Original Research

Validity of Fine Needle Aspiration Cytology in Diagnosis of Prostatic Lesions and Correlation with Trucut Biopsy

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Prostate fine needle aspiration (FNA) is an easy-to-perform outpatient procedure requiring no expensive equipment or anesthesia. The aim of this study was to analyze the cytomorphology of prostatic lesions and to correlate the findings in cytology with that of the histopathological appearance. In doing so we also assessed the diagnostic accuracy of fine needle aspiration cytology and identified possible pitfalls. The study was carried out in 100 patients who underwent tru-cut biopsy in the department of Urology at Kottayam Medical College, India during the period spanning from March 2010 to March 2011. Fine needle aspiration cytology (FNAC) was done with Franzen needle and followed by tru-cut biopsy after which the results of both were compared. FNAC gave a benign diagnosis in 64 cases and identified a malignant pattern in 36 cases. The overall accuracy of FNAC in this series in diagnosing prostatic lesions was 97% with a sensitivity of 100% and specificity of 95.5%. This shows that FNAC prostate is a reliable, relatively painless tool, which can be used for the diagnosis of prostatic carcinoma, especially in patients with high risk complications such as bleeding and infections in whom a tru-cut biopsy is more invasive. In addition it is also cost-effective and may sample a larger area.
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INTRODUCTION

Prostate cancer continues to be a major public health problem in both industrialized and developing countries worldwide. According to the World Health Organization, there are about 250,000 new cases of prostatic cancer every year. When diagnosed in time, the disease has a cure rate of over 90%. Elevated prostate specific antigen (PSA) levels suggest a likelihood of malignant disease however such levels can occur in benign prostatic diseases as well. Cytology and histopathology have been the forefront of cancer detection but how well these two correlate has been a content of debate.

In 1930, Russell Ferguson reported that prostate cancer could be diagnosed by transperineal fine needle aspiration (FNA); however, it took three decades before Sixten Franzen developed a trans-rectal approach to prostate biopsy and applied prostate FNA to diagnostic uropathology.[1] The development of a special instrument for prostatic aspiration led to a painless quick method of cytologic sampling of the prostate by trans-rectal FNA biopsy. In 1988, Benson[2] recommended that prostate FNA should be encouraged as a standard diagnostic tool that is performed by urologists, taught to urology residents, and diagnosed by pathologists. He mentioned that, while accuracy for cytodiagnosis was similar to that of histopathologic diagnosis, fine-needle aspiration was less traumatic and cost-effective compared to more invasive histologic biopsy methods. However, some pathologists find the core biopsies easier to interpret than aspiration cytology, and hence underestimate the role of FNA as a diagnostic tool. Whereas core biopsies offer the advantage of a more precise localization of the lesions within the target organ, FNA of the prostate offers its own unique advantages. First, it is an outpatient procedure, well tolerated by the patients because the discomfort and trauma from the 22-gauge needle are minimal.[3,4] Second, sampling area is larger and more representative[5] than that of core biopsies. Third, smears can be processed and interpreted rapidly. Finally, it is accurate in experienced hands and has low risk of complications[6] and seeding of tumor cells.

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METHODS

Our study was undertaken to elucidate the cytomorphological features of prostatic lesions and explore the diagnostic accuracy of FNA by comparing it with concurrent histopathology. Since the procedure was recently adopted by our institution, we standardized the technique by using different needles. Initially we tried with intravenous needle. It was technically easy because the needle is rigid but the smears were bloody, obscuring the cells. Subsequently, we used spinal needle. It was technically difficult because of the flexibility of the needle and we could not assess the depth of penetration. However, it gave better yield in the hands of experts. Most recently, we started using Franzen needle which is the recommended needle for prostatic FNAC. It was

technically easy and gave high yield, and we could easily assess the depth of penetration.

One hundred patients who were scheduled to undergo a tru-cut biopsy in the department of Urology during the study period spanning from March 2010 to march 2011 were selected for this study. Cases were chosen after proper history-taking, physical and imaging examination (including digital rectal examination, trans-rectal ultrasound) and informed consent. A single dose of quinolone was given one hour prior to the procedure. They were then subjected to FNA by trans-rectal route with the Franzen needle before tru-cut biopsy. The aspiration was done by specially constructed Franzen needle which is a 22-gauge, 20-cm in length flexible needle that is slightly thicker and rigid in the proximal 5 cm. The aspiration was performed with the patient in left lateral position. Patients with inflamed hemorrhoids or anal fistula were appropriately treated initially and received an anesthetic jelly prior to the procedure.

The suspected area of the prostate was palpated with the index finger of the non-dominant hand, after which the needle was advanced into the lesion with the plunger of the syringe down. When the needle entered the lesion, several small amplitude to-and-fro movements of the needle were performed to loosen the target tissue. Negative pressure was obtained by pulling on the syringe plunger in order to aspirate the material into the needle. Before withdrawing the needle from the prostate, the negative pressure was released, a most important step that will ensure that the aspirated material remained in the needle and does not enter the barrel of the syringe, where it would be irretrievably lost. If aspiration of several areas of the prostate was needed, the needle was withdrawn and replaced with another needle. It is not advisable to attempt to change the direction of the needle while being lodged in the target tissue, because of the risk of hemorrhage and injury to the prostate. The smears were then prepared from needle contents and processed as either air-dried May-Grunwald-Giemsa (MGG)-stained or alcohol-fixed Papanicolaou (PAP)-stained smears. The presence of 10-12 epithelial cell clusters were taken as adequate for diagnosis. This was followed by the tru-cut biopsy performed by the Urologist and was then subjected to histopathological examination.

The smears were evaluated on the very same day the FNA was done. The corresponding biopsy sections were studied and reported by a different pathologist when the H&E sections were ready after 2 days. The interpreters of the FNA and core biopsy were blinded to each other.

RESULTS

Benign prostate lesions in smears are usually composed of large clusters of normal, flat, non-stratified sheets of benign epithelial cells with regular architecture and cells in honey comb pattern (**Figures 1a, 1b, 1c)**. Another pattern of benign lesions is cell grouping as large multilayered plug of ductal epithelial cells (**Figure 1d**).

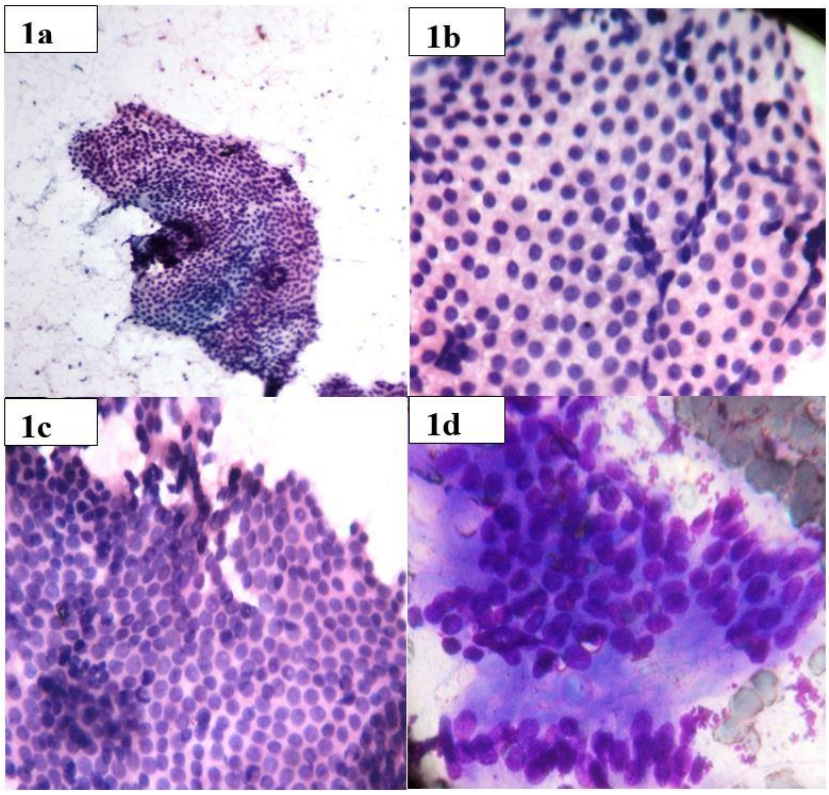


Figure 1. Characteristic patterns of benign prostate lesions on FNA smears (MGG stain). **1a-1c.** Large clusters of normal, flat, non-stratified sheets of benign epithelial cells with regular architecture and cells in honey comb pattern in a clean background (a. magnification ×100; **1b.** magnification ×400; **1c.** magnification ×400). **1d.** Clusters of ductal epithelial cells with no definite outline, overlapping and mild variation in size (magnification ×400).

The cytological criteria for diagnosing prostatic carcinoma in aspirates have been well-defined.[7,8] In smears from low-grade carcinoma (Grade I), sheets of cells in unicellular layer resembling benign pattern under low power view and cells in micro-adenomatous pattern can be seen (**Figure 2a**), and it can be considered as a malignant lesion even without significant nuclear polymorphism (**Figures 2b and 2c**). The adequate aspiration smears in prostatic adenocarcinoma are usually richer in cells than smears from benign conditions.

In moderately differentiated adenocarcinoma (Grade II), the micro-adenomatous pattern is still evident but the component cells are much larger (**Figures 3a, 3b and 3c**). However, the smears are mainly composed of more solid groups of malignant cells with significant nuclear polymorphism, large, irregular nuclei and prominent nucleoli. In smears from poorly differentiated prostatic cancers (Grade III), the malignant cells are often dissociated and may be strikingly polymorphic with bizarre forms and very large nuclei (**Figures 4a and 4b**). In the anaplastic variant, the picture is monotonous and may resemble the pattern of leukemia or lymphoma. Clustering and micro-adenomatous complexes are rare. This grading was applied to the FNA samples and was compared with the tru-cut biopsy interpretation.

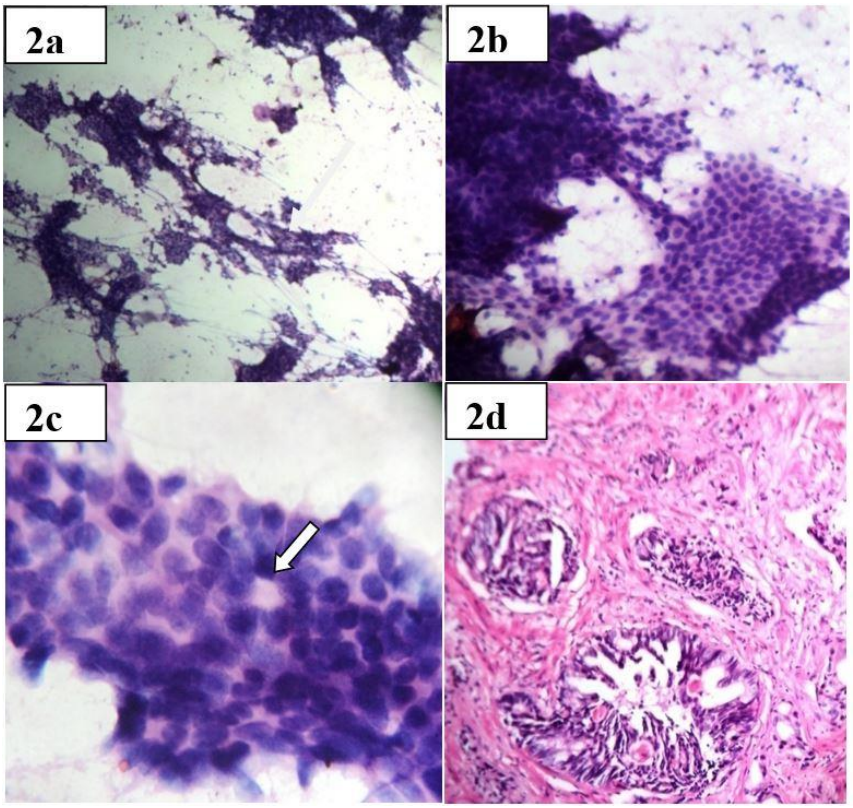


Figure 2. Grade I Adenocarcinoma. **2a.** Cohesive clusters of cells in unicellular layer resembling benign pattern under low power view (MGG stain, magnification ×100). **2b.** Higher power view shows that the cells have minimal atypia (MGG stain, magnification ×400). **2c.** Some cells may show micro-adenomatous pattern (arrow, PAP stain, magnification ×1000). **2d.** A concurrent tru-cut biopsy showing prostate adenocarcinoma with a Gleason score of 2+2 (H&E stain, magnification ×400).

After data on 100 patients was collected the results were analyzed. 64 cases were diagnosed as benign lesions and 36 were malignant as per cytology. On histological examination, the 64 cases which were cytologically diagnosed as benign were proven to be benign. This included 58 cases of benign prostatic hyperplasia (BPH), 4 cases of BPH with chronic prostatitis, and 2 cases of BPH with basal cell hyperplasia.

Of the 36 cases diagnosed cytologically as malignant, 33 cases were proven to be cancerous by histological examination, and 3 cases were proven to be false positive including 2 cases of basal cell hyperplasia and 1 case of chronic prostatitis. Using Fisher's exact test to correlate the results of FNAC and tru-cut in diagnosing prostatic lesions, the accuracy of FNAC was 97% with a sensitivity of 100% and a specificity of 95.5%. The positive predictive value and negative predictive value were 91.6% and 100%, respectively.

Of the 33 malignant cases, 5 cases (15%) were Grade I by cytology and correlated with Gleason score 2-5 in biopsy (**Figure 2d**), 23 cases (70%) were Grade II by cytology and correlated with Gleason score 6-8 in biopsy (**Figure 3d**), and 5 cases (15%) were Grade III by cytology and correlated with Gleason score 9-10 in biopsy (**Figures 4c and 4d**).

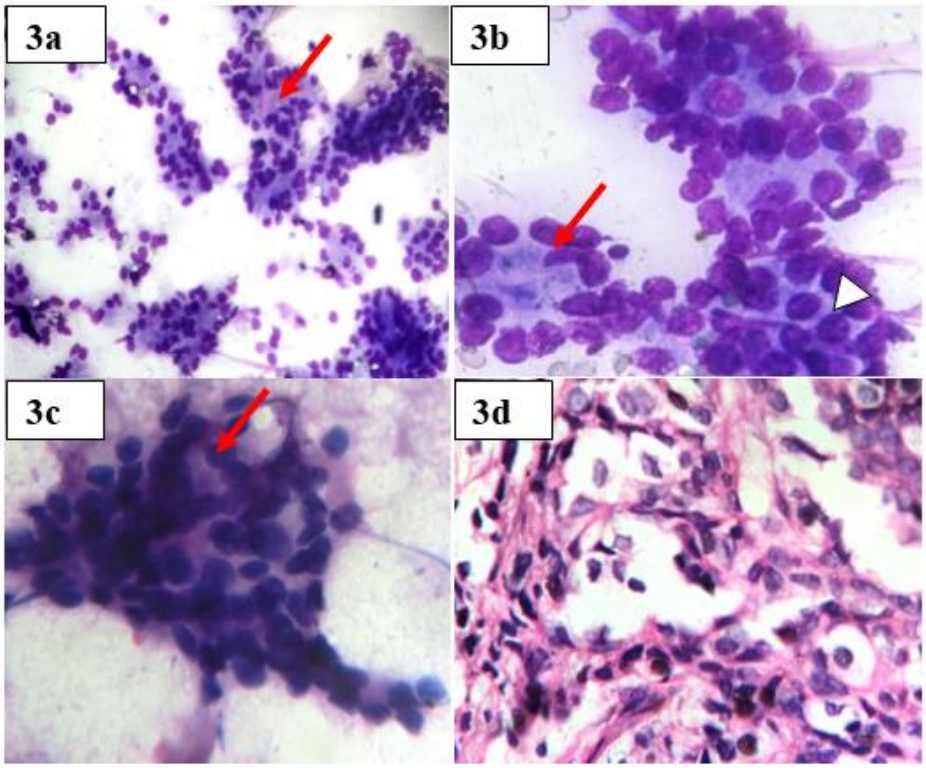


Figure 3. Grade II Adenocarcinoma. **3a-3c.** A case with predominantly micro-adenomatous pattern (arrows) and with solid cell clusters (arrowhead) showing increased nuclear atypia (a. MGG stain, magnification ×100; **3b.** magnification ×400; PAP stain, **3c.** magnification ×1000). **3d.** A concurrent tru-cut biopsy showing prostate adenocarcinoma with a Gleason's score of 3+4 (H&E stain, ×1000 magnification).

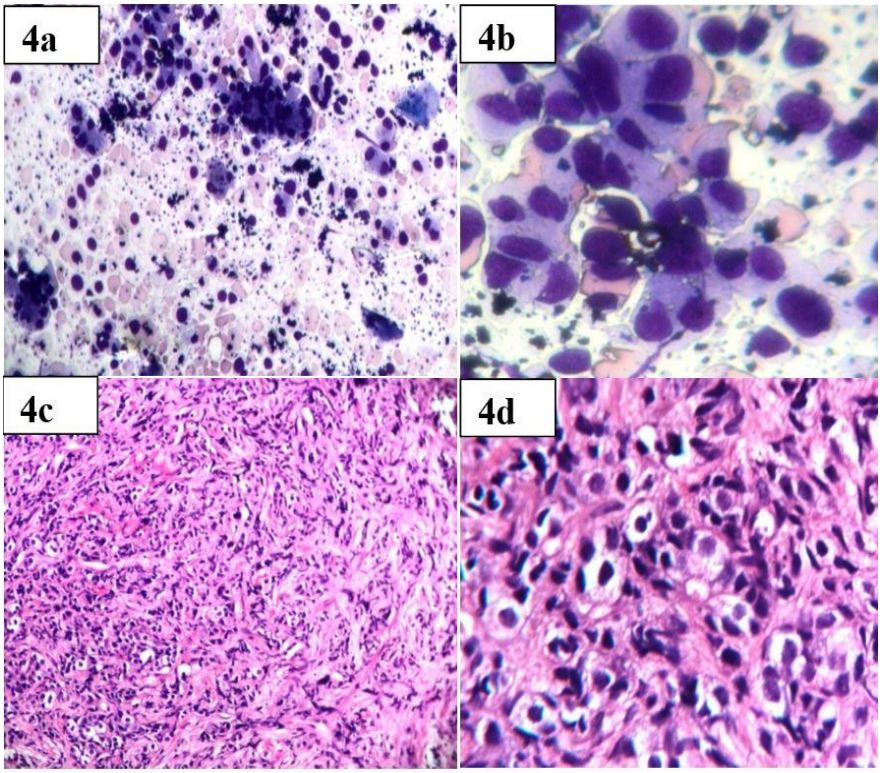
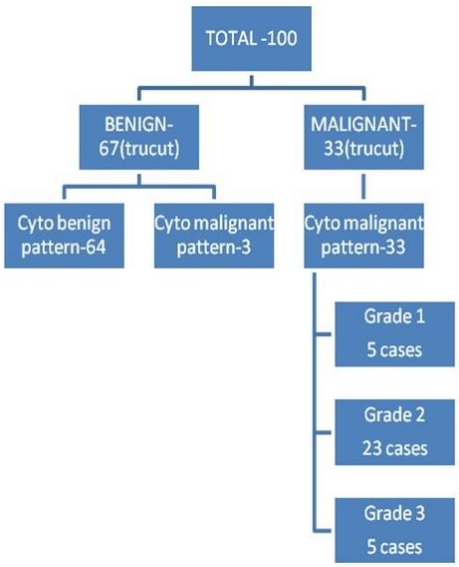


Figure 4. Grade III Adenocarcinoma. **4a-4b.** A case with mainly dissociated cells with marked atypia (MGG stain, a. magnification ×100; **4b.** magnification ×400. **4c-4d.** A concurrent tru-cut biopsy showing prostate adenocarcinoma with a Gleason score of 4+5 (H&E stain, **4c.** magnification ×400; **4d.** magnification ×1000**).**



TRU-CUT / FNAC	Malignancy positive	Malignancy negative
Malignancy positive	33	3
Malignancy negative	0	64

Figure 5. Correlation of results of fine needle aspiration and tru-cut.

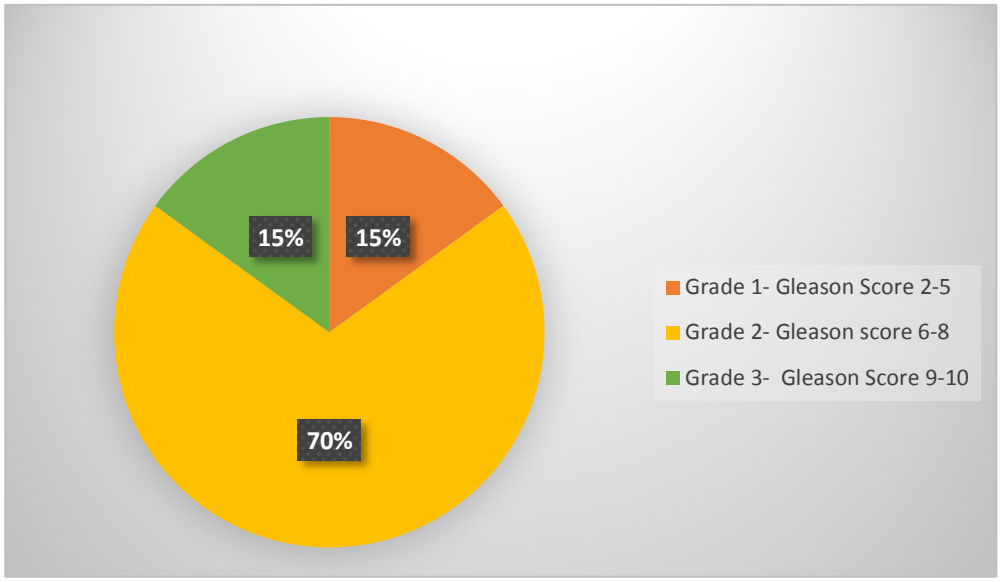


Figure 6. Cytological Grade and correlation with Gleason score obtained by tru-cut biopsy.

DISCUSSION

Prostatic carcinoma is one of the most important causes of mortality in elderly men mainly because of the late detection despite of the fact that it is a potentially curable disease. As FNA is painless, simple, low-cost, repeatable, with low risk of complications, it can be employed to detect occult or early prostatic carcinoma and in follow-up of confirmed cases. However the usefulness of FNA and the robust supportive data behind it in replacing or being an adjunct to tru-cut biopsy is a matter of contention.

There has been numerous research supporting the use and accuracy of FNA. In a study done by Saleh AF et al,[9] the sensitivity was 88% and specificity was 93% with an accuracy of 91.7%. FNA seems to be very effective in identifying benign lesions as shown in another prospective study by Singh et al where the accuracy for benign and malignant lesions of prostate were 98.33% and 81.88%, respectively.[10] These facts argue that FNA could have a high negative predictive value and be a useful tool in low prevalence populations who may not need a more invasive test.

By securing a larger sampling area FNA is less likely to miss early malignant pocket of cells. Tru-cut biopsies with more cores also carry higher rates of complications which can be avoided by FNA. Polito M, et al showed that FNA had a sensitivity of 98.2%, specificity of 98.1% and accuracy of 96% which is almost similar to our study.[11] A similar study

by Honig et al also showed that aspiration cytology of prostate increased the incidence of finding adenocarcinoma from 10% to 14% in patients undergoing transurethral resection of the prostate (TURP).[12] Klotz et al showed that all patients with positive findings on aspiration also had positive findings on core biopsy which could put the positive predictive value for aspiration close to 100%.[13] However, we found 3 false-positive cases in our study. On further investigation these three cases were found to be basal cell hyperplasia (n = 2) and chronic prostatitis (n=1). In the two cases of basal cell hyperplasia, smears showed high cellularity with solid clusters and crowed cells with hyper chromatic nucleus. In the case of chronic prostatitis, smears showed inflammatory atypia with background inflammatory cells. Though these diagnostic pitfalls afflict correct interpretation, the high negative predictive value of prostatic FNA is undeniable.

There is also an argument that cytological grade of FNA prostate correlates well with the Gleason score in prostate biopsy sections. In our study the correlation of cytological grade with histological score was 100%. This is in accordance to another study published by Willems et al. who showed that cytological grading of prostatic carcinoma into well, moderately, and poorly differentiated types had shown significant correlation with not only to histopathological grading, but also to clinical stage, response to hormonal therapy and survival.[7]

Another research by Maksem JA showed that when malignancies were classified as well differentiated, moderately differentiated, or poorly differentiated, there was 84% agreement between histology and cytology.[14] However not all researchers agree on the correlation of this grading to Gleason score. Hostetter AL showed a tendency toward underestimation of both the extent and degree of differentiation of the prostate carcinomas during cytological examination,[15] and Adolfsson J argued that core biopsies were generally graded higher than fine needle aspirations.[16] Since the technique of obtaining the sample and interpretation of FNA are highly operator dependent and relies heavily on the urologists' and pathologists' expertise, the correlation of the samples may not be universally concordant.

CONCLUSION

We conclude that FNAC prostate is a reliable tool for the diagnosis of prostatic lesions, especially in patients with high risk of complications, bleeding tendencies and in follow-up of previously diagnosed cases.

The accuracy of FNAC depends largely upon the skill of the examiner taking the cell samples and the alertness of the cytopathologist for possible diagnostic pitfalls. The procedure is quick, safe, and results are available the same day. Several aspirations can be done even in outpatients with minimal trauma. Complications are rare. Our results support the use of needle aspiration as an initial diagnostic maneuver especially in the low prevalence population.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

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