POSITIVE CYTOLOGY FOR MALIGNANT CELLS OF BLOOD STAINED NIPPLE DISCHARGE AMONG PATIENTS WITH PALPABLE BREAST MASS

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ABSTRACT

Background: Usually breast cancer presents as palpable mass. Suspicion of cancer is increased when nipple discharge is also present along with palpable masses. Triple assessment i.e clinical, radiological examination and biopsy is done to detect malignancy. However, this is expansive, operator dependent and is not readily available. **Objective:** To determine the sensitivity, specificity and diagnostic accuracy of positive malignant cell cytology of blood stained nipple discharge among patient with palpable breast mass for detection of breast carcinoma. **Methodology:** This cross- sectional study was conducted at Sir Ganga Ram Hospital, Lahore, from 1st July, 2011 to 31st July, 2013 and included 100 patients who presented with blood stained nipple discharge along with palpable breast mass. All the patients had cytology of nipple discharge which was labeled as positive (if malignant cells were found). Diagnosis was confirmed on histopathology of surgically removed breast lump (modified radical mastectomy for positive cases and wide local excision for negative cases). The data was entered and analyzed by using SPSS version 20. **Results:** Cytology of nipple discharge was positive among 30 (30%) and negative in 70 (70%) patients. Histopathology of patients with positive cytology confirmed intraductal carcinoma in all cases (100%). Sensitivity, specificity and diagnostic accuracy of cytological examination of blood stained nipple discharge was 100% each. **Conclusion:** Positive cytology for malignant cells in blood stained nipple discharge among patients with palpable breast masses is highly accurate and is suggestive of malignancy in almost all the cases.

Key Words: Positive cytology, Blood stained nipple discharge, Diagnostic accuracy, Palpable breast masses.

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INTRODUCTION

Breast cancer is the most common cancer in women.[1] The incidence is 10.9% of all the cancer among women worldwide.[2] In Pakistan it is more common at a young age contrary to the west where it is more common in old age.[3] It is estimated that one in every ninth Pakistani women is likely to suffer from breast cancer, which is the highest incidence rate in Asia.[4,5] The disease is associated with significant mortality in Pakistan as most cases present at an advanced stage where treatment options are limited.[6] This may in part be attributed to lack of awareness regarding the disease along with a lack of knowledge regarding the risk factors and the screening modalities.[7] The clinical presentation of breast carcinoma is palpable mass, nipple discharge, or clinically occult lesion diagnosed on mammography.[8] Usually the breast masses are evaluated with triple assessment i.e clinical, radiological examination and biopsy. With regular screening programs based on routine mammography, the breast cancer mortality rates have significantly decreased.[9,10,11] However, there is a dilemma in third world countries, these investigations are not freely available everywhere and many patients fail to follow these protocols due to ignorance, poverty, lack of resources or social behavior and patients are lost during their initial workup.

Moreover, the investigations like ultrasonography are operator dependent and sometimes may produce unreliable results which wastes precious time and money. Fine needle aspiration cytology/ core biopsy of breast mass may also become inconclusive in some scenarios. So in these circumstances there might be a need for simple, readily available, non invasive and quick tests, to be designed in developing countries where many patients are lost during diagnostic work up. The objective of this study was to determine sensitivity, specificity and diagnostic accuracy of positive cytology of blood stained nipple discharge for malignant cells among patient with palpable breast masses.

METHODOLOGY

This study was conducted in General Surgery Department of Sir Ganga Ram Hospital, Lahore from 1st July 2011 to 31st July 2013. This cross sectional study has a sample size of 100 cases with Confidence interval of 95%, 11% margin of error and taking expected percentage of carcinoma breast in females presenting with blood stained nipple discharge i.e.

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30.3%. With non-probability purposive sampling, the patient above 18 years of age with palpable breast lump and blood stained nipple discharge were included in the study. The patients with history of nipple trauma, bleeding disorders and advanced disease (irresectable and inoperable tumor) were excluded. Informed consent was taken and proforma developed. The result was categorized as blood stained nipple discharge positive (carcinoma breast), or negative benign breast lesion. Patients with positive cytology underwent modified radical mastectomy with metastatic work up and histopathology of the specimen to confirm the malignancy. Patients with negative cytology underwent excision biopsy of breast lump (wide local excision of lump with duct excision) and all specimens were sent for histopathology to confirm the diagnosis (benign breast lesion).

The data was entered in to SPSS version 20, computer program and analyzed accordingly. Study variables were analyzed by simple descriptive statistics. Mean and standard deviation was calculated for numerical variables and sensitivity, specificity was calculated.

RESULTS

The mean age of the patients was 41.2±10.9 years. Nipple discharge was present in all cases. It was seen from single duct 88 (88 %) and from multiple ducts 22 (22%). Clinical characteristics of breast lumps are shown in Table I.

Table I: Clinical characteristics of palpable breast lumps.

Breast lump		Number	Percentage
Site of breast lump	Right Upper Quadrant	23	23
	Right Lower Quadrant	26	26
	Right Upper Quadrant	13	13
	Left Lower Quadrant	2	2
	Central	36	36
Size of breast lump	< 2cm	29	29
	2-5 cm	53	53
	>5 cm	18	18
Mean size of breast lump (cm)	3.97 +_ 1.76		

Cytology was found positive in 30 (30%) patients and negative in 70 (70%) patients. Upon histopathology of 30 positive cases, all (100%) has intraductal carcinoma.

Table II: Histopathology of resected specimens (breast lump)

		Number	Percentage
Malignancy on histopathology (n = 30)	Intraductal	30	100
	Intralobular	0	0
	Medullary	0	0
	Papillary	0	0
	Tubular	0	0
	Colloid	0	0
Benign breast lesions on histopathology (n=70)	Fibrocystic disease	67	95.71
	Duct ectasia	3	4.28
	Papilloma	0	0
	Others	0	0

Among 70 negative cases (benign), 67 (95.71 %) has fibrocystic disease and 3 (4.28 %) were ductectasia. (Table II).

The sensitivity, specificity ,positive predictive value, negative predictive value and diagnostic accuracy of cytology of blood stained nipple discharge was 100% each. (Table III)

Table III: Histopathological analysis of the breast lump in comparison to cytological examination of the blood stained nipple discharge.

Histopathology of specimen	Cytology of blood stained nipple discharge (100 patients)	
Carcinoma breast	Positive	Negative
	30	0
Benign breast lesion	0	70

DISCUSSION

Breast cancer is the leading cause of death in women. In Pakistan the prevalence of carcinoma of breast is 9 in 100 females.[12] Investigation of nipple discharge includes triple assessment which consist of physical and radiological examination and biopsy (Fine needle aspiration cytology/ core biopsy).[13] Treatment offered is based on triple assessment and ranges from lumpectomy to toilet mastectomy depending on the stage of disease.[14] The overall five year survival rate is 63%.[15] The reported incidence of breast carcinoma in pathological nipple discharge is between 7 to 15%.[16,17] A majority of patients with breast cancer who manifest with isolated nipple discharge have an early stage disease associated with in situ ductal carcinoma.[18] Montroni et al in one study had reported that cancer is present in 18% of patients with watery nipple discharge. Cancer was detected in 100 of 330 (30.3%) patients with bloody nipple discharge and in 42 of 239 (17.6%) patients with serous discharge.[19] The main diagnostic tool in our study was nipple discharge cytology which is contrary to triple

assessment. We adopted this test only for patients with blood stained nipple discharge and palpable breast lumps because this has been previously recognized that the possibility of cancer increases when the discharge is accompanied by a lump. So this may also increases the probability of detecting patients with carcinoma.

Comparing the cytology of blood stained nipple discharge with biopsy, the cytology of discharge is noninvasive test while biopsy (FNAC, core biopsy) is an invasive technique and patient sometimes refuses biopsy because of fear of needle. However, breast FNAC has a sensitivity ranging from 76% to 99%, a specificity from 60% to 100%, and a diagnostic accuracy from 72% to 95%. The false positive diagnosis are rare (0-3%) and false negative diagnoses have been reported to be in the range of 3% to 18%. [20] The sensitivity and specificity of nipple discharge fluid cytology in diagnosing malignancy range from 16% to 46% and from 60% to 62%. [21,22]

Nipple discharge cytology is specific in cases of malignancy but often inadequate for routine assessment.[23] Similarly, presence of red blood cells in nipple discharge is not a reliable marker for breast cancer.[24,25] However, the significance of nipple discharge cytology among patients with palpable breast mass is not known upto our information. This might be pilot study in this context. Mammography is recommended to any patient presenting with abnormal nipple discharge. However, some studies have reported that mammography has a poor positive predictive value (16.7%). [26] It is also reported to have a low sensitivity (59%) in the diagnosis of malignant duct pathology.[27] However, most experts recommends that a mammogram should be performed in a women over 30 years presenting with non lactation , spontaneous nipple discharge. [28] Ultrasonography, particularly with high frequency probes (11-13mHz) is complementary to mammography and could be useful in many patients but main drawback of it is, it is operator dependent. [26]

Cytology of blood stained nipple discharge and clinical examination (palpable breast lump), both noninvasive techniques can diagnose and manage breast cancer by bypassing biopsy and radiological investigations of triple assessment in our setup where most of the patients are poor, illiterate and non-complaint and where resources like mammography are out of reach. So in these circumstances, nipple discharge cytology along with clinical examination of breast is reliable alternative to establish diagnosis of breast cancer and manage the patient accordingly. There were some limitations in our study. This was a single centre trial with a limited sample size.

CONCLUSION

It is concluded from our study that blood stained nipple discharge cytology among patients with palpable breast mass is very useful in diagnosis of breast cancer.

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