cases (64.61%) were benign and 232 cases (21.3%) were found to be malignant and most common benign lesion was fibroadenoma and commonest malignant lesion was Duct carcinoma.

Siddegowda MS et al[20] prospective study found of the 34 malignant cases, 28 were reported as Infiltrating Ductal Carcinoma, Not Otherwise Specified (NOS) type, three cases were reported as mucinous carcinoma breast on cytology, one case was reported as medullary carcinoma breast, one case was reported as papillary carcinoma breast and one case was reported as metaplastic carcinoma breast on cytology.

The histopathological diagnosis of breast lesions in our study noted that 32 (45.7%) patients had benign breast lesions while 38 (54.3%) patients had malignant breast lesions. The most common benign breast lesion was fibroadenoma (25.7%) followed by fibrocystic disease (12.8%), epithelial hyperplasia (4.3%) and benign phyllodes (2.8%). The most common malignant breast lesion was invasive ductal carcinoma (48.6%) followed by Ductal Ca in situ (2.8%), invasive lobular carcinoma (1.4%) and medullary carcinoma (1.4%). This is in concordance to the studies of Mahadevappa A et al[19] and Sheikh SA et al[16].

Mahadevappa A et al[19] descriptive cross-sectional study assessing the IC and FS features of breast lesions with correlation of final Histopathologic (HP) diagnosis observed on final Histopathology, 33(53.23%) cases were diagnosed as malignant lesion and 29(46.77%) as benign lesion. Fibroadenoma (42.86%) and infiltrating

duct carcinoma (75.76%) were the commonest lesions in benign and malignant groups respectively.

Sheikh SA et al[16] cross-sectional study observed among 15 cases of benign breast lesions, 7(46%) patients had fibroadenoma, 5(33%) had fibrocystic changes and 1(7%) case each had fat necrosis, duct ectasia and benign phyllodes tumour. Out of 61 malignant cases, 59(96%) were diagnosed correctly on touch imprint cytology, while 2(4%) were given false negative results. The histology of the false negative cases turned out to be invasive lobular carcinoma and invasive ductal carcinoma on paraffin section.

It was observed in the present study that frozen section findings correlated with the histopathological findings in 69 of 70 cases (98.6%), which included 32 of 32 (100%) of the benign lesions and 37 of 38 (97.4%) of the malignant lesions. 1 case of malignant lesion was wrongly diagnosed as benign on frozen section findings. The correlation of frozen section and histopathological findings was found to be statistically significant as per Chi-Square test ($p < 0.05$). Mahadevappa A et al[19] and Sheikh SA et al[16] noted similar observations in their studies.

Mahadevappa A et al[19] descriptive cross-sectional study observed more condensed hyperchromatic nuclei and chatters even in HP study of the same frozen tissue. On comparing the FS diagnosis of 62 cases with the final HP study, FS showed correlation of 100% for all malignant lesions and 96.6% for benign lesions. Sensitivity and specificity of FS was 100% and 96.55% respectively. The overall accuracy was 98.39%. p-value for IC and FS were < 0.001 indicating significant correlation with HP study.

Sheikh SA et al[16] cross-sectional study comparing the diagnostic accuracy cytology and frozen section with histopathology malignant breast lumps keeping reported accurate diagnosis's of all histologically proven malignant ($n=61$) as well as benign ($n=15$) breast cases on frozen section. The sensitivity, specificity and diagnostic accuracy were 100%.

It was observed in our present study, FNAC findings correlated with the histopathological findings in 65 of 70 cases (92.9%), which included 31 of 32 (96.9%) of the benign lesions and 34 of 38 (89.5%) of the malignant lesions. 1 case was wrongly diagnosed as malignant on FNAC findings while 4 cases were wrongly diagnosed as benign. The correlation of FNAC and histopathological findings was found to be statistically significant as per Chi-Square test ($p < 0.05$). This finding was consistent with the studies of Das M et al[18], Mahadevappa A et al[19], Siddegowda MS et al[20] and Abraham B et al[21].

Das M et al[18] study evaluating of diagnostic accuracy of FNAC in diagnosis of breast lesions reported sensitivity and specificity of FNAC for cyto-histo correlation were found to be 97.16% and 92.83% respectively.

Mahadevappa A et al[19] descriptive cross-sectional study reported IC correlated 100% with final HP in all malignant lesions and for benign lesions and it showed 93.1% correlation. Sensitivity and specificity of IC was 100% and 96.43% respectively. The overall accuracy was 98.36%.

Siddegowda MS et al[20] prospective study reported among these 34 cases, 27 cases were available for histopathological correlation which proved to be malignant on histopathology also. FNAC proved to be 100% sensitive and specific in the diagnosis of malignant lesions.

Abraham B et al[21] study assessing the validity of MMSI by the evaluation of cytomorphological features of various breast lesions compared with histopathological findings found of the total 65 cases, all cases in MMSI category I and IV showed good histopathological correlation. The agreement between MMSI and histopathology was 93.8% which is more when compared with 72.3% agreement between cytology without scoring and histopathology. MMSI has increased the diagnostic accuracy of FNAC to 93.8% from 80%.

In the present study, the Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of Frozen section were 97.37%, 100%, 100% and 96.97% respectively. Accuracy of Frozen section was 98.57%. Similar observations were noted in the study of Sheikh SA et al[16].

Sheikh SA et al[16] cross-sectional study reported all the 61(80%) malignant cases as well as 15(20%) benign cases were diagnosed correctly on frozen section. No false positive or false negative cases were recorded. Therefore, the sensitivity, specificity, PPV, NPV and diagnostic accuracy turned out to be 100%.

In our study, the Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of FNAC were 89.47%, 96.88%, 97.14% and 88.57% respectively. Accuracy of FNAC was 92.86%. This is similar to the studies of Sheikh SA et al[16] and Bukhari MH et al[22].

Sheikh SA et al[16] cross-sectional study reported no false positive on touch imprints. Specificity and positive predictive value (PPV) turned out to be 100%. However, the sensitivity rate was 96.72% and negative predictive value (NPV) was 88.24%. Hence, the diagnostic accuracy of touch imprint cytology was 97.37%. The PPV and NPV were 100% and 88.24% respectively.

Bukhari MH et al[22] study on Comparison of accuracy of diagnostic modalities for evaluation of breast cancer revealed the sensitivity, specificity and accuracy rates as 100% for class II and class V cytology lesions on touch imprints. The sensitivity, diagnostic accuracy and NPV were 87%, 95% and 85% respectively for class III and IV lesions.

It was observed in the present study that frozen section was more accurate than FNAC with higher sensitivity (97.37% vs. 89.47%), specificity (100% vs. 96.88%), PPV (100% vs. 97.14%), NPV (96.97% vs. 88.57%) and accuracy (98.57% vs. 92.86%). Similar observations were noted in the studies of Mahadevappa A et al[19][104], El-Bolkainy TM et al[23] and Bianchi S et al[8].

Mahadevappa A et al[19] descriptive cross-sectional study reported associated Ductal Carcinomas In Situ (DCIS) were better appreciated in FS especially comedo pattern. One case of false positivity on IC and FS was noted due to error in interpretation of gross, IC and FS features. On HP study it was confirmed as benign adenomyoepithelioma. Out of 33 malignant cases, 25 cases were evaluated by IC with FS for surgical resected margin involvement by malignancy and lymph node metastasis. One case showed a positive resected margin for malignancy, while remaining (24 cases) were negative. Among them, 20 cases were positive for lymph node metastasis and rest (05) was negative, which were confirmed by HP study with an accuracy rate of 100%. In male patients all three cases had gynecomastia. IC and FS correlated with final HP diagnosis in all malignant lesions giving 100% correlation and in benign lesions 93.1% correlation for IC while 96.6% correlation for FS. The accuracy rate was 98.36% for IC and 98.39% for FS.

El-Bolkainy TM et al[23] comparative study on Intra-operative diagnosis of breast mass-lesions on 130 patients reported sensitivity, specificity and accuracy rates of frozen section as 100%. However, their sensitivity and specificity rates of touch imprint cytology were 92.22% and 93.33% respectively. The NPV and PPV were 80% and 97.65% respectively.

Bianchi S et al[8] study on accuracy and reliability of frozen section diagnosis reported frozen sections accurately diagnosed 623 out of 650 cases. The frozen section diagnosis was deferred to paraffin section in 22 cases, 3 false positive and 24 false negative cases were diagnosed. The sensitivity and specificity were 91.7% and 99.2% respectively.

Conclusion

To conclude, F.N.A.C. is a simple, rapid, cost effective, non-invasive procedure in the early diagnosis of breast lesions and not associated with any complications of the procedure. Despite increasing popularity and undisputed utility of FNAC, there are cases where frozen section still stands out as the method of choice for rapid diagnosis mainly for determining the resection margins of the lesion and the extent of metastasis in case of malignant lesion to ensure no residual tumour mass thus helping in further treatment and follow-up of patients. Final histopathological study is required to accurately arrive at a definitive diagnosis along with IHC marker study which is considered as a gold standard for patient care. Thus, a judicious

selection of one or more of these modalities is essential in every patient presenting with a suspicious breast lump.

References

1. WHO Global Burden of Disease, 2004 update.
2. Coleman MP et al. Cancer survival in five continents: a worldwide population based study (CONCORD). *Lancet Oncol.* 2008, 9:730–56.
3. Jones SB. Cancer in the developing world: a call to action. *BMJ.* 1999, 21, 319(7208): 505–508
4. Parkin DM, Fernández LMG: Use of statistics to assess the global burden of breast cancer. *Breast J.* 2006, 12(s1): S70–S80
5. Organization WH. The Global Burden of Disease: 2004 Update. 20 Avenue Appia, 1211 Geneva 27, and Switzerland: Department of Health Statistics and Informatics, WHO Press, World Health Organization, 2008.
6. Dennison G, Anand R, Makar SH. A prospective study of use of FNAC and core biopsy in the diagnosis of breast cancer. *Breast Journal.* 2003, 9(6), 491-493
7. Pradhan M, Dhakal H. Study of breast lump of 2246 cases by fine needle aspiration. *J Nepal Med Assoc.* 2008, 47, 2008, 205-9.
8. Bianchi S, Palli D, Ciatto S et al. Accuracy and reliability of frozen section diagnosis in a series of 627 non palpable breast lesion. *Am J Clinical Pathology.* 1995, 103, 199-205.
9. Florell SR, Layfield LJ, Gerwels JW. A comparison of touch imprint cytology and Mohs frozen-section histology in the evaluation of Mohs micrographic surgical margins. *J Am Acad Dermatol.* 2001, 44, 660-664.
10. Wazer DE, Sinesi M, Schmidt-Ulrich R et al. Importance of surgical and pathologic determinants of tumor margin status for breast conservation therapy. *Breast Dis.* 1991, 4, 285-92.
11. http://ec.europa.eu/health/ph_projects/2002/cancer/fp_cancer_2002_ext_guid_01.p
12. Pandey JS, Sayami G, Dali S, Shrestha HG, Shrestha B, Adhikari RC, et al. Fine needle aspiration cytology of breast lump in TU Teaching Hospital. *Nep. Med Assoc.* 2002;41:388-91.
13. Manohar P, Adhikari RC, Sigdel B, Basnet RB, Amatya VJ. Present cancer status in TU teaching hospital. *JSSN.* 1992;2:16-23.
14. Hughes JE, Royle GT, Buchanan R, Taylor I. Depression and social stress among patients with benign breast disease. *British Journal of Surgery.* 1986;73 (12): 997-9.
15. Ellman R, Angeli N, Christians A, Moss S, Chamberlain J, Maguire P. Psychiatric morbidity associated with screening for breast cancer. *British Journal of Cancer.* 1989;60(5):781.
16. Sheikh SA, Singh PP, Ganguly S et al. Frozen section of breast lesions, its correlation with fnac and histopathology: a tertiary centre experience. *Journal of Science.* 2016, Vol 6(3),191-201.
17. Sultana N, Kayani NJ. Validity of frozen section in the diagnosis of breast lumps: 5 years experience at the Aga Khan University Hospital. *J Pak Med Assoc* 2005; 55: 533-6.
18. Das, M., & Koirala, A. (2018). Cytological evaluation of breast lesion and its histopathological correlation in a tertiary care center. *Journal of Nobel Medical College,* 6(2), 66-71.
19. Mahadevappa A, Nisha TG, Manjunath GV. Intra-operative Diagnosis of Breast Lesions by Imprint Cytology and Frozen Section with Histopathological Correlation. *J Clin Diagn Res.* 2017, 11(3):EC01–EC06.
20. Siddegowda MS, Ara T. Correlation of fine needle aspiration cytology with histopathology of malignant breast lesions in a tertiary care hospital, Mandya. *J. Evid. Based Med. Healthc.* 2019, 6(41), 2697-2701.
21. Abraham B, Sarojini TR. Cytological scoring of breast lesions and comparison with histopathological findings. *J Cytol.* 2018, 35:217-22.
22. Bukhari MH, Akhtar ZM. Comparison of accuracy of diagnostic modalities for evaluation of breast cancer with review of literature. *Diagn Cytopathol* 2009; 37: 416-24.
23. El-Bolkainy TM, Shabaan HA, Abodeif WT, El-Bolkainy MN, El-Tony A. Intra-operative diagnosis of breast mass-lesions: Comparison of the validity of touch smear preparation and frozen section techniques. *J Egypt Nati Canc Inst* 2008; 20: 63-9.

Conflict of Interest: Nil Source of support: Nil