DOI: 10.7860/JCDR/2021/46932.15116

Original Article

Pathology Section

Diagnostic Accuracy of Fine Needle Aspiration Cytology in Breast Masses among Children and Adolescents Aged Below 21 Years- A Cross-sectional Study

T RAJINI[1], K AMITA[2]

ABSTRACT

Introduction: Breast diseases in paediatric and adolescence are unusual. Fine Needle Aspiration Cytology (FNAC) has an important role in triaging breast masses, more so in younger population, wherein preoperative accurate diagnosis has significant impact on selecting and planning treatment. Role of FNAC in breast lesions amongst children and adolescents has not been explored much.

Aim: To study the role of FNAC in diagnosis of breast lesions in children and adolescents.

Materials and Methods: A cross-sectional study was conducted between June 2017 to May 2019 at Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India. All the patients presenting with breast lesion aged below 21 years, referred to FNAC clinic during this period were included in the study. The diagnoses were categorised as inflammatory, benign, atypia, suspicious and malignant. Cytohistopathology concordance was attempted wherever possible. Analysis was done using Statistical Package for the Social Sciences (SPSS) software version 17.0.

Results: Out of total 45 cases, 37 (82.22%) were females and 8 (17.78%) were males. Breast lesions in paediatric and adolescents accounted for 15.20% (45/296) of total breast FNAC performed during the study period. The morphologic spectrum seen most commonly was fibroadenoma (FA) 62.22% (28/45), benign breast disease 8.88% (4/45), mastitis 4.44% (2/45). Morphologic variations observed in FA were epithelial hyperplasia 32.14% (9/28), cystic change 28.57% (8/28), hypercellular stoma 21.42% (6/28), multinucleate giant cells 32.14% (9/28), apocrine change 14.28% (4/28), adenosis 10.71% (3/28), columnar cell change 10.71% (3/28), squamous metaplasia 3.57% (1/28) and atypia 3.57%(1/28). Histopathologic association was obtained in 31 cases (68.88%). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of FNAC was found to be 50%, 100%, 100%, 96.6%, 96.77%, respectively.

Conclusion: Majority of the breast lesions in paediatric and adolescents are benign in nature with FA being the most common. The FNAC had high specificity and diagnostic accuracy, thereby establishing its role in selecting appropriate treatment for this age group of patients.

Keywords: Breast neoplasms, Cytology, Paediatric

INTRODUCTION

Breast diseases in paediatric and adolescence are unusual and different from that seen in adults [1]. Presence of breast mass in this age group creates anxiety among patients and family members, necessitating early and accurate diagnosis. The FNAC is an established tool in diagnosis of breast lesions in adults. Though true cut biopsy has replaced FNAC in many higher centres, FNAC still has precedence over biopsy in establishments where infrastructure is not appropriate. In children and adolescents, a biopsy in breast is not favoured in view of injury to the breast bud amounting to abnormalities in development and also the anxiety associated with the procedure [2]. In contrast, FNAC has an advantage of being a simple, cost-effective, less painful tool performed in Outpatient Department (OPD) without use of local anaesthesia and provides quick results there by relieving the parents of the apprehensions associated with the disease [3].

The role of FNAC in paediatric population has been studied by various authors [4-8]. These studies have highlighted high diagnostic accuracy of FNAC in paediatric population, most of these studies being conducted on tumours of head and neck region. The cause of breast enlargement in children and adolescents is in diverse. It ranges from hormonal enlargement, juvenile hypertrophy, the larche, inflammatory to neoplastic causes [3].

The most common cause of neoplastic breast enlargement in this age group is a FA [3]. The FNAC plays a key role in deciding whether a surgical intervention is required or not. Though the morphological features of a FA are quite well established, FA occurring in the adolescent age group pose difficulties in view of the hormonal influence and it may be difficult to differentiate it from phyllodes tumour [3].

Studies portraying utility of FNAC of breast lesions in paediatric and adolescence are few [3,7]. The studies done so far have reported high diagnostic accuracy of FNAC in paediatric population and discussed the pitfalls encountered with possible solutions for the same. The present study was undertaken with an aim to determine the role of FNAC on diagnosis of breast lesions in children and adolescents aged below 21 years.

MATERIALS AND METHODS

This was a cross-sectional study conducted from June 2017 to May 2019 at Adichunchanagiri Institute of Medical Sciences, BG Nagara, Mandya, Karnataka, India. Study protocol was approved by the Institutional Ethical Committee (IEC) on human research, AIMS (2176 dated 14th September 2019). Written informed consent from the participant was obtained from the parents and assent was obtained from the children and adolescents. Purposive sampling was performed. All consecutive cases in the age group below 21 years presenting to FNAC OPD with breast lesions during the study period were taken for the study. Sample size was 45.

Inclusion criteria: All cases below 21 years of age and presenting with breast masses were included in the study.

Exclusion criteria: Cases wherein participant refused to provide informed consent, (assent in case of minor) were excluded from the study.

Study Procedure

The FNAC was done by a trained cytopathologist using 23G needle by non-aspiration technique. The material was expressed on slides, 50% of which were fixed in 50% ethanol for Haematoxylin and Eosin (H&E) stain and rest were air dried for Giemsa stain. All the cases were categorised into five categories as inadequate, benign, atypical, suspicious and malignant as per Yokohama system for reporting breast cytology [9]. Histopathology concordance was done wherever possible. Cytological findings were compared with histopathology to determine the sensitivity and specificity.

STATISTICAL ANALYSIS

The SPSS software version 17.0 was used for statistical analysis. Data was expressed as mean, proportions and Standard Deviation (SD). The sensitivity, specificity, positive predictive value and negative predictive value for FNAC were calculated with histopathology as gold standard. Comparison between continuous variables between two groups (cellular fibroadenoma and classic fibroadenoma) was done by unpaired student's t-test. The $p<0.05$ was considered as statistically significant.

RESULTS

The FNAC of palpable breast masses among children and adolescents constituted (15.20%) 45/296 of all cases. Mean age of presentation was 16.2 years. Maximum number of cases was females (37/45). Female to male ratio was 4.6:1. Distribution of breast lesions with respect to age and gender is shown in [Table/Fig-1].

Age group (years)	Total no. of cases (%)	No. females	No. of males
1-11	1 (2.22)	-	1
12-15	6 (13.33)	3	3
16-18	11 (24.45)	8	3
19-21	27 (60)	26	1
Total	45	37	8

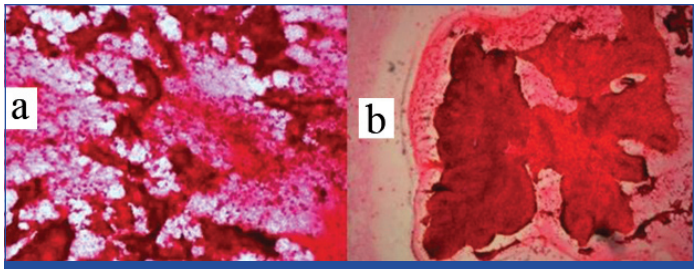
[Table/Fig-1]: Distribution of breast lesions with respect to age and gender.

The distribution of cases as per the cytologic diagnosis is shown in [Table/Fig-2]. Maximum number of cases was that of fibroadenoma 28 (62.22%) [Table/Fig-3,4] followed by gynaecomastia 6 (13.33%), benign breast disease 4 (8.88%) and lactational changes 2 (4.44%) [Table/Fig-5]. One case (2.22%) of galactocele was reported. Two cases of mastitis were reported with one being each of acute mastitis [Table/Fig-6] and granulomatous mastitis.

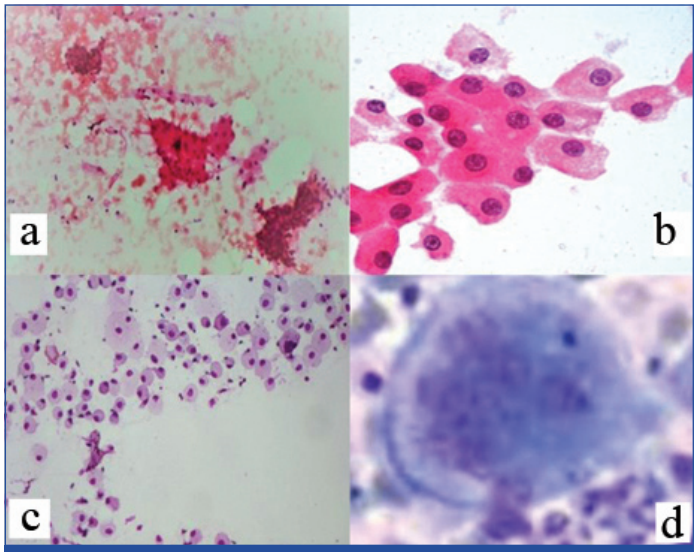
FNAC	No. of case (%) Cytology
Fibroadenoma	28 (62.22)
Acute mastitis	1 (2.22)
Granulomatous mastitis	1 (2.22)
Galactocele	1 (2.22)
Lactational changes	2 (4.45)
Lactating adenoma	1 (2.22)
Benign breast disease	4 (8.89)
Gynaecomastia	6 (13.34)
Infiltrating ductal carcinoma	1 (2.22)
Total	45 (100)

[Table/Fig-2]: Distribution of cases as per cytologic diagnosis.

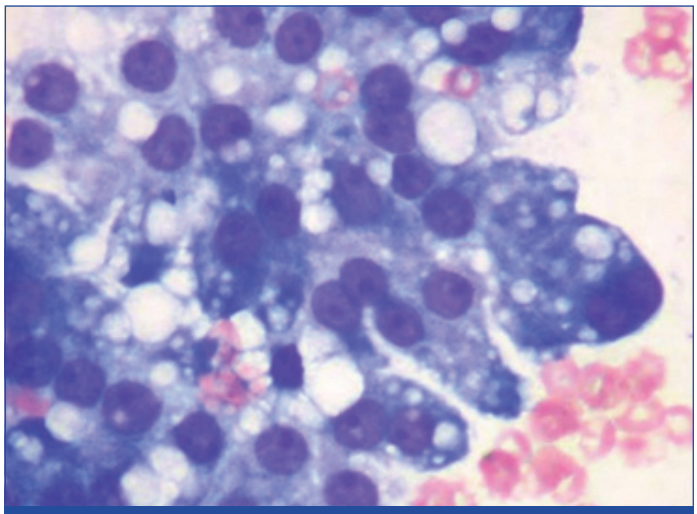
Inflammatory lesions included mastitis, two cases (4.44%) both of whom were seen between 19-21 years of age. Four cases (8.88%) of benign breast disease were noted, three were between 12-15 years of age and one was between 19-21 years of age.



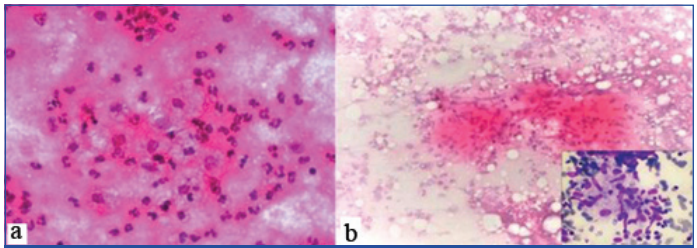
[Table/Fig-3a-b]: a) Cytology smears from cellular fibroadenoma depicting epithelial hyperplasia (H&E, 40X). b) Cytology smears from cellular fibroadenoma shows cellular stroma in a leaf like pattern mimicking a phyllodes tumour (H&E, 40X).



[Table/Fig-4a-d]: a&b) Cytology smears from fibroadenoma showing apocrine change. (a- H&E,100X, b-H&E,400X). c) Smear showing cystic change in fibroadenoma. (H&E,100X). d) Smear showing giant cell in a fibroadenoma (H&E, 400X).



[Table/Fig-5]: Cytology smears from lactational change showing vacuolated cytoplasm and nuclei with prominent nucleoli. (H&E,400X).



[Table/Fig-6]: a) Cytology smears from acute mastitis depicting neutrophils (H&E, 40X). b) Smears showing granulomas admixed with fibrous stroma and neutrophils in granulomatous mastitis (H&E, 40X). Inset shows high power of epithelioid clusters. (H&E,100X).

There were 28 (62.22%) cases of FA, most of whom (20/28) were between 19-21 years of ages, with remaining eight cases between 16-18 years of age. Lactational changes were seen to occur between 19-21 years of age group. There was one case of invasive ductal carcinoma in the age group of 19-21 years.

An attempt was made to determine the various morphologic changes seen in fibroadenoma [Table/Fig-7]. The most common change noted was hyalinised stroma in 15/28 (53.57%) and epithelial hyperplasia in 9/28 (32.14%).

Variable	No. of case (%)
Columnar cell change	3/28 (10.71)
Giant cells	9/28 (32.14)
Epithelial hyperplasia	9/28 (32.14)
Hypercellular stoma	6/28 (21.42)
Hyalinised stroma	15/28 (53.57)
Myxoid stroma	2/28 (7.14)
Cystic change	8/28 (28.57)
Apocrine change	4/28 (14.29)
Adenosis	3/28 (10.71)
Adipocyte change	4/28 (14.29)
Squamous metaplasia	1/28 (3.57)
Atypia	1/28 (3.57)

[Table/Fig-7]: Various morphologic changes in fibroadenoma.

Morphologic variations seen among classic FA and cellular FA were analysed by using student's t-test [Table/Fig-8]. Epithelial hyperplasia, stromal hypercellularity, bare nuclei, adenosis and giant cells seen more commonly in cellular FA as compared to classic FA and this was found to be statistically significant. Cytohistological was obtained in 31 out of 45 cases [Table/Fig-9]. Cytohistopathological concordance was obtained in all cases except in one case wherein an adenomyoepithelioma of low malignant potential was misdiagnosed as FA on FNAC accounting to one false negative case.

S. No.	Parameters	Cellular fibroadenoma	Classic fibroadenoma	Test of significance
1	Epithelial hyperplasia			
	Usual ductal hyperplasia	7	2	<0.001
	Atypical ductal hyperplasia	-	-	
2	Stromal hypercellularity			
	Hypercellular	6	-	<0.001
	Hyalinised	-	15	0.0019
	Myxoid	2	-	0.0059
3	Bare nuclei			
	Plenty	6	-	<0.001
	Moderate	-	21	
4	Columnar cell change			
	Present	1	2	0.623
	Absent	-	-	
5	Giant cells			
	Present	7	2	0.001
	Absent	-	-	
6	Adenosis			
	Present	2	1	0.049
	Absent	-	-	
7	Cystic change			
	Present	3	5	0.215
	Absent	-	-	
8	Apocrine change			
	Present	1	3	0.884
	Absent	-	-	
9	Squamous metaplasia			
	Present	1		0.076
	Absent	-	-	
10	FCC like changes			
	Present	-	4	0.247
	Absent	-	-	

[Table/Fig-8]: Comparison of various morphologic changes seen in cellular fibroadenoma and classic fibroadenoma.
Student unpaired t-test, statistical significance at p<0.001

Cytology	Histopathology		n
	Benign	Malignant	
Benign	29 (True Negative)	1 (False Negative)	30
Malignancy	0 (False Positive)	1 (True Positive)	1
Total	29	2	31

[Table/Fig-9]: Depicts cytohistopathologic concordance among 31 cases where histopathology was available.

The Risk of Malignancy (ROM) was calculated by dividing the number of cases in each category by the total number of malignant cases in that category [Table/Fig-10]. ROM was 100% in category V while it was 3.33% in benign category. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of FNAC in diagnosing FA was 100%, 75%, 96.43%, 100%, 96.77%, respectively. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of FNAC was found to be 50%, 100%, 100%, 96.6%, 96.77%, respectively.

Cytodiagnostic categories	Number of cases in each category	Risk of malignancy in each category
Unsatisfactory	0	-
Benign	30	3.33%
Atypia	0	-
Suspicious	0	-
Malignancy	1	100%

[Table/Fig-10]: Distribution of cases in cytodiagnostic categories (for which histopathology was available) as proposed by Yokahama et al., with Risk of Malignancy (ROM) in each category [24].

DISCUSSION

Breast masses in adolescents are uncommon. Their presence creates anxiety among the parents and hence early and accurate diagnosis goes a long way in bringing relief to the caregivers.

The FNAC is an important first line investigative tool in the diagnosis of breast lesions in adults. Several studies have established a high accuracy for this procedure. Recently, trucut biopsy has emerged as an alternative to FNAC at many institutes. Though its role in rural areas with restricted infrastructure is limited, however in category III lesions reported on FNAC and in cases where there is cytoradiological dissonance, trucut biopsy is irreplaceable [9].

In children and adolescents presenting with breast masses, FNAC plays a crucial role in selecting patients for surgical versus medical line of management. Biopsy in this age group is contraindicated as damage to the breast buds may lead to developmental abnormalities like aplasia or hypoplasia [2].

The role of FNAC in paediatric population has been studied by various authors [4,5]. Though universally accepted in adults, FNAC in children is not unanimously utilised as an initial mode of investigation. Literature on FNAC of various anatomic sites in paediatric population is scarce, more so in breast lesions [6-8]. In a study by Shirian S et al., involving 1000 cases of FNAC in paediatric population, the most

common lesions aspirated were thyroid and lymphnode, albeit no breast lesions underwent FNAC in their study [10].

The causes of breast enlargement in children and adolescents are diverse. It includes plethora of lesions like development abnormalities, hormone related enlargement like virginal hypertrophy, the larchy, inflammatory lesions, and pregnancy associated changes and neoplastic lesions. In the present study, out of total 296 cases of breast lesions in whom FNAC was done 15.20% (45/296) were children and adolescents. In the present study, FNAC was requested for a breast lesion most frequently in the age group of 19-21 years followed by 16-18 years. Similar to the present study, Kapila K et al., reported breast lesions to occur commonly in similar age groups [3]. Females more commonly present with breast masses as compared to males. Similar findings were reported in the present study wherein 82.22% were females while 17.78% were males. Among total 1404 breast aspirates studied by Kapila K et al., aspirates from male accounted for 12.6% cases. There are very few studies on FNAC of breast lesions in males. Gyanecomastia was the most common lesion encountered in the present study in adolescent males accounting for 13% of the cases. Other studies have encountered similar findings [1-3]. Many gynaecomastia are fibrotic and hence obtaining adequate material for interpretation is a challenge. Sampling from multiple sites along with aspiration using 10cc syringe attached to comeco syringe holder to provide sufficient negative pressure will yield adequate material in most of the cases. Most of the gynaecomastia smears depicted benign ductal epithelial cells with overriding myoepithelial cells and scanty fibrotic stroma. These were consistent with the findings described in literature [9]. Epithelial hyperplasia and atypia is commonly encountered in gynaecomastia and should be viewed with caution. In the present study, epithelial hyperplasia was encountered in 45% of gynaecomastia. These cases showed epithelial hyperplasia consistently in resection specimens as well.

Most common lesions detected in females was FA. In the present study FA was the most common lesion encountered in 62.22% cases. In a study by Pacinda SJ and Ramzy I, involving 59 cases of breast FNAC in children and adolescents FA was noted in 49% of cases. In a study, among 49 benign tumours diagnosed by FNAC in paediatric population, FA was the most common tumour (20.8%) [11]. The most common age group of FA in present study was 19-21 years and 16-18 years which was similar to the study by Kapila K et al., [3]. The FA in adolescents have a tendency to assume large size under the influence of hormone. Four percent of all FA is juvenile FA [12]. These giant or juvenile FA are highly cellular with both epithelial and stromal hypercellularity and hence the synonym of cellular FA. There are very few studies documenting the characteristic features of cellular FA at FNAC. Cellular/juvenile FA are rare accounting for 4% of all FA [13].

In cellular FA, presence of the extensive stromal hyperplasia and increased cellularity in stromal component makes it difficult to distinguish it from phyllodes tumour which needs a different surgical approach [Table/Fig-3,4]. Diagnosing cellular or juvenile FA is a challenge for the cytopathologist. Awareness of this entity and its cytomorphologic features is important for accurate diagnosis. In the present study, morphological variations seen among classic FA and cellular FA were analysed by using student's t-test. Epithelial hyperplasia, stromal hypercellularity, bare nuclei, adenosis and giant cells were seen more commonly in cellular FA as compared to classic FA and this was found to be statistically significant. Adenomyoepithelioma is another entity which is a nightmare for a cytopathologist as well as the surgeon. Adenomyoepithelioma is an extremely rare tumour known to occur in adolescents. Accurate diagnosis at cytology is not possible in most of the cases, especially when one is unaware of this entity. It is a tumour with a modest recurrence rate and needs wide surgical excision and follow-up. Apart from this, malignancy occurring in adenomyoepithelioma can be easily missed at cytology [14]. In the present study, one case of adenomyopeithelioma was misdiagnosed at cytology. The smears of adenomyoepithelioma closely resemble cellular FA. High cellularity, epithelial hyperplasia and plenty of myoepithelial cells in the form of bare nuclei or small clusters of cells with epithelioid like morphology are important clues to diagnosis of adenomyoepithelioma, albeit without the awareness of this entity diagnosis is difficult [14]. One case in present study presented six months later with recurrence of the mass in the same breast as well as a new mass in the opposite breast. The FNAC at this time of both the lesions was cautiously reported as adenomyoepithelioma which was later confirmed on histopathology and immunohistochemistry. In a series of 12 cases of adenomyoepithelioma by Iyengar P et al., the accurate diagnosis of adenomyoepithelioma was not rendered in any of the cases [15]. Careful identification of myoepithelium and a conservative diagnosis with histologic follow-up will help prevent mismanagement.

Characteristically FA smears show a triad of ductal epithelial cells, myoepithelial cells and fibromyxoid stroma [16]. However, several variations from usual morphology have been described in 48 to 50% of fibroadenoma. Geethamala K et al., reported pathological variations in 42.5% of fibroadenoma [17]. In the present study the morphological variations were seen in 40% of FA [Table/Fig-4]. The most common variation was epithelial hyperplasia seen in 32.14% (9/28) of cases. Spectrum of proliferative lesions can be noted in FA akin to that in normal breast. Literature reveals that epithelial hyperplasia occurs in 13.2% of FA [17,18]. In a study by Kuijper A et al., epithelial hyperplasia was seen in 43.9% of all age groups [19]. Since, epithelial hyperplasia in FA is attributed to increase in risk of invasive carcinoma caution should be entertained in the diagnosis. Similarly, close follow-up should be recommended in the final report in such cases. Fibrocystic change was noted in 28.57% (8/28) analogous to that reported by Geethamala K et al., (24.3%) [17].

Multinucleate giant cells in breast lesions are usually of stromal origin and non-neoplastic in nature. The first report of multinucleate stromal cells was by Rosen P, in 1979, wherein he documented their presence in invasive ductal carcinoma [20]. Later on Jaiswal R et al., reported the presence of multinucleate giant cells in one out of four cases of FA in series of teenage patients [13]. In the present study multinucleate giant cells were seen in 32.14% (9/28) of FA which was quite high compared to that described in literature. Apocrine metaplasia is another entity which was noted in 14.28% (4/28) of all FA reported in present study. Kuijper A et al., reported a slightly higher prevalence of apocrine metaplasia in fibroadenoma (28%). Stand alone, presence of apocrine metaplasia in fibroadenoma has no clinical or prognostic implications [19]. However, when apocrine change is accompanied with epithelial hyperplasia and calcification, possibility of complex FA has to be considered, since complex FA is associated with increased ROM warranting a close follow-up in such scenario [21].

At time FA can show extensive hypercellular stoma especially the juvenile variant. Presence of this finding makes it simulate a phyllodes tumour the distinction between two being of utmost importance in view of different management and biologic behaviour. Phyllodes are a neoplasm of intermediate grade and occur exclusively in females above 35 years of age. In a study by Kapila K et al., phyllodes tumour was reported in 1.4% of the adolescents [3]. In a recent study, on immunohistochemistry and proteomics on FA and low

grade phyllodes tumour, it was observed that both are similar and distincition of one from another is neither crucial nor necessary [16]. Approximately, 0.9% of FA can show focal phyllodes like areas [17]. The FA can progress to phyllodes tumour by clonal expansion of the stromal component [17]. In the present study, hypercellular stroma was noted in 21.42% of FA. All these cases turned out to be classic FA on histopathology.

Columnar cell lesions of the breast have been studied extensively in the last decade. Use of mammography has increased the detection for columnar cell lesions [22]. However, the exact clinical significance and management guidelines for these lesions are still matter of debate. Columnar cell lesions include columnar cell hyperplasia and columnar cell change without atypia and columnar cell hyperplasia and columnar cell change with atypia, the latter two being synonyms to flat epithelial atypia [21]. In the present study, columnar cell change was noted in 3 out of 28 cases (10.71%). However, a thorough literature review did not yield any results on the presence of columnar cell hyperplasia in FA.

Squamous metaplasia was not noted in one case (3.57%) in the present study. This was similar to that reported by other studies in literature [17]. Squamous metaplasia begins in the myoepithelium and then extends to involve the ducts and acini. It is essential to be aware of this entity in order to avoid a misdiagnosis of squamous cell carcinoma.

Mastitis was observed in 4.44% of cases in the present study. Inflammatory lesions in the breast are uncommon and their aetiology is obscure [Table/Fig-6]. However, identification avoids unnecessary surgical procedure. In a study by Kapila K et al., inflammatory lesions accounted to 4% of the cases [3].

Pregnancy induced changes in the breast accounted for 8.88% of cases in the present study [Table/Fig-2]. These included galactocele (2.22%), lactational changes (4.44%) and lactating adenoma (2.2%). In India, prevalence of teen age pregnancy is high as compared to developed world. Under the influence of hormones, the lactating breast show increased acinar tissue which exhibits abundant fragile cytoplasm and round nuclei with prominent nucleoli. These acinar cells undergo cytoplasmic fragmentation during smearing as a result plenty of bare nuclei are noted in the background. These bare nuclei can be easily mistaken for malignancy. Hence, history taking plays a major role in avoiding over diagnosis at cytology [9].

The smears of benign breast disease showed scanty cellularity with benign ductal epithelial cell and bare bipolar myoepithelial cells in the background. Benign breast disease was reported in 8.8% of cases in the present study, while Kapila K et al., observed benign breast disease in 20% of their cases [3].

Prevalence of breast malignancy in paediatric population is rare accounting for 0.1% below 30 years of age [23]. Most common primary carcinoma in this age group is secretory carcinoma which has a better prognosis as compared to invasive ductal carcinoma. Metastatic malignancies are more common than primary invasive ductal carcinoma in paediatric population. Common metastatic malignancies in children include lymphoreticular malignancies, rhabdomyosarcoma, esthesioneuroblastoma and rarely adenocarcinomas [1]. Presence of metastasis in breast from a primary elsewhere portends a poor prognosis. In the present study, invasive ductal carcinoma was observed in 2.22% of cases in accordance with that reported in literature (0.3%).

Recently, Yokahama et al., proposed a new system for reporting of breast lesions at cytology with the aim to bring uniformity in reporting patterns among cytopathologists and to provide risk-based stratification which will direct clinicians in deciding management. In the present study, it was attempted to categorise breast lesions based on this system. The ROM obtained was 100% in category V and 3.33%% in benign category. This was in accordance with that published in literature [24].

Limitation(s)

Small sample size with a smaller number of cytohistopathologic association was the major limitation of the present study.

CONCLUSION(S)

In the present study, majority of the breast lesions paediatric and adolescents were benign in nature with FA being the most common. The FNAC is very useful in reducing anxiety and providing an accurate diagnosis, thus avoiding open surgery to prevent later deformity.

Acknowledgement

Authors acknowledge Dr. MG Shivaramu, Dean, Health Sciences, Medical, Adichunchanagiri Institute of Medical Sciences, Adichunchanagiri University, for the support and guidance provided for conducting the study.

REFERENCES

[1] Kaneda HJ, Mack J, Kasales CJ, Schetter S. Pediatric and adolescent breast masses: A review of pathophysiology, imaging, diagnosis, and treatment. American Journal of Roentgenology. 2013;200:W204-12.
[2] García CJ, Espinoza A, Dinamarca V, Navarro O, Daneman A, García H, et al. Breast US in children and adolescents. RadioGraphics. 2000;20:1605-12.
[3] Kapila K, Pathan SK, Mosawy FA, George SS, Haji BE, Ayadhy B. Fine needle aspiration cytology of breast masses in children and adolescents: Experience with 1404 aspirates. Acta Cytol. 2008;52:681-86.
[4] Rapkiewicz A, Thuy Le B, Simsir A, Cangiarella J, Levine P. Spectrum of head and neck lesions diagnosed by fine-needle aspiration cytology in the pediatric population. Cancer. 2000;111:242-51.
[5] Razack R, Michelow P, Leiman G, Harnekar A, Poole J, Wessels G, et al. An interinstitutional review of the value of FNAB in pediatric oncology in resource limited countries. Diagn Cytopathol. 2012;40:770-76.
[6] Jain M, Majumdar DD, Agarwal K, Bais AS, Choudhury M. FNAC as a diagnostic tool in pediatric head and neck lesions. Indian Pediatr. 1999;36:921-23.
[7] Prathima S, Suresh TN, Harendra Kumar ML, Krishnappa J. Fine needle aspiration cytology in pediatric age group with special reference to pediatric tumours: A retrospective study evaluating its diagnostic role and efficacy. Ann Med Health Sci Res. 2014;4:44-47.
[8] Dhingra V, Misra V, Mishra R, Bhatia R, Singhal M. Fine Needle Aspiration Cytology (FNAC) as a diagnostic tool in pediatric lymphadenopathy. J Clin Diag Res. 2010;4:2452-57.
[9] Wong S, Rickard M, Earls P, Arnold L, Bako B, Field AS. The International Academy of Cytology Yokohama System for reporting breast fine needle aspiration biopsy cytopathology: A single institutional retrospective study of the application of the system categories and the impact of rapid onsite evaluation. Acta Cytologica. 2019;63(4):280-91.
[10] Shirian S, Daneshbod Y, Haghpanah S, Khademi B, Noorbakhsh F, Ghaemi A. Spectrum of pediatric tumours diagnosed by fine-needle aspiration cytology. Medicine. 2017;96:e5480.
[11] Pacinda SJ, Ramzy I. Fine-needle aspiration of breast masses. Journal of Adolescent Health. 1998;23:03-06.
[12] Islam S, Saroop S, Bheem V, Naraynsingh V. Largest giant juvenile fibroadenoma of the breast. BMJ Case Rep. 2019;28(12):pii: e227277.
[13] Jaiswal R, Dwivedi U, Ghaoghave S. Unusual variants of fibroadenoma breast. Journal of Evolution of Medical and Dental Sciences. 2013;2:3687-91.
[14] Mathur SR, Karak K, Verma K. Adenomyoepithelioma of the breast: A potential diagnostic pitfall on fine needle aspiration cytology. Indian J Pathol Microbiol. 2004;47:243-45.
[15] Iyengar P, Ali SZ, Brogi E. Fine-needle aspiration cytology of mammary adenomyoepithelioma: A study of 12 patients. Cancer. 2006;25:108:250-56.
[16] Zhang L, Yang C, Pfeifer JD, Caprioli RM, Judd AM, Patterson NH, et al. Histopathologic, immunophenotypic, and proteomics characteristics of low-grade phyllodes tumour and fibroadenoma: More similarities than differences. Breast Cancer. 2020;27:01-09.
[17] Geethamala K, Vani BR, Murthy VS, Radha M. Fibroadenoma: A harbor for various histopathological changes. Clin Cancer Investig J. 2015;4:183-87.
[18] Pike AM. Juvenile (cellular) adenofibromas, a clinicopathologic study. Am J Surg Pathol. 1985;9:730-36.
[19] Kuijper A, Mommers ECM, Wall E, Diest PJ. Histopathology of fibroadenoma of the breast. Am J Clin Pathol. 2001;115:736-74.
[20] Rosen P. Multinucleated mammary stromal giant cells-A benign lesion that simulates invasive carcinoma. Cancer. 1979;44:1305-08.
[21] Logullo AF, Nimir C. Columnar cell lesions of the breast: A practical review for the pathologist. Surg Exp Pathol. 2019;2:02-08.

[22] Sanchez R, Ladino-Torres MF, Bernat JA, Joe A, DiPietro MA. Breast fibroadenomas in the pediatric population: Common and uncommon sonographic findings. Pediatric radiology. 2010;40:681-89.
[23] Murphy JJ, Morzaria S, Gow KW, Magee JF. Breast cancer in a 6-year-old child. J Pediatr Surg. 2000;35:765-67.
[24] Field AS, Raymond WA, Rickard M, Arnold L, Brachtel EF, Chaiwun B, et al. The International Academy of Cytology Yokohama System for reporting breast fine-needle aspiration biopsy cytopathology. Acta Cytol. 2019;63:257-73.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India.
2. Professor, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. K Amita,
BG Nagara, Nagamangala Taluk, Mandya District-571448, Karnataka, India.
E-mail: dramitay@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 26, 2020
- Manual Googling: Jun 10, 2021
- iThenticate Software: Jun 30, 2021 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Sep 26, 2020**
Date of Peer Review: **Dec 05, 2020**
Date of Acceptance: **Jun 12, 2021**
Date of Publishing: **Jul 01, 2021**