

PATTERN OF BENIGN BREAST LESIONS ON FNAC IN CONSECUTIVE 100 CASES: A STUDY AT TERTIARY CARE HOSPITAL IN INDIA

Shirish Chandanwale¹, Mohit Rajpal², Pradeep Jadhav³, Sonam Sood⁴,
Kanika Gupta⁵, Nidhi Gupta⁶

^{1, 2, 3, 4, 5, 6} Department of pathology, Padm. Dr D Y Patil Medical College Pimpri, Pune, 411018

*Corresponding Author Email: shirishchandanwale@gmail.com

ABSTRACT

Aim: The aim of this study is to study the cytomorphologic features of benign breast lesions and correlate with clinical and histological findings. To find diagnostic accuracy of fine needle aspiration cytology (FNAC) in benign lesions of breast. Methods: Consecutive 100 patients of benign breast lesions which included 94 females and 6 males were subjected to FNAC. Clinical findings including general, systemic and local examination were noted. Cytomorphologic features of the breast lesions were studied in detail and correlated with clinical and histological features. Diagnostic accuracy of FNAC was calculated. Results: The most common age group affected in our study was 21-30 years (39%). The most common lesion encountered in our study on FNAC was fibroadenoma (49%) followed by fibrocystic disease (14%), and acute mastitis (5%). Tuberculous mastitis was 3%. Diagnostic accuracy of FNAC was 86.66%. Conclusion: FNAC is a safe outpatient procedure and is cost effective. FNAC provides highly accurate preoperative diagnosis (86.66%) in patients with benign breast lesions. It is highly sensitive and specific in diagnosing benign breast lesions. FNAC is quite useful in early diagnosis and management of the inflammatory lesions of the breast.

KEY WORDS

Breast, Benign, FNAC, Fibroadenoma, Fibrocystic, Mastitis.

INTRODUCTION

Fine needle aspiration cytology (FNAC) is widely accepted as a reliable technique in the initial evaluation of palpable and non-palpable breast lumps. The procedure is simple, safe, cost effective, minimally invasive and rapid. FNAC has high sensitivity, specificity and diagnostic accuracy.[1-5] The overall accuracy of FNAC in diagnosis of breast lesions is reported to be about 97.40%. FNAC is very well established as a diagnostic modality for elucidating the etiology of breast lumps and definitive therapy is instituted on the basis of FNAC results.[6] The primary goal of aspiration cytology is to separate malignant lesions that require more radical therapy from benign ones that may be conservatively managed.

With the growing awareness in general population about the breast pathology, females with breast lump is one of the commonest presentation in surgical outpatient department.[7] Though exact incidence of benign breast lesions is not known, majority of the patients attending a breast clinic have a benign breast lump.[8]

Benign breast lesions encompass a heterogeneous group of lesions that may present with a variety of symptoms. Frequently seen benign lesions of the breast are inflammatory lesions, epithelial and stromal proliferative lesions and neoplasms. The incidence of benign breast diseases begins to rise in the second decade and peaks in the fourth and fifth decade of life.[9] While much has been written about the cytomorphology of the atypical and malignant

lesions of breast, little covers the benign lesions which represent a sheer number in all fine needle aspiration cytology cases.[4]

A variety of inflammatory lesions can be seen in breast. Some of them are as a result of infectious agents while others do not have well understood etiology. Tuberculosis of the breast is relatively a rare occurrence with reported incidence varying from 3-4.5% in developing countries like India.[10] Sir Astley Cooper recorded the first case of mammary tuberculosis in 1829, and called it 'Scrofulous swelling of the bosom'. Hamit and Ragsdale in 1982 documented 500 cases of tuberculous mastitis, from world literature.[11] The significance of breast tuberculosis is due to its mistaken identity with breast cancer and pyogenic breast abscess.

CLASSIFICATION OF BREAST LESIONS

Rosai J (2004) and Chinoy RF(1997) mentioned a recent classification of breast lesions according to recent histogenetic concepts, gross and histological characteristics of these lesions.[12,13]

1) Non-Neoplastic

(I) Inflammatory-

A) Acute mastitis.-1) Lactational mastitis 2)Subareolar abscesses.

B) Chronic mastitis.- 1) Nonspecific mastitis- a) Fat necrosis b) Granulomatous mastitis. c) Mammary duct ectasia 2) Specific mastitis- a) Tuberculosis, b) Leprosy, c) Syphilis d) Actinomycosis e) Fungal infections f) Parasitic infections g) Viral infections, h) Reaction to foreign bodies i) Sarcoidosis.

II) Benign proliferative lesion.

1. Fibrocystic disease
2. Adenosis
3. Collagenous spherulosis

III) Miscellaneous. A) Galactocele. B) Gynecomastia.

2) Neoplastic

Benign

Epithelial lesions- Intraductal papilloma, Lactating adenoma

Fibroepithelial lesions- Fibroadenoma, Phyllodes tumor

B Malignant

MATERIALS AND METHODS

The present study was a prospective study of clinical, cytological and histopathological (wherever available) correlation of benign breast lesions done in the cytology and histopathology sections of our institute.

Inclusion criteria: Women having clinically benign breast lumps attending the hospital were the subject of study. **Exclusion criteria:** Breast lumps which are suspected clinically and diagnosed by ultrasonography or mammography as malignant.

Total 100 patients, were subjected to FNAC of the breast. Before doing FNAC, detailed findings of clinical history, clinical examination including general, systemic and local examinations were noted. The written consent of the patients was taken before FNAC, after explaining the procedure in their language. The aspirations were performed without USG guidance in this study.

Standard technique was followed during the procedure. FNAC gun along with disposable 10cc syringe and 22 gauze needle was used for aspiration. Needle contents were smeared over the glass slides. The smears of the aspirated material were made. In case of diffuse swellings left and right regions were aspirated separately. In case of cystic swellings, the cyst contents were aspirated, centrifuged and the slides were made from the sediment for the cytological analysis. No serious complications occurred in our study. The slides were carefully labeled, few slides were air dried and stained with Leishman's stain, other slides were stained with Haematoxylin and eosin stain (H and E).

Cytomorphologic features of the smears were studied in detail. Special stains like Ziehl Neelsen stain (ZN) were used whenever needed. The lumpectomy specimens were received in 10% formalin. If the specimen was small (up to 5 cm in diameter) then the entire circumference of the specimen was sectioned. In case of larger specimens additional sections were taken. Sections were paraffin processed. 3-5 microns sections were cut and stained with haematoxylin and eosin stain.

FNAC results were compared with histopathological diagnosis. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of FNAC in each lesion was calculated. The diagnostic

accuracy of FNAC was calculated by correlating with histopathological results.

RESULTS

The most common age group affected in our study was 21-30 years (39%) with maximum (94%) female patients. **Table 1** show detailed age and sex distribution of 100 cases. The most common lesion encountered in our study on FNAC was fibroadenoma (49%). **Table 2** show detailed FNAC diagnosis of 100 cases. Right breast was the most commonly involved (55%). Left breast was involved in 35% of the cases. Bilateral involvement was in 10% of the cases. All the cases presented with lump in the breast. Pain was the second most common presentation seen in 29% of the cases. **Table 3** show detailed signs and symptoms of 100 cases.

Out of the 49 cases of fibroadenoma on FNAC, 39(79.50%) were given a definitive diagnosis of fibroadenoma based on the presence of characteristic cytomorphologic features, while 10 cases were given a diagnosis of suggestive of fibroadenoma as these cases lacked specific cytomorphologic features of fibroadenoma. **Table 4** show detailed

cytomorphologic features of fibroadenoma. **Table 5** show detailed cytomorphologic features of other benign breast lesions.

Table 6 show FNAC diagnosis and cytological features of inflammatory and related lesions. Of the 3 cases of tuberculous mastitis, 2 cases had presence of epitheloid granulomas with caseous necrosis (66.6%). The third case had a suppurative abscess like picture but showed acid fast bacilli on Z N stain. In 2 cases of granulomatous mastitis, no infectious etiology could be established after staining with Ziehl Neelsen (ZN), Grocott Methenamine silver (GMS) and Periodic Acid Schiff (PAS) or culture studies which led to the provisional diagnosis of granulomatous mastitis in these cases. None of these cases were received for histopathological examination so the diagnosis of granulomatous mastitis could not be confirmed.

Out of the 100 cases studied, we received 45 specimens for histopathological examination. Fibroadenoma was the most common diagnosis given on histopathology in 30 cases followed by fibrocystic disease in 6 cases (**Table 7**). **Table 8** show cytohistological correlation of 45 cases.

Table 1: Age and Sex of 100 patients of Benign breast lesions

Age Group(yrs)	Sex		Total (%) (N=100)
	Males (%) (N=6)	Females (%) (N=94)	
0-10	0	0	0
11-20	1	19	20
21-30	1	38	39
31-40	1	31	32
41-50	1	4	5
51-60	1	2	3
61-70	1	0	1

Table 2: FNAC Diagnosis of 100 Benign Breast Lesions

FNAC Diagnosis	No. of Cases(N=100)	Percentage (%)
1.Fibroadenoma	49	49%
2.Fibrocystic disease	14	14%
3.Acute Mastitis	5	5%
4.Tubercular Mastitis	3	3%
5.Granulomatous Mastitis	2	2%
6.Fat Necrosis	1	1%
7.Galactocoele	3	3%
8.Gynaecomastia	6	6%
9.Lactational adenoma	1	1%
10.Simple cyst	2	2%
11.Benign breast disease	14	14%

Table 3: Signs and symptoms in 100 cases

Signs and symptoms	No of cases (%)
Lump	100
Pain	29
Fever	9
Nipple discharge	5
Nipple retraction	2
Cyclic mastalgia	7
Axillary lymphadenopathy	2

Table 4: Pattern of cytomorphological features in fibroadenoma

FNAC Diagnosis	No.of Cases	Fibromyxoid Stroma	Bare Bipolar Nuclei	Cohesive sheets	Cyst macrophages /Giant cells	Anisonucleosis
1.Definitive Diagnosis	39	39	39	39	6	5
2.Suggestive of Fibroadenoma	10	2	7	10	4	3

Table 5: Pattern of cytomorphologic features of other Benign lesions

FNAC Diagnosis	No.of cases	Ductal Cells	Apocrine cells	Bare Bipolar Nuclei	Proteinaceous Background	Cyst macrophages
Fibrocystic Disease	14	11	10	7	1	8
Galactocoele	3	3	-	-	3	1
Gynaecomastia	6	6	-	3	-	-
Lactating adenoma	1	1	-	-	-	-
Simple Cyst	2	-	1	-	-	2

Table 6: Cytomorphologic pattern of Inflammatory and related lesions

FNAC Diagnosis	No.of cases	Epitheloid Granulomas	Suppurative Necrosis	Caseous Necrosis	Giant Cells	Inflammatory Cells
1.Acute Mastitis	5	-	4	-	1	5
2.Tubercular astitis	3	2	1	2	1	3
3.Granulomatous Mastitis	2	2	-	-	-	2
4.Fat Necrosis	1	-	-	-	-	1

Table 7: Histopathological diagnosis of patients with benign breast lesions

Diagnosis(N=45)	No. of cases	Percentage (%)
1. Fibroadenoma	30	30%
2. Fibrocystic disease	6	6%
3. Gynaecomastia	5	5%
4. Benign Phyllodes	1	1%
5. Adenomyoepithelioma	1	1%
6. Galactocoele	2	2%

Table 8: Cytohistopathological correlation

FNAC Diagnosis/ No of cases.	HISTOPATHOLOGICAL DIAGNOSIS					TOTAL	
	FA	Adenomyoepithelioma	Benign Phyllodes	FCD	Galactocoele	Gynaecomastia	
FA-30	27	1	1	1	-	-	30
FCD-8	3	-	-	5	-	-	8
Galactocoele-2	-	-	-	-	2	-	2
Gynaecomastia-5	-	-	-	-	-	5	5
Total	30	1	1	6	2	5	45

Table No 9: Comparison of Diagnostic accuracy of our study with other studies

STUDIES	DIAGNOSTIC ACCURACY OF FNAC
Our study	86.66%
Tiwari M	90%
Arjun Singh et al	92.3%
Clive et al	94%
Wanebo et al	74%

STATISTICAL RESULTS

Diagnostic accuracy of FNAC is 86.66%. Sensitivity, specificity, positive predictive value and negative predictive value of FNAC in fibroadenoma lesions came out to be 90%, 80%, 90% and 80% respectively. Cohen's kappa is 0.7. Sensitivity, specificity, positive predictive value and negative predictive value of FNAC in fibrocystic disease came out to be 83.33%, 92.31%, 62.5% and 97.3% respectively. Cohen's kappa is 0.73. All statistical parameters- sensitivity, specificity, positive predictive value and negative predictive value of FNAC in gynaecomastia and galactocoele lesions came out to be 100%.

DISCUSSION

In this study, FNAC was done in 100 patients with benign breast lesions out of which histopathology was available in 45 cases. Diagnostic accuracy of FNAC was calculated by correlating with histopathological results.

AGE AND SEX INCIDENCE: The most common age group in our study was from 21-30 years (39%). This is also supported by Farkhanda and coauthors [14] and Echejoh et al [15] in their study. In contrast, Haque et al [16] reported 30-40 years of age as the most common age group in their study. Out of 100 patients, 6 were male and all were diagnosed as gynaecomastia. Similar observations were made by Echejoh et al [15] and Arjun singh et al. [17]

SITE OF INVOLVEMENT: In our study, right breast was more commonly involved than left. This was in contrast to the study conducted by Prakash et al [18] who found more involvement of the left breast in their study.

FNAC DIAGNOSIS: The most common diagnosis on FNAC in our study was fibroadenoma (49%) followed by fibrocystic disease (14%). Similar results were observed by Farkhanda and co authors [14] and Tiwari M [19]. However, she reported very few cases of fibrocystic disease (5.5%). Arjun singh and co authors [17] in their study on 102 patients also reported fibroadenoma to be the most common diagnosis in their study(45.08%). Majority of the patients of fibroadenoma in our study were in the 2nd and 3rd decade of their life. Similar finding was corroborated in the study conducted by Farkhanda et

al.[14] Fibrocystic disease in our study was found mainly in patients of 3rd and 4th decade of life. Similar findings were also in the study done by Echejoh et al[15] and Farkhanda et al.[14]

Inflammatory lesions in our study were 11%. Similar findings were observed by Baptist et al [20] in their study (11%), Baravkar LV [21]found 5.60% and Haque et al [16] reported 4% inflammatory lesions in their study. Tubercular mastitis in our study were 3% which was in accordance with studies of Dharkar et al [22] and Haque et al. [16]

SIGNS AND SYMPTOMS: All the patients presented with lump in the breast. The next common symptom was pain in 29% of the cases followed by fever in 9% (Table 3). Pain (54.54%) and fever (33.33%) were the common symptoms of inflammatory lesions of the breast. Nipple discharge was observed in cases of chronic mastitis viz tuberculous mastitis, granulomatous mastitis and in 2 cases of fibrocystic disease. Axillary lymphadenopathy was observed in 2 patients who were subsequently diagnosed as tuberculous mastitis on FNAC. Similar findings were corroborated by Echejoh and co-workers.[15]

Cytomorphologic findings in our study:

Cytomorphologic features of 100 benign breast lesions were studied and histopathological correlation was done wherever possible. Out of the 100 cases, 49 cases were diagnosed as fibroadenoma on cytology. Out of these, 39 cases (79.59%) were given a definitive diagnosis of fibroadenoma (Table 4). Definitive diagnosis of fibroadenoma was made when cytology smears showed the presence of characteristic cytomorphologic features viz presence of cohesive sheets of ductal epithelial cells, fibromyxoid stroma and presence of numerous bare bipolar nuclei in the background. Degenerative changes like presence of cyst macrophages, giant cells and mild anisonucleosis were also noted which are known to occur in fibroadenoma. Presence of marked nuclear atypia in cases of fibroadenoma makes it a common cause of a false positive diagnosis on breast cytology. [23] Though mild anisonucleosis was seen in some cases (n=8) of fibroadenoma, none of our cases showed marked nuclear atypia. Bottles and associates demonstrated that stromal fragments, antler- horn clusters and marked cellularity were the three most useful cytological variables for a definitive diagnosis

of fibroadenoma.[24] The diagnosis of suggestive of fibroadenoma was made when cytological smears lacked all the three specific features characteristic of fibroadenoma i.e. either one or two of the characteristic cytomorphologic features were present. There were 10 such cases (20.40%). All of these cases showed cohesive sheets of ductal epithelial cells. Bare bipolar nuclei were seen in 8 cases (80%) and fibromyxoid stroma was present in only 5(50%) of these cases. Other features were cyst macrophages, giant cells and mild anisonucleosis.

Out of the 49 cases diagnosed as fibroadenoma on FNAC, 30 cases were received for histopathological examination. Of these, 27 cases showed cytohistological concordance. The three discordant cases diagnosed were: benign phyllodes, adenomyoepithelioma and fibrocystic disease.

Cytohistological discordance in the case of benign phyllodes diagnosed as fibroadenoma on cytology is attributed mainly to the considerable amount of overlap in the cytological appearance of both these diagnosis and only few spindle shaped stromal cells were seen on cytology in this case which led to the misdiagnosis.

The case of fibrocystic disease diagnosed as fibroadenoma on cytology was because the cytology smears were dominated by presence of cohesive sheets of ductal epithelial cells and bare bipolar nuclei with only a scant number of cyst macrophages and apocrine cells.

One case was diagnosed as adenomyoepithelioma on histopathology. Adenomyoepithelioma is an extremely uncommon tumor. Kurashina described two cases of adenomyoepithelioma in 2002. Our case on cytology showed only a few stromal cells (spindle cells) which are diagnostic of adenomyoepithelioma and the correct diagnosis was therefore overlooked.

14% cases were given a diagnosis of benign breast disease (BBD) in our study. These diagnoses were made in view of scant cellularity of the aspirate, presence of a haemorrhagic background, cell debris and presence of degenerate epithelial cells. These cases were also diagnosed as benign breast disease in view of overlapping features with other benign proliferative breast lesions like epithelial hyperplasia,

adenosis, papillomatosis, radial scar and atypical ductal hyperplasia.

In our study, 14 cases were given a diagnosis of fibrocystic disease. The characteristic cytologic features of these cases were presence of apocrine cells (71.4%), cyst macrophages (57.14%) and bare bipolar nuclei (50%) on the background.

Histopathology was available in 8 cases diagnosed as fibrocystic disease. Out of these 5 cases were confirmed on histology. Remaining 3 cases which were diagnosed as fibrocystic disease on cytology turned out to be fibroadenoma on histology. This was attributed to predominance of cyst macrophages in these cases and only a scant population of cohesive sheets of ductal epithelial cells and bare bipolar nuclei which resulted in misdiagnosis of fibrocystic disease. In fibroadenoma, degenerative changes are known to occur, possibly the aspirate was taken from the site where degenerative changes were more marked. This is also stated by Kline who concluded that the cytological features of fibroadenoma cannot always be distinguished from those of fibrocystic disease. [25]

There were 3 cases of galactocoele on cytology, out of which 2 were subjected to histopathology. Both the cases subjected to histopathology were given a diagnosis of galactocoele. All the 3 cases gave a history of lactation. The cytomorphologic features were presence of dispersed large epithelial cells (acinar cells) with vacuolated cytoplasm against a proteinaceous background. Cyst macrophages were present in 1 case (Table 5).

There was 1 case of lactating adenoma in our study. Cytomorphology of the case showed the presence of flat sheets of acinar cells studded with abundant amount of vacuolated cytoplasm (Table 5). Recognition of this lesion on cytology can prevent unnecessary radical surgery and cure it by local excision only. [26]

6 male patients with the FNAC diagnosis of gynaecomastia were present in our study. 2 patients (33.33%) had history of alcoholic liver disease. Clinically, all the patients presented with a subareolar mass. Aspirates of these cases showed moderately cellular smears with cohesive sheets of ductal epithelial cells. Bare bipolar nuclei were observed in 3 cases (50%) Out of the 6 cases of gynaecomastia on

cytology, 5 were received for histopathological examination. Cytohistological concordance in gynaecomastia was 100%. This is further corroborated by Das et al [27] who found 100% diagnostic accuracy of fine needle aspiration cytology in cases of gynaecomastia.

In our study, 5 patients were given a diagnosis of acute mastitis on cytology. Clinically, 2 of these patients (40%) had history of lactation. This was also concluded by Knight et al [28] who reported that acute mastitis is a common complication of nursing. All the patients of acute mastitis in our study were in 20-40 year age group, this was also observed by Ekland and Zeigler [29] who reported majority of the patients of acute mastitis in their study belonging to the same age group. Pain and fever were common presentations being seen in 60% and 40% of the patients with acute mastitis respectively in our study. Cytology revealed the presence of inflammatory infiltrate of neutrophils in all the cases, suppurative necrosis in 4 cases (80%) and giant cells in 1 case. Aspirates from 4 out of the 5 patients with acute mastitis were subjected to microbiologic culture studies, and staphylococcus was identified in 2 of these cultures. All the patients were treated effectively with antibiotics. The early diagnosis of acute mastitis can be made by fine needle aspiration cytology and can be treated effectively with antibiotics.

There were 3 cases diagnosed as tuberculous mastitis on cytology. 2 out of the 3 patients were in the 20-30 year age group. This was also observed in the study conducted by Baravkar [21] from 1985 to 1990 in his study of 9 patients of tuberculous mastitis who observed the maximum number of patients in the same age group. Clinically, these patients presented with a firm mass in the breast.

In 2 of these cases, there was no difficulty in establishing a diagnosis of tuberculous mastitis since they showed presence of epithelioid granulomas and caseous necrosis. Tuberculosis is the commonest cause of caseating granulomas. Ziehl Neelsen staining revealed the presence of acid-fast bacilli in one case. The detection of acid-fast bacilli on FNAC is not mandatory, since for AFB to be seen microscopically, their number must be 10,000 to 100,000/ml of the aspirate.[30] Other cytological features were

presence of chronic inflammatory cells like lymphocytes and plasma cells.

In the third case, cytology showed presence of numerous neutrophilic inflammatory cells, suppurative necrosis, cyst macrophages and occasional giant cells. Diagnosis of tuberculous mastitis was confirmed on ZN stain which demonstrated the presence of numerous acid fast bacilli. Leo Francis et al [31] reported a case of tuberculous mastitis presenting as breast abscess. Similar cases were also studied by Kumar et al [32] in their study in 2004.

These patients were started standard antitubercular treatment and showed improvement clinically on subsequent follow up, thereby concluding the usefulness of FNAC in managing this condition. Mehrotra [33] studied cytomorphology of 20 cases of tuberculous mastitis and concluded FNAC to be very reliable in diagnosing this condition.

There were 2 cases diagnosed as granulomatous mastitis in our study. Both these cases showed the presence of epithelioid granulomas on a background of chronic inflammatory cells like lymphocytes and plasma cells on cytology. Caseous necrosis was not seen. No infectious etiology could be established in these cases after doing Ziehl Neelsen (ZN), Grocott Methenamine Silver (GMS) and Periodic Acid Schiff (PAS) and culture studies. A provisional diagnosis of granulomatous mastitis was made. However, the diagnosis of granulomatous mastitis could not be confirmed as histopathology was not available for these cases.

There was 1 case of fat necrosis. The patient had history of prior surgical intervention on the affected side of the breast (right side). Cytological features were presence of fat droplets and fragments of adipose tissue along with presence of chronic inflammatory cells. 2 cases were diagnosed as simple cyst. They showed complete disappearance of the lump after aspiration of the fluid. Thus, FNAC is a diagnostic as well as therapeutic procedure in these cases. Cytology showed presence of numerous neutrophils and cyst macrophages in one of the cases which was given a diagnosis of infected cyst. The other case showed presence of few apocrine cells along with cyst macrophages.

Relatively low diagnostic accuracy(86.66%) in our study as compared to studies by Tiwari M and Singh A can be attributed to smaller size of the lesion, deep seated lesions and inadequate sampling.

CONCLUSION

FNAC is a safe outpatient procedure. The procedure is cost effective. FNAC is quite useful in early diagnosis and management of the inflammatory lesions of the breast, this was highlighted by the fact that none of the inflammatory lesions in our study were subjected to histopathology and were managed effectively on basis of FNAC diagnosis. Success of FNAC is contingent upon several important contributing factors like aspirator's experience, skillful cytological interpretation and a rational analysis based upon correlation of cytological and clinical information in the context of the patient. FNAC provides highly accurate preoperative diagnosis (86.66%) in patients with benign breast lesions. It is highly sensitive and specific in diagnosing benign breast lesions. FNAC can reduce significant morbidity and mortality of patients by making an early diagnosis. Benign breast lesions commonly affect the younger age group. Fibroadenoma is the most common lesion encountered amongst the benign lesions.

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***Corresponding Author:**

Dr Shirish Chandanwale,
Professor Pathology,
Padm Dr D Y Patil Medical College,
Pimpri, Pune, 411018.