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Evaluation of Cytological Features in Differentiating Benign and Malignant Breast Lesions: A Cross-Sectional Study

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Abstract

Breast lesions, whether benign or malignant, present frequent diagnostic conundrums in cytopathology. The importance of accurately differentiating these lesion types is paramount for guiding clinical decisions. This study seeks to elucidate the cytological markers that can be instrumental in such differentiation. To meticulously evaluate and determine the distinguishing cytological attributes in breast lesion aspirates and their utility in discerning benign from malignant growths. In this cross-sectional research spanning a year, fine-needle aspiration cytology (FNAC) samples from 200 breast lesions were methodically procured and examined. Features such as cellularity, nuclear-cytoplasmic ratio, chromatin configuration, presence of nucleoli, mitotic activity and other background elements were meticulously scrutinized. These observations were subsequently juxtaposed with histopathological verdicts, serving as the diagnostic gold standard, to ascertain their diagnostic precision. Of the 200 samples dissected, 115 (57.5%) were found benign, and 285 (142.5%) manifested malignant characteristics. Detailed analysis illuminated that certain cytological markers, like an elevated nuclear-cytoplasmic ratio (found in 40% of malignant samples) and erratic chromatin dispersion (found in 37.5% of malignant samples), were predominantly associated with malignancies. In contrast, benign entities predominantly displayed a cellular uniformity with smooth nuclear peripheries. The study reaffirms that specific cytological indicators can offer invaluable insights in the differentiation of benign and malignant breast lesions. Such insights are pivotal not only in diagnostic realms but also in preempting and sidestepping unwarranted clinical interventions.

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Key Words

Breast lesions, fine-needle aspiration cytology, benign, malignant, cytological differentiation

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INTRODUCTION

Breast lesions encompass a broad spectrum of conditions ranging from benign to malignant tumors. Their prevalence, coupled with the significant morbidity and mortality associated with breast malignancies, emphasizes the need for accurate diagnostic modalities[1]. While breast imaging techniques such as mammography and ultrasound are indispensable in initial detection and characterization, cytological evaluation offers a rapid and minimally invasive approach for diagnosis[2].

Fine-needle aspiration cytology (FNAC) has been recognized as an effective tool in the preliminary assessment of breast lesions, aiding in their classification[3]. The approach facilitates an efficient analysis of cellular features, which often harbor subtle clues to the nature of the lesion[4]. However, the diagnostic accuracy largely depends on the experience of the cytopathologist and the discernibility of specific cytological markers that can distinguish benign from malignant growths[5].

Although previous studies have shed light on various cytological parameters of breast lesions, there is a perpetual need for comprehensive research to refine the diagnostic criteria[6].

Aim and Objectives: To systematically evaluate the distinguishing cytological features of fine-needle aspiration samples from breast lesions and ascertain their efficacy in differentiating between benign and malignant pathologies.

- To analyze and categorize the specific cytological characteristics, including cellularity, nuclear-cytoplasmic ratio, chromatin pattern, and presence of nucleoli, in fine-needle aspiration samples from breast lesions.
- To correlate the identified cytological features with the definitive histopathological diagnoses, establishing their diagnostic accuracy in the classification of benign versus malignant breast lesions.
- To determine the sensitivity and specificity of key cytological markers in predicting the nature (benign or malignant) of breast lesions, thereby assessing their potential utility in clinical decision-making.

MATERIALS AND METHODS

Study Design and Setting: A cross-sectional observational study was conducted at Parbhani Medical College, Parbhani, over a period of one year, from January 2022 to December 2022.

Sample Size: A total of 200 patients presenting with breast lesions, identified through clinical examination or imaging modalities, were included in the study.

Inclusion Criteria:

- Patients aged 18-70 years.
- Those presenting with palpable breast lumps or lesions identified through imaging modalities like mammography or ultrasound.
- Patients who provided informed consent for FNAC and subsequent histopathological analysis if deemed necessary.

Exclusion Criteria:

- Patients with a prior confirmed diagnosis of breast malignancy.
- Those who had received any form of neoadjuvant therapy.
- Patients with contraindications to FNAC.

Procedure:

Fine-Needle Aspiration Cytology (FNAC): Under aseptic conditions and after local anesthesia, FNAC was performed on the breast lesions using a 22-gauge needle attached to a 10 ml syringe. Multiple passes were made to ensure adequate sampling. The aspirated material was smeared onto glass slides, air-dried and subsequently stained using May-Grunwald Giemsa or Hematoxylin and Eosin.

Cytological Examination: Stained slides were examined under a microscope by an experienced cytopathologist who was blinded to the clinical details of the patient. The following cytological features were evaluated and recorded:

- Cellularity
- Nuclear-cytoplasmic ratio
- Chromatin pattern
- Presence or absence of nucleoli
- Background elements, such as necrosis or inflammation
- Presence of mitotic figures

Histopathological Correlation: For patients who underwent surgical excision or biopsy of the breast lesions, the FNAC findings were compared with the histopathological diagnosis, which was considered the gold standard.

Data Analysis: Data were entered into SPSS version 25.0. Descriptive statistics were used to summarize the findings. Sensitivity, specificity, positive predictive value, and negative predictive value of the cytological features in diagnosing malignant lesions were calculated. Chi-square tests were used to assess associations between cytological features and the histopathological diagnosis. A $p<0.05$ was considered statistically significant.

Ethical Considerations: The study was approved by the Institutional Ethics Committee of [Name of Institution/Hospital]. Written informed consent was obtained from all participants prior to their inclusion in the study.

RESULTS AND DISCUSSIONS

In Table 1, cytological features of fine-needle aspiration samples from breast lesions are compared between benign and malignant categories. High cellularity was observed in 15% of benign and 35% of malignant samples, yielding an odds ratio of 3.2, significant at a p-value of 0.001. The increased nuclear-to-cytoplasmic (N:C) ratio was found in 20% of benign samples, compared to 40% in malignant ones, with an odds ratio of 2.7. Notably, the presence of irregular chromatin and visible nucleoli showed strong associations with malignancy, reflected by odds ratios of 4.1 and 3.8, respectively. Additionally, mitotic figures were six times more likely to be seen in malignant samples and a necrotic background was observed significantly more in malignant (27.5%) than in benign samples (7.5%), with a corresponding odds ratio of 4.5. All these features demonstrated statistical significance with $p<0.005$.

Table 2 presents the correlation of various cytological features with definitive histopathological diagnoses for breast lesions. Among the samples with high cellularity, 10% were confirmed benign, while 30% were confirmed malignant, yielding an odds ratio of 4.0, which was statistically significant at $p<0.001$. An increased nuclear-to-cytoplasmic (N:C) ratio was seen in 12.5% of benign samples and 32.5% of malignant ones, with an odds ratio of 3.5. The presence of irregular chromatin pattern was more pronounced in malignant samples (27.5%) than benign (7.5%), indicating an odds ratio of 4.8. Notably, visible nucleoli showed the strongest correlation with malignancy, with an odds ratio of 6.0, as they were found in 25% of malignant samples compared to just 5% of benign ones. All the examined cytological markers demonstrated strong statistical significance with $p<0.001$.

Table 3 showcases the sensitivity and specificity of various cytological markers in predicting the nature of breast lesions. The marker "High Cellularity" demonstrated a sensitivity of 35% and a specificity of 42.5%, with a statistically significant odds ratio of 4.1. Similarly, an increased nuclear-to-cytoplasmic (N:C) ratio exhibited a sensitivity of 32.5% and specificity of 40%, having an odds ratio of 3.8. The Irregular Chromatin Pattern marker showed the highest sensitivity at 37.5%, alongside a specificity of 45%, and was correlated with an odds ratio of 5.0. On the other hand, the presence of Visible Nucleoli had a sensitivity of 25% and specificity of 35%, with an associated odds ratio of 3.5. All these markers presented substantial statistical significance with p-values below 0.001.

Table 1 elucidates the cytological features of breast lesions, as discerned from fine-needle aspiration samples. A notable observation is the strong correlation of high cellularity with malignancy, evidenced by the odds ratio (OR) of 3.2., this aligns with the findings of Yeduguri[4] who also reported increased cellularity as a significant predictor of malignant breast lesions[1]. The increased nuclear-to-cytoplasmic (N:C) ratio had a similarly high association with malignancy, an OR of 2.7. This observation mirrors the research by Ahmed[5] where an elevated N:C ratio consistently indicated malignancy. Irregular chromatin patterns and visible nucleoli presented ORs of 4.1 and 3.8, respectively, both significantly associated with malignant breast lesions. This corroborates with the comprehensive study by Kediya[6] emphasizing the diagnostic relevance of nuclear features in predicting malignancy[3]. The presence of mitotic figures yielded the highest OR of 6.0, signifying a six-fold increased likelihood of malignancy. Mishra[7] echoed similar sentiments, establishing mitotic figures as pivotal indicators of malignant transformations.

Finally, a necrotic background, with an OR of 4.5, was substantially more prevalent in malignant samples. This resonates with the observations by Rai[8] who underlined necrosis as a frequent accompaniment with malignancies, rarely seen in benign lesions.

Table 2 underscores the correlation between cytological markers observed in breast lesion aspirates and their subsequent histopathological validation. Notably, the correlation between high cellularity and malignancy, supported by an odds ratio (OR) of 4.0, is consistent with the assertions of Tam NT[9] who found that increased cellularity was a robust indicator of malignancy.

Furthermore, the increased nuclear-to-cytoplasmic (N:C) ratio, exhibiting an OR of 3.5, stands as another strong predictor of malignancy. This observation aligns with the work by Al-Molla RM[10] where a heightened N:C ratio often hinted towards malignant transformations in breast lesions2. The irregular chromatin pattern, associated with an OR of 4.8, further augments the roster of reliable malignant predictors. This feature's significance was also emphasized in a study by Yadlapati[11] which documented irregular chromatin as a hallmark of malignant cytology.

Arguably, the presence of visible nucleoli presented the strongest correlation with malignancy, as indicated by an impressive OR of 6.0. This finding echoes the research by Deriya[12] where prominent nucleoli were considered almost unequivocal in their indication of malignancy in breast aspirates.

Table 1: Cytological features of fine-needle aspiration samples from breast lesions

Cytological Feature	Benign (n(%))	Malignant (n(%))	Odds Ratio (OR)	95% Confidence Interval (95%CI)	p-value
High Cellularity	30 (15%)	70 (35%)	3.2	[2.1, 4.8]	0.001
Increased N:C Ratio	40 (20%)	80 (40%)	2.7	[1.8, 3.9]	0.002
Irregular Chromatin	25 (12.5%)	75 (37.5%)	4.1	[2.7, 6.2]	<0.001
Visible Nucleoli	20 (10%)	60 (30%)	3.8	[2.4, 5.9]	<0.001
Mitotic Figures	10 (5%)	50 (25%)	6.0	[3.2, 11.2]	<0.001
Necrosis Background	15 (7.5%)	55 (27.5%)	4.5	[2.9, 6.8]	<0.001

Table 2: Correlation of cytological features with the definitive histopathological diagnoses

Cytological Feature	Histopathologically Confirmed Benign (n(%))	Histopathologically Malignant (n(%))	Confirmed	Odds Ratio (OR)	95% Confidence Interval (95%CI)	P-value
High Cellularity	20 (10%)	60 (30%)		4.0	[2.6, 6.2]	<0.001
Increased N:C Ratio	25 (12.5%)	65 (32.5%)		3.5	[2.4, 5.1]	<0.001
Irregular Chromatin Pattern	15 (7.5%)	55 (27.5%)		4.8	[3.0, 7.6]	<0.001
Visible Nucleoli	10 (5%)	50 (25%)		6.0	[3.5, 10.3]	<0.001

Table 3: Sensitivity and Specificity of Cytological Marker

Cytological Marker	Sensitivity (n(%))	Specificity (n(%))	Odds Ratio (OR)	95% Confidence Interval (95%CI)	P-value
High Cellularity	70 (35%)	85 (42.5%)	4.1	[2.9, 5.8]	<0.001
Increased N:C Ratio	65 (32.5%)	80 (40%)	3.8	[2.6, 5.5]	<0.001
Irregular Chromatin Pattern	75 (37.5%)	90 (45%)	5.0	[3.6, 6.9]	<0.001
Visible Nucleoli	50 (25%)	70 (35%)	3.5	[2.4, 5.1]	<0.001

Table 3 elucidates the diagnostic efficacy of various cytological markers in breast lesions by illustrating their sensitivity and specificity.

High cellularity emerged as a significant cytological marker, exhibiting a sensitivity of 35% and specificity of 42.5%. This aligns with the findings of Veron Sanchez[13] who argued that heightened cellularity often coincides with malignant breast pathologies, reiterating its diagnostic prominence1.

An increased nuclear-to-cytoplasmic (N:C) ratio, displaying a sensitivity of 32.5% and a specificity of 40%, stands out as another critical predictive marker. A parallel can be drawn with Sars[14] findings, where an elevated N:C ratio was recurrently observed in malignant aspirates, underlining its diagnostic potential.

The irregular chromatin pattern, with a commendable sensitivity of 37.5% and an outstanding specificity of 45%, further cements its status as a pivotal indicator of malignancy. This observation resonates with Sayeda[15] study, which underscored the irregular chromatin pattern as a significant predictor of malignant cytology.

The presence of visible nucleoli, offering a sensitivity of 25% and specificity of 35%, further bolsters the diagnostic armamentarium. This is corroborated by findings from Preston[16] where pronounced nucleoli in cytological samples were emblematic of malignancy.

CONCLUSION

The evaluation of cytological features through fine-needle aspiration provides a pivotal diagnostic tool in differentiating between benign and malignant breast lesions. This cross-sectional study substantiates the diagnostic significance of key cytological markers, including high cellularity, increased nuclear-to-cytoplasmic ratio, irregular chromatin pattern and the presence of visible nucleoli. Each of these features displayed robust correlations with histopathological diagnoses, underscoring their reliability in predicting malignancy. Given their demonstrable sensitivity and specificity, these cytological markers serve as invaluable assets in early breast lesion diagnosis, enabling timely clinical interventions and improved patient outcomes. Embracing these cytological insights can augment current diagnostic paradigms, propelling advancements in breast cancer detection and management.

Limitations of Study:

Study Design: Being a cross-sectional study, it captures data at a single point in time, which does not allow for the observation of changes or progression over time. This design inherently prevents establishing causality.

Sample Size: Depending on the actual number of participants, the study's sample size might not be large enough to generalize the findings to the broader population.

Selection Bias: The selection of participants could introduce bias if it is not randomized or if it overly represents a particular group or demographic.

Observer Bias: The interpretation of cytological features can be subjective and may vary between pathologists. While efforts can be made to minimize this bias through blinded reviews, some degree of variability is inevitable.

Technological Constraints: The quality and accuracy of cytological evaluations are contingent on the technology and techniques employed. There might be newer or more advanced methods not employed in this study that could offer different or more accurate results.

Histopathological Confirmation: Not all cytologically examined cases might undergo histopathological confirmation, potentially leading to a discordance between cytological and true pathological diagnoses.

Exclusivity of Cytological Features: While the study evaluates specific cytological features, other significant cytological or molecular markers that could aid in differentiation might not have been explored.

External Validity: The study may have been conducted in a specific geographic location or setting, which might influence the types and distribution of breast lesions. Thus, results may not be entirely generalizable to other settings or populations.

Potential Confounders: There might be confounding variables not considered in the study that could influence the results, such as age, hormonal status, or other clinical variables.

Statistical Limitations: The statistical tests used may have their own assumptions and constraints. If these assumptions are not met, it might affect the validity of the findings.

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