Int. J Med. Pharm. Res. (P-ISSN: 2958-3675 | E-ISSN: 2958-3683)
Available on: https://ijmpr.in/

International Journal
of Medical and Pharmaceutical Research

ORGINAL ARTICLE **OPEN ACCESS**

EXPLORING THE DIAGNOSTIC SIGNIFICANCE OF GREY LESIONS IN BREAST: A SYSTEMATIC REVIEW AND META-ANALYSIS

Dr. Sabiha A Maimoon, Dr.Ibtisam Fatima Salim Shaikh[2], Dr.Shreyabose[3], Dr Lata Tapnikar[4]
Department is pathology, Lata Mangeshkar Hospital, Hingna, Nagpur,Maharashtra,India

OPEN ACCESS

***Corresponding Author**
Dr.Sabiha A Maimoon,
Lata Mangeshkar Hospital,
Hingna,
Nagpur,Maharashtra,India

Received: 05-01-2025
Accepted: 23-02-2025
Available online: 27-02-2025

A B S T R A C T

Systemic review and meta-analysis of grey lesions in breast pathology.The current systematic review & meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, making sure that reporting is rigorous and transparent. Our search strategy focused on identifying relevant studies published between May 2020 and May 2021, with an emphasis on English language articles. Medline was systematically queried, and an extensive search of the PubMed Central (PMC) literature was conducted to pinpoint journal articles featuring both FNAC and HPE comparisons. Particularly in a situation where resources are limited, this systematic review and meta-analysis that compares the effectiveness of Fine Needle Aspiration Cytology (FNAC) against Histopathological Examination (HPE) is unique. FNAC exhibits substantial predictability in identifying malignancies within the grey zone of breast lesions, reinforcing its efficacy in resource-limited settings.

KEYWORDS: Meta-analysis, FNAC, HPE, Odds ratio, Forest plot

INTRODUCTION

Breast carcinoma stands out as the most prevalent malignancy among women, with a staggering 1.7 million new cases reported in 2012, constituting approximately 12 percent of newly diagnosed cases of cancer.In the last ten years, breast cancer incidence has exhibited a consistent upward trajectory, now ranking as the leading cancer among Indian females. This alarming trend underscores the critical importance of swift and precise diagnostic methods, given the potential for disease curability when detected early.

Commonly, breast lesions manifest as palpable lumps, with additional clinical picture including nipple discharge, pain, or incidental findings. The triple approach to diagnosis, encompassing clinical, radiological, and fine needle aspiration cytology examinations, is essential in the comprehensive assessment of breast abnormalities.

FNAC, a vital component of the triple approach, offers a highly sensitive, specific, rapid, and easily performed diagnostic tool. While the majority of breast lumps are benign, the anxiety surrounding potential malignancy necessitates efficient preoperative diagnosis for accurate surgical and therapeutic planning. FNAC proves invaluable in this regard, aiding in the assessment of breast lesions prior to surgery and facilitating the differentiation between malignant and benign cases.

The primary objective of the present study is to delineate the spectrum of grey lesions within the breast, leveraging the resources of a tertiary care centre. Concurrently, the study aims to assess the diagnostic validity of FNAC by juxtaposing cytological results with later histopathological diagnoses. Such an investigation promises to enhance our understanding of the diagnostic accuracy and efficacy of FNAC in the context of breast lesions, contributing valuable insights for improved patient care and treatment planning.

SEARCH STRATEGY AND SELECTION CRITERIA

The current systematic review & meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, making sure that reporting is rigorous and transparent. Our search strategy focused on identifying relevant studies published between May 2020 and May 2021, with an emphasis on English language articles. Medline was systematically queried, and an extensive search of the PubMed Central (PMC) literature was conducted to pinpoint journal articles featuring both FNACand HPE comparisons.

Electronic databases Medline and Google Search were employed, with a specific focus on free PMC articles. Articles recommended by other researchers or identified through cross-referencing in included studies were excluded from consideration. Case series were excluded, except for references. Additionally, review articles, case reports, editorials, and similar types were excluded from our analysis.
Data extraction was carried out exclusively from eligible articles, with three investigators (SM, LT, FS) independently reviewing and screening journal titles and abstracts. Two reviewers (LT, SM) then independently screened the full-text papers. Discrepancies in between reviewers at both abstract and fulltext stages were resolved by a third reviewer. A sensitive screening methodology was employed either in the abstract or title, with choosing by at least two reviewers deemed sufficient for a study to undergo a full-text evaluation.
In the systematic review, all studies falling under the FNAC/HPE comparison label were thoroughly examined. Among these, studies with a measure for Comparative Performance Evaluation (CPE) were isolated for meta-analyses. The keyword search utilized specific terms such as FNAC, HPE, and comparison. Meta-analyses were conducted using Review Manager 5.4, ensuring a robust and comprehensive synthesis of the available evidence.

REVIEW OF LITERATURE

1)AMRITHA MALINI. ET AL (2018);Amritha Malini et al. conducted a comprehensive study in 2018, involving 350 patients who sought medical attention at a tertiary care hospital over a four-year period from June 2013 to 2017. The focus of the investigation was on individuals presenting with a breast lump, and all cases underwent evaluation through Fine Needle Aspiration Cytology (FNAC). Lesions were meticulously categorized into C1-C5 groups based on the "National Health Service Breast Screening Programme (NHSBSP)" reporting criteria.
A comprehensive evaluation of the diagnostic accuracy of FNAC was made possible by the cyto-histopathological correlation performed on 240 of the 350 cases. Defining the range of benign and malignant breast lesions and assessing the diagnostic utility of FNAC were the principal goals of the research.This was accomplished by comparing the results of FNAC with later histological findings.
The study's findings are expected to contribute valuable insights into the accuracy and reliability of FNAC in diagnosing breast lesions, shedding light on its effectiveness in distinguishing between benign and malignant conditions. The four-year duration of the study enhances the robustness of the data, capturing a diverse range of cases and providing a comprehensive understanding of the diagnostic landscape in the specified population.

2)SUSMITHA N. S. ET AL (2016);Fine Needle Aspiration Cytology was performed on 124 breast lesions over an18-month prospective research that ran from January 2012 to June 2013. Of those cases, 45 underwent correlation with Histopathological Examination (HPE). Of the 124 FNACs that were conducted, 102 cases included benign breast lesions, and the remaining 22 cases involved malignant tumors. All malignant lesions and 23 cases of benign lesions had biopsies taken. Interestingly, of the 23 benign cases, all excisional samples correlated with the cytological diagnosis.
Nevertheless, two of the 22 malignant breast lesions were mistakenly reported as benign on FNAC, resulting in misleading negative results. 95.55%, 100%, and 4.44%, respectively, were found to be the overall sensitivity, specificity, and false negative percentage values.
The study's key conclusion underscores the importance of biopsy and subsequent histopathological examination in cases where there is a lack of concurrence between clinical and cytological diagnoses. This recommendation is particularly pertinent when cytological indications of malignancy are deemed suspicious. The recognition of occasional false negatives highlights the necessity for a judicious approach to confirmatory procedures, especially when the stakes involve decisions such as mastectomy.

3)PRASHANT S. MANE. ET AL (2017);This study conducted a retrospective analysis spanning from January to December 2016, evaluating the results of needle aspiration in one hundred women who arrived with breast lumps. HPE correlation was performed in 33 cases, revealing fibroadenomas as the most prevalent lesions, while malignancy was observed in 13 cases.
With a sensitivity of 85%, specificity and positive predictive value of 100%, negative predictive value of 96.3%, and an overall accuracy of 97%, the results showed strong diagnostic performance metrics for fine needle aspiration cytology. This underscores the effectiveness FNAC as aneasy, simple, affordable outpatient department (OPD) basedprocedure for the diagnosis of breast lumps, offering high sensitivity, specificity, and accuracy.[3]

4)JESSICA ALINE TOMELIN DE CURSI. ET AL (2020); This study systematically examined all anatomopathological reports of Fine Needle Aspiration Cytologies (FNACs) obtained from a private community pathology service between January 1, 2000, and December 31, 2019, comprising a total of 24,721 cases. Focusing specifically on lesions measuring up to 1.0 cm (≤1.0 cm), which accounted for 8,334 cases, the study employed the categorization recommended by the "International Academy of Cytology Yokohama System for Reporting Breast Fine Needle Aspiration Biopsy Cytopathology".

Lesions were classified in the following categories: "(1) insufficient/inadequate; (2) benign; (3) atypical, probably benign; (4) suspicious of malignancy; and (5) malignant". In order to assess the precision of FNAC, the outcomes were then contrasted with those of the comparable histological analyses, which included 785 cases in total.
The principal aim of the research was to assess the accuracy of FNAC in the diagnosis of minor breast lesions which are less than 1cm. The findings of the research indicate that FNAC proves to be a dependable and reliable method for accurately diagnosing small breast lesions, reinforcing its utility in clinical practice.[4]

5)ADETOLA OLUBUNMI DARAMOLA.ET AL (2015);Over a 5-year span, 1,790 patients underwent FNAC for breast lumps, with 436 of them undergoing subsequent biopsies. Finding out how accurate FNAC was in diagnosing palpable breast lesions throughout this period was the goal. The study's conclusion underscores that breast FNACs exhibit strong concordance with histological findings from excisional biopsies. Moreover, when performed by experienced professionals, FNAC emerges as an exceedingly valuable tool in the effective management of breast lumps.[5]

6) DAVID E. IBIKUNLE.ET AL (2017) 6;This study encompassed all individuals who underwent FNAC for breast swellings with subsequent histopathological confirmation during the specified time frame. Over the course of 5 years (2010-2014), a total of 289 FNAC procedures were conducted, involving 275 females (95.2%) and 14 males (4.8%). Histological correlation was available for 161 FNAC cases, giving rise to a 55.7% biopsy rate.
With a matching specificity of 100%, the sensitivity of FNAC in identifying the final histologic diagnosis was exceptionally high at 99.4%.The ultimate histologic diagnosis in 86.3% of cases was definitively established by FNAC, which is an important finding. The study's clear results validate our centre's use of FNAC as a trustworthy diagnostic technique for breast masses. Given its rapid and cost-effective nature, as underscored by prior research, we advocate for the continued incorporation of FNAC in the surgical management of breast lumps by clinicians.[6]

7) PHIRTHANGMOI FIMATE. ET AL (2020) 7;In this retrospective two-year study, we examined the Fine Needle Aspiration Cytology (FNAC) results of 382 female patients with breast lesions, classifying them according to the NCI guidelines. Out of these cases, 156 had subsequent histopathological follow-up, facilitating a comprehensive analysis and comparison of FNAC diagnoses.
Notably, all 156 cases had satisfactory FNAC results, with none falling into the unsatisfactory category (C1). The majority, comprising 105 cases (67.1%), were diagnosed as benign (C2). Additionally, 7 cases (4.4%) were classified as atypical but likely benign (C3), 2 cases (1.1%) were suspicious, favoring malignancy (C4), and 43 cases (27.4%) were confirmed as malignant (C5).
Following the initial FNAC assessments, a subsequent cyto-histopathological correlation was diligently performed to enhance the reliability and accuracy of the diagnostic findings.
Just three of the 112 instances that fell into categories C2 and C3 (false negative) were found to be malignant, whereas the remaining 109 cases were confirmed as benign (true negative). There were 45 instances in categories C4 and C5, all of which were verified as malignant (true positive) and none of which were benign (false positive).
This research's key finding supports the assertion that Fine Needle Aspiration Cytology is a prompt and efficient technique. Moreover, smear reporting in accordance with NCI guidelines exhibited a high correlation with histopathological diagnoses. This reinforces the reliability and effectiveness of FNAC in facilitating swift and accurate diagnoses in the context of breast lesions.[7]

8) ABHIJIT SAHA.ET AL (2016) 8;The Department of Pathology performed Fine Needle Aspiration Cytology (FNAC) and Core Needle Biopsy (CNB) on 50 patients as part of a prospective study. The Department of General Surgery then performed excision surgeries on the remaining patients.
Particularly in a developing country, FNAC has shown to be a quick, simple, affordable, accurate, and relevant approach for preoperative pathological diagnosis of breast cancer. Core Needle Biopsy (CNB) is an invaluable secondary approach for pathological diagnosis in cases where the original FNAC proves insufficient. It lowers the likelihood of missed diagnoses in cases of breast cancer. This approach ensures a comprehensive and accurate diagnostic pathway in the context of breast carcinoma within the constraints of a developing healthcare environment.[8]

9) ADITI DHARMESH VASAVADA.ET AL (2017) 9; In the current study, a meticulous correlation between cytological findings and histological diagnoses was established for all cases, encompassing benign, malignant, and suspicious presentations. The findings showed that Fine Needle Aspiration Cytology (FNAC) performed exceptionally well for palpable breast masses, with a 97.7% sensitivity, 98.8% specificity, and 97.7% positive predictive value.
This study's overarching conclusion asserts that FNAC, when applied to breast lumps, proves to be an effective, rapid, and cost-efficient diagnostic procedure. Despite its simplicity, it exhibits exceptional patient compliance. Furthermore, the high accuracy rates achieved by experienced practitioners underscore FNAC's position as one of the most reliable modalities for evaluating palpable breast masses.[9]

10) PRASHANT S. MANE. ET AL(2017)10;In this retrospective investigation, Fine Needle Aspiration (FNA) was administered to 100 patients exhibiting breast lumps, and histopathological correlation was carried out in 33 cases. Malignancy was identified in 13 cases through FNA.

The metrics that were obtained were as follows: 85%, 100%, 100%, 96.3%, and 97% for sensitivity, specificity, positive predictive value, negative predictive value, and accuracy, respectively.

The study's overarching conclusion emphasizes that FNAC stands out asstraightforward, easily administered, outpatient department (OPD) based, and cost-effective procedure. Its effectiveness in diagnosing breast masses is shown by its impressive performance indicators, which include high specificity, sensitivity, and accuracy.[10]

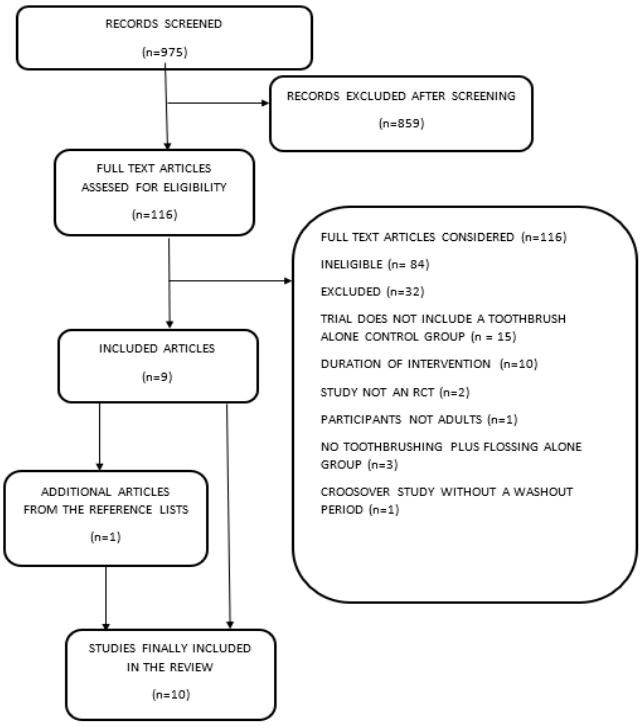

FIG 1. SHOWS A PRISMA DIAGRAM FOR SELECTION AND EXCLUSION OF JOURNAL ARTICLES

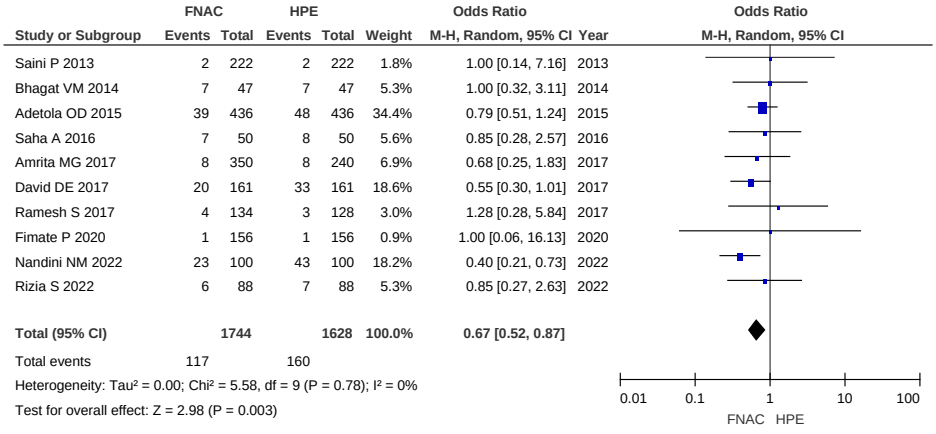

FIG 2 SHOWS META ANALYSIS OF FNAC VS HPE

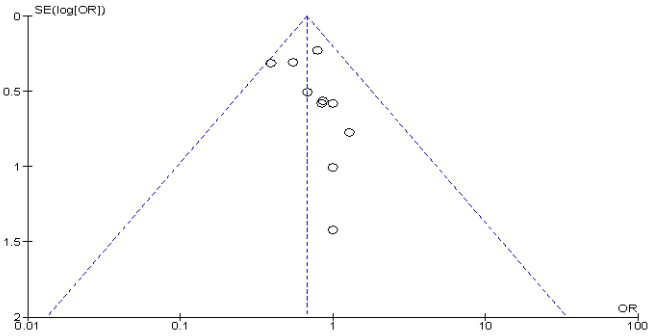

FIG NO.3 SHOWS FUNNEL PLOT OF THE ARTICLES CHOSEN FALLING WITHIN AT FUNNEL RANGE

DISCUSSION

The two most popular techniques for the preliminary assessment of breast lesions are FNAC and core-needle biopsy; nevertheless, there has been debate on the accuracy of FNAC. With a specificity of 99.6%, sensitivity of 97.4%, PPV of 99.6%, NPV of 97.6%, and accuracy of 98.5%, the study conducted by Cursi et al[4]discovered that Fine Needle Aspiration Cytology (FNAC) is a dependable medical diagnostic technique for tiny breast lesions less than or equal to 1 cm. A few writers recommend FNAC as the initial method of evaluating breast lesions, with the exception of those that merely have microcalcifications.[4]

It is widely believed that FNAC for a palpable breast lump is a rapid, affordable and painless. As far as early breast cancer detection is concerned, it also produces trustworthy results. Applying little pressure to the operation site for a brief period of time might avoid the occurrence of hematomas, which is the only complications that occur.

According to a study by Amritha et al. [(1),]breast lumps were most common in those between the ages of 21 and 40. The same was stated by Hussain Et al[(11)] and Ariga Et al[(12)] . For females, fibroadenoma and for males, gynecomastia was the most prevalent benign lesion. The most frequent type of cancerous tumor was infiltrating ductal carcinoma. Results from studies by Kamal Et al [(13)] Tiwari Et al[(14)] were similar.

In the research undertaken byPhirthangmoi Fimate[7], the right breast was found to be engaged more frequently, which was in contradiction with some published data; nevertheless, the most common area was the upper outer quadrant, which was consistent with findings by the same researchers.[15,16]

In the majority of studies reviewed, the absence of a C1 category was notable, as rapid stain was consistently performed for every case to assure the specimen adequacy[1,2,5,7].This practice aimed to enhance the reliability of results. Groups C2 &C5 were relatively clear-cut and demonstrated a consistently high degree of diagnostic accuracy, ranging between 99 percent and 100 percent.

Conversely, the analysis of categories C3 & C4 posed challenges, as these categories lacked strict criteria for diagnosis. The inherent difficulty and ambiguity in interpreting C3 and C4 underscored the need for clearer and more standardized criteria to improve the accuracy and consistency in diagnosing specimens falling within these categories.

Fine Needle Aspiration (FNA) outcomes revealed that the benign and malignant rates for category C3 were 71.4 percent& 28.6 percent, respectively. Notably, the cancerous effect for category C4 was hundred percent, aligning closely with findings from comprehensive studies featuring histopathological correlation[7].

In the Amritha et al. research, seven of the eight cases that were cytologically identified as C4 - suspicious of malignancy turned out to be malignant upon histology. The majority of lesions in the suspected of malignancy category in the investigations by Bak M Et al [17]& Ranjan agarwalEt al[18]showed up on histology to be malignant.

For the duration of a year, Ishita performed 125 FNAs on breast tissue. Of these, histological confirmation was obtained in 60 cases. The FNA technique had specificity of 97.06%, sensitivity of 93.10%, and a positive predictive value of 96.43%.19. Another study involving 334 fine needle breast aspirations conducted over a two-year time frame with histological confirmation, Sushma reported 100 percent sensitivity, 88.5 percent specificity, and an 84 percent predictive value for a positive outcome.[20].

In the study by Cursi et al. [4], 79.4% of the lump in C3 (atypia, most likely benign) were found to be non-malignant upon histological examination, with just 20.6% being classified as malignant. 71.6% of C4 lesions (atypia, presumably malignant) had their malignancy confirmed by histopathology. All things considered, these data demonstrate that FNAC has good agreement with histological investigation, especially in instances that are questionable (groups 3 and 4), providing crucial information for making a correct diagnosis.

Following an extensive review of multiple studies, our investigation concludes that Cytodiagnosis through Fine Needle Aspiration Cytology (FNAC) proves to be exceptionally valuable in assessment of breast lumps. A benign diagnosis obtained through FNAC affords a temporal window during which surgical interventions can be strategically planned or deferred. Conversely, a positive carcinoma diagnosis on cytology enables preoperative discussions and counselling with

the patient, facilitating more informed treatment planning and contributing to the reduction of morbidity associated with breast conditions.

CONCLUSION

Particularly in a situation where resources are limited, this systematic review and meta-analysis that compares the effectiveness of Fine Needle Aspiration Cytology (FNAC) against Histopathological Examination (HPE) is unique.

It succinctly concludes that opting for FNAC as the initial investigative procedure under any circumstance is a robust approach. This is especially valuable as it effectively predicts malignancy in the often ambiguous "grey zone" of breast lesions.

Acknowledging the necessity for a more extensive pool of studies to mitigate potential selection biases, the forest plot depicting Odds Ratios for events within the FNAC group revealed a statistically significant outcome. This underscores the conclusive finding that FNAC exhibits substantial predictability in identifying malignancies within the grey zone of breast lesions, reinforcing its efficacy in resource-limited settings.

REFERENCES

1. Amritha Malini. G1 , Mary Nandini Singh, K.A. AisabiIndian; Journal of Pathology and Oncology, April-June, 2018;5(2):254-261. [1]
2. Susmitha NS, Sathyaki DC. Accuracy of fine needle aspiration cytology in diagnosing various breast lesions with histopathological correlation. Journal of Evolution of Medical and Dental Sciences. 2016 Sep 19;5(75):5564-8. [2]
3. Hasan MY, Al Hashimi BA, Al-Khalidy NA, Al Ameen MI, Al Diwan JK. Fine Needle Aspiration Cytological Study of Palpable Breast Lump Among Sample of Iraqi Women Attending Al Elweiya Teaching Hospital Breast Cancer Screening Unit in Baghdad.[3]
4. de Cursi JA, Marques ME, de Assis Cunha Castro CA, Schmitt FC, Soares CT. Fine-Needle Aspiration Cytology (FNAC) is a reliable diagnostic tool for small breast lesions (≤ 1.0 cm): a 20-year retrospective study. Surgical and Experimental Pathology. 2020 Dec;3:1-8.[4]
5. Daramola AO, Odubanjo MO, Obiajulu FJ, Ikeri NZ, Banjo AA. Correlation between fine-needle aspiration cytology and histology for palpable breast masses in a Nigerian tertiary health institution. International journal of breast cancer. 2015 Oct 8;2015..[5]
6. Ibikunle DE, Omotayo JA, Ariyibi OO. Fine needle aspiration cytology of breast lumps with histopathologic correlation in Owo, Ondo State, Nigeria: a five-year review. Ghana medical journal. 2017 Apr 30;51(1):1-5.[6]
7. Fimate P. A Correlative Study of Fine Needle Aspiration Cytology with Histopathology of Female Breast Lesions. Journal of Evolution of Medical and Dental Sciences. 2020 Apr 6;9(14):1135-40.[7]
8. Saha A, Mukhopadhyay M, Das C, Sarkar K, Saha AK, Sarkar DK. FNAC versus core needle biopsy: a comparative study in evaluation of palpable breast lump. Journal of clinical and diagnostic research: JCDR. 2016 Feb;10(2):EC05.[8]
9. Vasavada AD, Kher S. Cytohistological correlation of palpable breast mass: A study of 300 cases. Annals of Pathology and Laboratory Medicine. 2017 Dec 11;4(6):A632-637.[9]
10. Mane PS, Kulkarni AM, Ramteke RV. Role of fine needle aspiration cytology in diagnosis of breast lumps. Int J Res Med Sci. 2017 Aug;5(8):3506-[10]
11. Hussain MT. "Comparison of Fine needle aspiration Cytology with excision biopsy of breast lump". J Coll Physicians Surg Pak. 2005;15(4):211-21. [11]
12. . Ariga R I,Bloom K, Reddy V B, KluskensL, Francescatti D, Dowlat K, Siziopikou P, Gattuso P. "Fine needle aspiration of clinically suspicious palpable breast mass es with histopathological correlation." Am J Surg. 2002;184 (5):410-3.PMID:12433603.[12]
13. Kamal Malukani, Garima Malpani, Gaurav Malpani, Amit V. Varma, Prashant S. Yeshwante. "Diagnostic Accuracy of Fine Needle Aspiration Cytology in Benign and malignant Breast lesions". Indian Journal of Pathology and Oncology.2016;3(2):145-151. [13]
14. Tiwari M. "Role of fine needle aspiration cytology in diagnosis of breast lumps." Kathmandu Univ Med J. 2007;5(2);215-7.PMID:18604022[Pubmed] [14]
15. [1] Arul P, Masilamani S. Application of National Cancer Institute recommended terminology in breast cytology. J Can Res Ther 2017;13(1):91-6 [15] .
16. Sankaye SB, Dongre SD. Cytological study of palpable breast lumps presenting in an Indian rural setup. Indian J Med Paediatr Oncol 2014;35(2):159-64[16].
17. Bak M, Szabo E, Mandoky L. "The grey zone in fine needle aspiration cytology of Breast". Magy Seb. 2005; 58(1):3-7[17].
18. Ranjan Agarwal, Nitesh M, Jagdamba.S, Garima.G, Parbodh.K. "Spectrum of breast diseases with cyto–histopathological correlation in a tertiary care hospital of Western Uttar Pradesh". Indian Journal of pathology and Oncology.2017;4(1):1-7[18].

19. 3. Ishita P, Singh PK. Cytomorphologic study of palpable breast lesions and histopathologic correlation. J Cytol 2003;20:129-32[19].
20. Sushma Y, Tanikella R, Prabhala S, et al. Histopathological and cytological correlation of tumors of breast. Medical Journal of Dr. D. Y. Patil University 2014;7(3):326-31[20].