

Accuracy of Perineal Percutaneous Fine Needle Aspiration Cytology (FNAC) of Prostate under Ultra-Sound in Comparism with Transrectal Aspiration in Diagnosis of Prostatic Cancer

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Abstract:

Background: Prostatic carcinoma is the commonest internal malignancy of adult males. Patients usually presenting with voiding symptoms. Clinical suspicion of prostatic carcinoma depends on finding of one or more of the followings; hard prostatic nodule(s) on digital rectal examination (DRE), hypoechoic lesion on transrectal ultrasonography (TRUS), and/or high serum level of prostatic specific antigen (PSA). Final diagnosis depends on FNAC and/or histopathology. Objective: This is a case control prospective study designed to evaluate the usefulness of FNAC of prostate through perineal skin under ultrasound instead of transrectal aspiration in diagnosis of suspicious prostatic conditions.

Patients and Methods: One hundred and ten males with voiding symptoms and clinical suspicion of prostatic carcinoma were participated in the study. Their ages were between 45 and 92 years. The aspiration was carried out as outpatient procedure.

Results: Cytopathological results were; 64 (58.18%) positive, 4 (3.64%) suspicious, and 40 (36.36%) negative for prostatic cancer. Two specimens (1.82%) were inadequate for proper cytopathology. Results of histopathological examination of resected specimens from the same patients was very close to that of cytopathology with only two false positive and one false negative results. There was no any mentioned complication following aspiration, and sensitivity, specificity, and accuracy were 98%, 95%, and 91.81% respectively, and all results were statistically significant with p-values <0.05.

Conclusion: Percutaneous perineal FNAC of prostate under ultrasound is a safe, reliable, cost effective, and as accurate as transrectal FNAC in diagnosis of prostatic cancer.

Keywords: Perineal prostatic FNAC, Prostatic Cytopathology, PSA, TRUS.

Introduction:

Carcinoma of the prostate is a common malignancy in adult males, and in the United States it is the commonest internal malignancy, and accounting for about 10% of cancer related death [1, 2]. It is only second to lung cancer as a cause of deaths from cancer in adult men [1, 2]. Patients usually presented to doctors because of voiding symptoms. Clinical evaluation is usually performed by digital rectal examination (DRE), transrectal ultrasonography (TRUS), and serum prostate Specific Antigen level (PSA) [1, 2, 3, 4]. Digital rectal examination (DRE) by the hands of experts can detect hard peripheral prostatic nodule(s) of prostatic carcinoma [3]. Nevertheless, there are many other conditions confused with pros-

tatic carcinoma on DRE by giving the same feeling such as nodular hyperplasia, infarction, granulomatous prostatitis, and lithiasis [4]. The estimation of serum prostate specific antigen (PSA) level is also of great help in detection of prostatic cancer as more than 50% of prostatic cancer have elevated serum level of PSA over 10 ng/ml [4,5]. Nevertheless, a moderate elevation of serum PSA level was seen in many non-neoplastic prostatic conditions such as benign prostatic hyperplasia and prostatitis [3, 4, 5]. On contrary, many cases of prostatic carcinoma were found to have even normal serum level of PSA [3, 4, 5]. Although transrectal ultrasonography (TRUS) can detect early cases of prostatic cancer as hypoechoic nodule(s) but also may miss up to 30% of cancer cases that produce isoechoic nodules, and 10% may even have hyperechoic nodules [4]. The combination of DRE, TRUS, and Serum PSA level are good triad for early clinical suspicion of prostatic cancer cases. Final diagnosis depends on results of fine needle

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aspiration cytopathology (FNAC) and/or histopathology [4, 5, 6, 7]. Majority of prostatic cancer cases were diagnosed at advanced stages which are beyond radical treatment [7, 8]. Radical prostatectomy or radiotherapy can control localized prostatic cancer and improving survival and may even results in complete cure [7]. The aspiration from prostatic lesions is usually performed through the rectum (transrectal FNAC) under guidance of transrectal sonography (TRUS) using special needles and special intrarectal sonic probes [6, 7, 8]. Prior to aspiration patients should be prepared to have empty colon by fluid diet for three days, purgatives and rectal enemas. Painful anal and peri-anal conditions such as anal fissures and inflamed hemorrhoids should be treated before the procedure. The current study was designed for aspiration from clinically suspicious prostatic lesions, using disposable spinal needle gauge 23, through perineal skin above anus to one side under ultrasonic guidance. Aspirations were performed after sterilization of area by povidone iodine and local application of anesthesia, usually 2% lidocaine without adrenaline, to the site aspiration. Percutaneous transperineal prostatic FNAC doesn't require preliminary bowel preparation and painful anal and peri-anal conditions are not contraindications.

Patients and Methods:

This case control prospective study was conducted at the department of pathology/ Al-Yarmouk Teaching Hospital. One hundred and ten (110) patients with voiding symptoms and clinical suspicion of prostatic carcinoma (PCa) were enrolled. Patient were recruited at Al-Yarmouk Teaching Hospital/Department of urology during the period from January 2013 to January 2017. Ethical approval of this work was taken from Al-Mustansiria Medical College/Ethical Committee and a signed consent was taken from each participant before taking the sample.

INCLUSION CRITERIA

All patients included in the study were presented with voiding symptoms and clinical suspicion of prostatic carcinoma.

EXCLUSION CRITERIA

All patients without histopathological examination to confirm or exclude prostatic carcinoma were excluded from the study, because histopathology was taken as a gold standard method for final diagnosis.

TOTAL SERUM PSA ESTIMATION

Total serum PSA level was estimated on frozen sera taken from patient after visiting the hospital. The PAS level for each patient measured using Enzyme Linked Immunosorbent Assay method (ELIZA) employing Biotech system and kits from Ebwe company.

FINE NEEDLE ASPIRATION PROCEDURE

Prior to aspiration the coagulation status of the patients was checked by taking history for hemorrhagic diseases, history of drugs that interfere with coagulation, and relevant hematological tests. The area of aspiration was sterilized by povidone iodine and infiltrated by 2% lidocaine. The suspicious prostatic lesion was identified by ultrasound and then spinal

needle gauge 23 inserted into the perineum above anus to one side, according the site of prostatic lesion, and guided by ultrasound into the suspicious area. The stellate then removed from the spinal needle and 10 ml syringe attached. The aspiration was performed by negative pressure and rotation of needle with to and fro movement for many times until specimen appeared, then negative pressure is released and the needle withdrawn. Aspirated specimen then forced onto labeled slides, and smeared by ordinary method. Smears then fixed immediately in 95% ethanol for at least ½ hour before staining by Papanicolaou stain [9].

STAINING AND CYTOPATHOLOGY

After staining of fixed slides by Papanicolaou stain, the slides were examined by two pathologists and the results were categorized into the following four categories [10, 11];

Category-1: Inadequate for cytopathological examination. These include samples with very scanty or no cells adequate for a reliable cytopathological diagnosis.

Category-2: Negative for prostatic cancer.

Category-3: Suspicious for prostatic cancer. These include samples with epithelial cells atypia that did not reach degree of malignant cells.

Category-4: Positive for prostatic cancer.

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM SPSS version 23 statistical software and Microsoft Excel 2010 [12]. Mean and standard error was formulated for numerical data. The t-test was used for comparison between data that were normally distributed, and data that were not normally distributed the non-parametric Mann-Whitney U test was used [12]. The data were considered statistically significant when the (p-value) is < 0.05 [12].

Results:

Clinical findings

All of 110 studied patients were presented with voiding symptoms and clinical suspicion of prostatic carcinoma. The ages of patients ranged from 45 to 96 years with a mean of 66.5 and standard deviation of ± 9.97 . Ninety-Two (83.63%) of patients had elevated serum PSA level >4.0 ng/ml, 76 (69.09%) had peripheral hard prostatic nodule(s) on DRE, and 88 (80%) had hypoechoic prostatic nodule(s) on TRUS examination, figure-1.

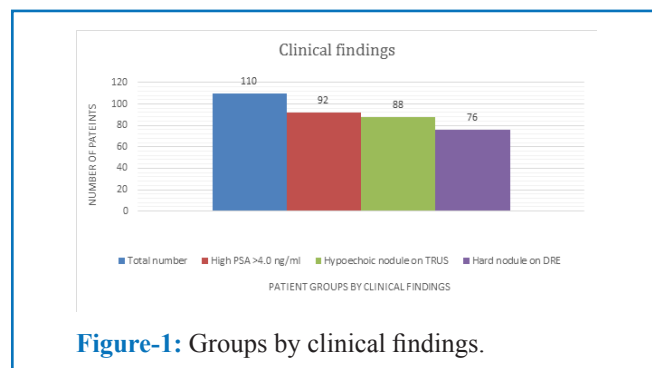


Figure-1: Groups by clinical findings.

Cytopathological findings

Two out of all the 110 studied cases were inadequate samples accounting for 1.81% of whole cases, in whom the aspiration was advised to be repeated. The remaining 108 specimens

were satisfactory and accounting for 98.19% of cases. Prostatic cancer was present in 64 (58.18%), negative in 40 (36.36%), and suspicious in 4 (3.63%), all results were statistically significant with p-values <0.05, (figures-1, 2, 3, & 4).

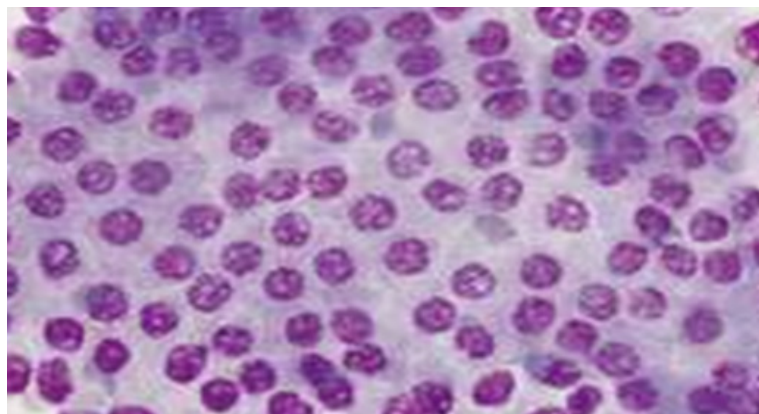


Figure-2: Sheet of benign uniform epithelial cells of benign prostatic hyperplasia.

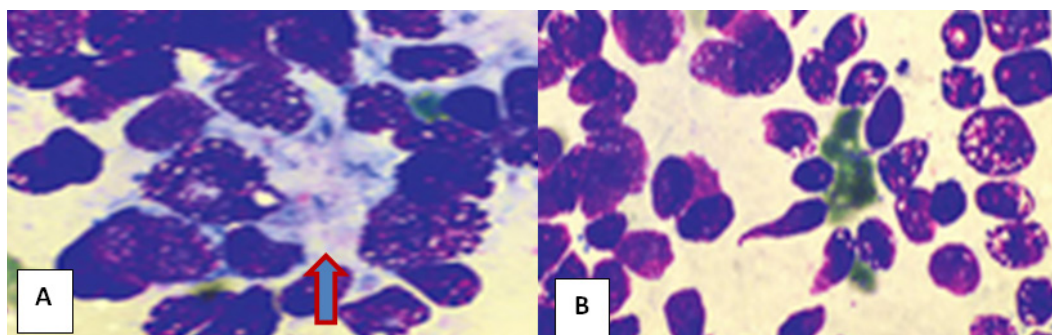


Figure-3: Clusters of malignant epithelial cells of prostatic adenocarcinoma, A-well differentiated forming gland (arrow), B- Poorly differentiated.

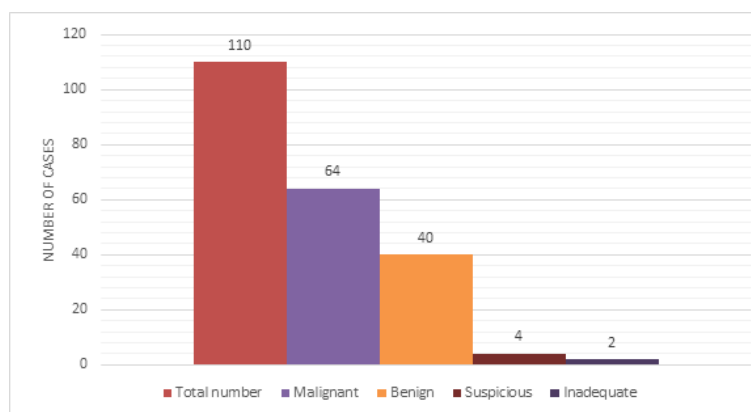


Figure-4: Showing number of cases in cancer, benign, suspicious, and inadequate.

Histopathological findings

The final diagnosis was achieved by histopathological examination of prostatic specimens which is the gold standard of diagnosis and included histopathology (needle biopsy, open prostatectomy or transurethral resection of prostate TUR-P). Histopathology proved prostatic adenocarcinoma (true positive cases) in 62 (96.87%) out of 64 cases positive cases by

FNAC and fail to confirm diagnosis in 2 (3.13%) of them (false positive cases). The histopathology also confirmed the benign prostatic conditions (true negative) in 39 (97.5%) and prostatic adenocarcinoma (false negative) in 1 patient out of 40 FNAC benign conditions. The histopathological examination also proved prostatic carcinoma in 3 (75%) and benign condition in 1 (25%) out of the 4 suspicious cases, figure-5.

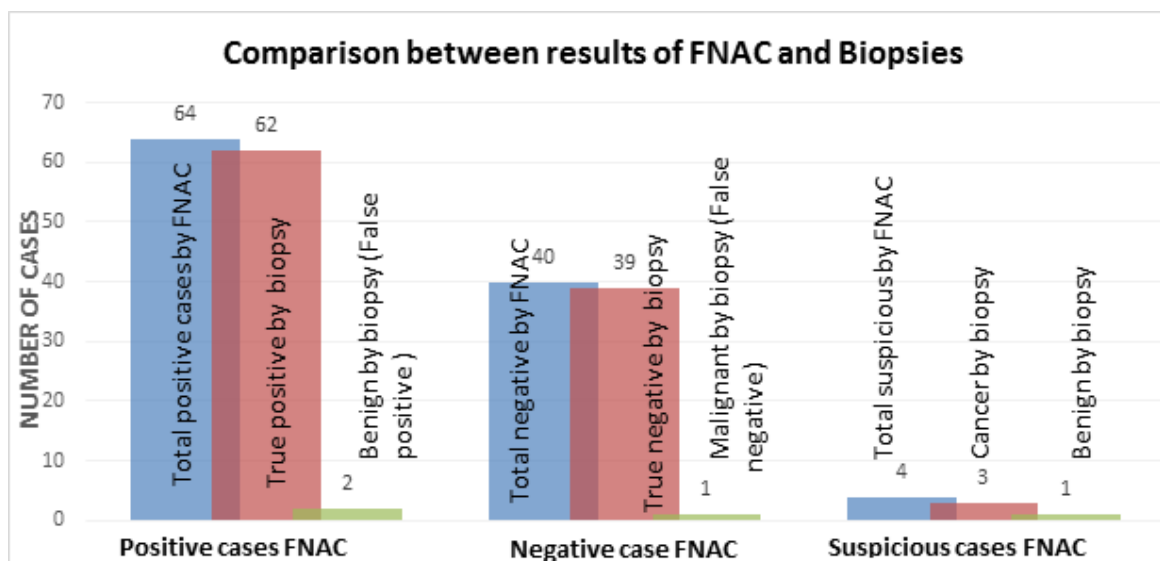


Figure-5: Positive, negative and suspicious in FNAC and histopathology.

Statistical findings

The sensitivity, specificity, and accuracy of current study were 98%, 95%, and 91.81% respectively while positive and negative predictive values were 97% and 98% respectively. All results were statistically significant with p-values <0.05. True positive cases proved by histopathology accounted for 96.87% of total positive cases by FNAC, while false positive cases were 3.13%. True negative cases proved by histopathology were 97.5% of total negative cases by FNAC, and false

negative were 2.5%. Cases with inadequate specimens were 2 out of total 110 cases and accounted for 1.81% of cases, all results were statistically significant with p-values <0.05. Fifty patients (75.75%) out of the 66 patients that were positive for prostatic cancer by histopathology showed high serum PSA level over 10 ng/ml. Twelve of cancer patients (18.18%) showed serum PSA level >4.0 ng/ml but <10 ng/ml, and in 4 patients (6.06%) less than 4.0 ng/ml, figure-6.

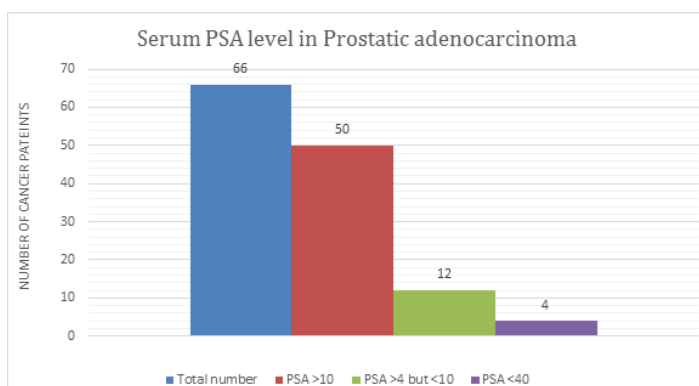
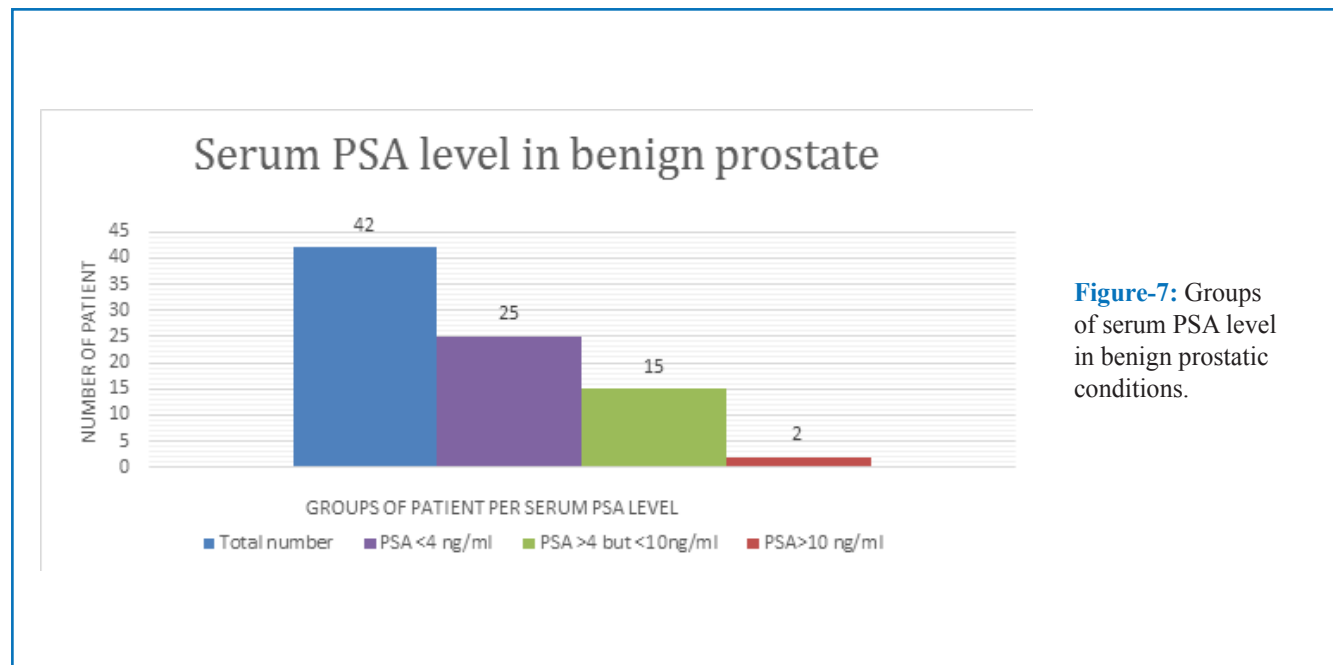


Figure 6: Level of PSA in prostatic adenocarcinoma.

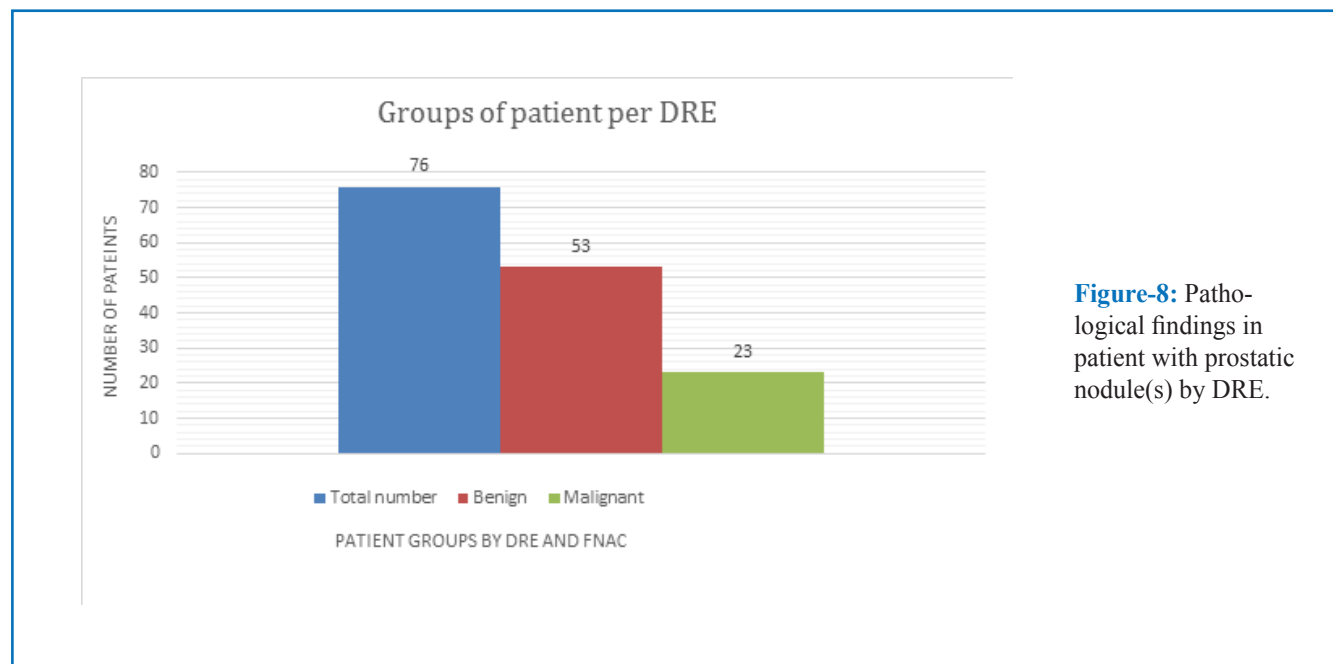
The serum level of PSA in benign prostatic conditions proved by cytopathology and histopathology was >10 ng/ml in 2 (4.76%), >4.0 ng/ml but <10 ng/ml, in 15 (35.72%), and

<4.0 ng/ml in 25 cases (59.52%) out of 42 total benign cases, all results were statistically significant with p-values<0.05, figure-7.



The digital rectal examination (DRE) revealed hard peripheral prostatic nodule[s] in 76 (69.09%) of the 110 studied cases. Twenty-three (30.26%) cases proved to be prostatic adeno-

carcinoma, and 53 (69.74%) benign by cytopathology and histopathology, results were statistically significant with p-values<0.01, figure-8.



Eighty-eight (80%) out of 110 studied cases showed hypoechoic prostatic nodule{s} on TRUS examination, 52 cases (59.09%) of them showed benign prostatic conditions, and 36

(40.91%) were malignant on cytopathologic and histopathologic examination. All results were statistically significant, p-value <0.04, figure-9.

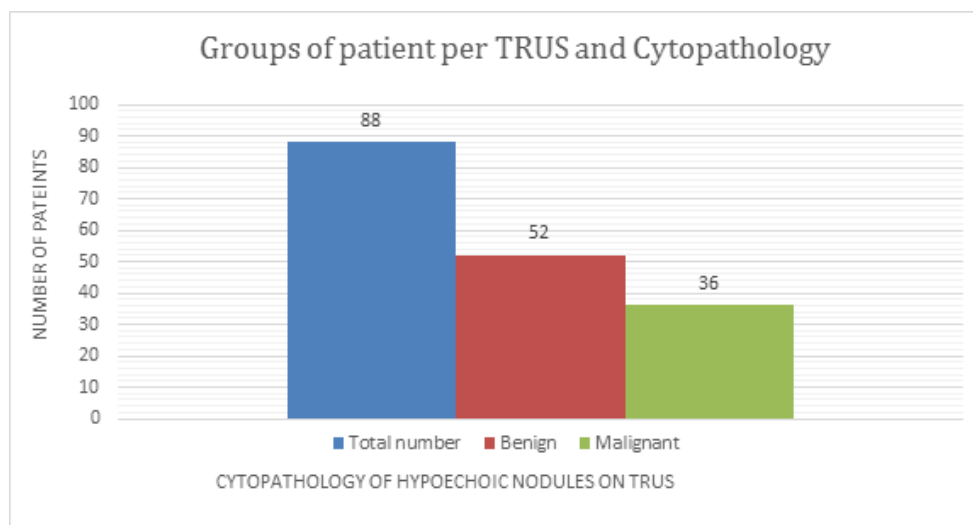


Figure-9: Results of FNAC on hypoechoic nodules by TRUS.

Twenty-six (23.63%) out of the 110 patients in present study showed a combination of the three suspicious clinical findings for prostatic cancer (high serum >4.0 ng/ml, hard peripheral prostatic nodule(s) by DRE, and hypoechoic nodule on

TRUS). Twenty-three (88.46%) out of them proved to have prostatic adenocarcinoma by cytopathology and histopathology, figure-10.

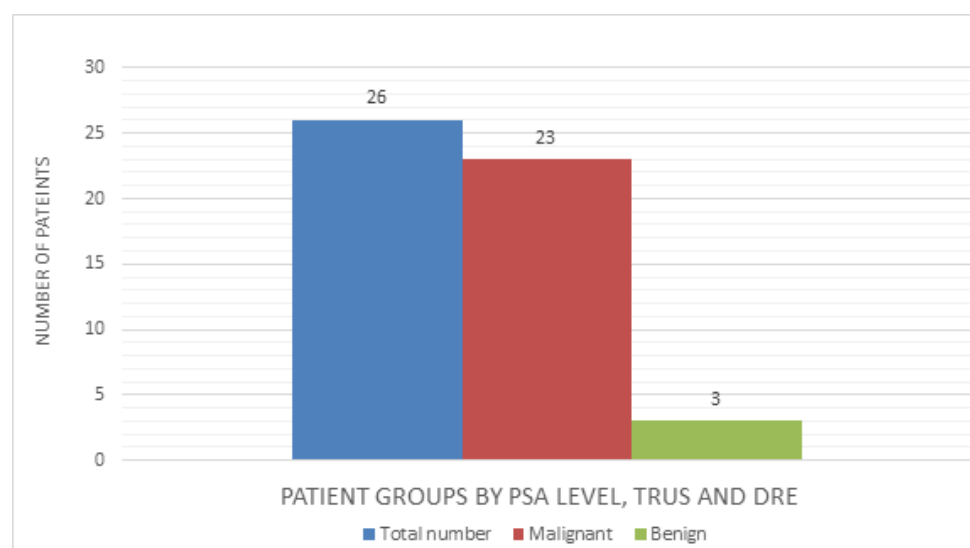


Figure-10: Malignant and benign conditions in patient with positive combinations of hard peripheral prostatic nodule(s) on DRE, high serum PSA level >4.0 ng/ml, and hypoechoic lesions on TRUS.

DISCUSSION:

Carcinoma of the prostate is a common internal malignancy in adult and elderly men [1, 2, 3, 4], and is an important cause of morbidity and mortality because of late diagnosis in spite of being curable by radical treatment in the early stages

[3, 4, 5, 6].

There are numerous researches all over the world support the role of FNAC, in confirming or excluding prostatic cancer in patients with clinical suspicion of prostatic cancer by digital rectal examination (DRE), serum PSA level estimation, and transrectal ultrasonography (TRUS) [5, 6, 7, 8]. Fine needle

aspiration from prostate is a safe, simple, cost effective, rapid, and accurate method in diagnosis of prostatic cancer [7, 8, 9, 10, 11]. Prostatic FNAC necessitates prior bowel preparation by fluid diet for three days accompanied by rectal enemas and purgatives. It is usually performed through the rectum using transrectal ultrasound (TRUS) with a special guide and special needle for aspiration [9, 10, 11]. The current study was designed to aspirate from clinically suspicious prostatic lesions through skin of perineum to overcome a lot of drawbacks to transrectal prostatic aspiration (FNAC) of these are; Transrectal aspiration from prostate performed by using transrectal ultrasound with guide and special aspiration needles, patient should have prior to aspiration a large bowel preparation by fluid diet for atleast three days with purgative and rectal enemas [13, 14, 15], the presence of anal and perianal painful conditions such as anal fissures, skin ulcerations and infections are contraindication for this procedure and should be treated before commencing the procedure [16, 17], and aspiration through rectum may result in an intra-abdominal infection. According to results from current study, prostatic lesions can easily aspirate through perineal skin using disposable spinal needle under ultrasound guidance. Aspiration from 110 patients yielded 108 (98.18%) adequate and 2 (1.82%) inadequate specimens. The procedure was quite safe, uncostly, rapid, and without any mentioned complication. Painful anal and perianal conditions were not contraindications for this procedure. Results from current study showed that none of the three parameters used for clinical suspicion of prostatic cancer (serum PSA level, DRE, and TRUS) can be effectively used alone as a screening method for early detection of prostatic cancer. Serum PSA level was high (>4.0 ng/ml in 62 (93.94%) out of 66 patients with prostatic cancer), and in 17 (40.47%) out of 42 benign prostatic conditions. Serum PSA levels were normal (<4.0 ng/ml) in 4 (6.06%) patients with prostatic cancer and 25 (59.52%) out of 42 benign prostatic conditions. The higher the serum PSA level, the higher the possibility of prostatic, in addition to that high serum PSA level does not mean prostatic carcinoma and vice versa (normal level does not mean benign prostatic condition). The results were in accordance other studies by Al-Abadi [19], Usama S. Al-Nasiri et al [22], Cho M et al [24], Nakamura et al [25], and Saleh AFM et al [23].

Results from present study showed peripheral prostatic nodule(s) in 76 (69.09%) out of 110 patients, and pathological examination confirmed prostatic cancer in 23 (30.26%) and benign conditions in 53 (69.74%) of them. Most of cancer patients detected by DRE were in advanced stages, and the findings again suggested that not all patients with hard peripheral prostatic nodule(s) have prostatic cancer. Results agreed with studies by Al-Abadi [19], Usama S. Al-Nasiri et al [22], and Cullmann et al [27]. Transrectal sonography of prostate (TRUS) in current study detected hypoechoic prostatic lesions in 88 (80%) out of 110 studied patients. Thirty-six (40.90%) out 88 patients confirmed to have prostatic cancer and 52 (59.09%) had benign conditions by FNAC and histo-

pathological examination. This finding again suggested that not all prostate with hypoechoic lesion on TRUS were malignant. These findings also agreed with those of Saleh AFM et al [23], Vision E et al [26], and Cullmann et al [27]. Results from current study showed that 26 (23.63%) out of 110 studied patients had all three following findings at the same; hard peripheral prostatic nodule(s), high serum PSA level >4.0 ng/ml, and hypoechoic prostatic lesions on TRUS. Cytopathology and histopathology confirmed prostatic cancer in 23 (88.46%) of them. This result was unique because none of the published studies mentioned the rate of prostatic cancer in patients with a combination these three-clinical findings.

Comparing the sensitivity of current study which was 98% with those of other studies performed by transrectal prostatic FNAC it was the same as that of Al-Abadi [19], but was slightly lower than result of study by Judith J Thangaiah et al [21], which was 100% and was higher than those of Dhanamjaya Rao Teeda et al [20], Usama S. Al-Nasiri et al [22], Cho M et al [24], Nakamura et al [25], Saleh AFM et al [23], Vision E et al [26], and Cullmann et al [27] which were 88.89%, 85%, 86%, 90%, 89%, 87%, and 83.7% respectively. The specificity of current study was 95% which was similar to results by Vision E et al [26] of 95%, and higher than those of Dhanamjaya Rao Teeda et al [20], and Saleh AFM et al [23] which were 85% and 93% respectively, but lower than results by Cho M et al [24], Judith J Thangaiah et al [21], Nakamura et al [25], Al-Abadi et al [19], Cullmann et al [27], and Usama S. Al-Nasiri et al [22] which were 100%, 95.5%, 100%, 100%, 100%, and 100% respectively. The accuracy of current study is 91.81% which is higher than result by Cho M et al [24] which was 90%, but lower than results of studies by Dhanamjaya Rao Teeda et al [20], and Nakamura et al [25], Al-Abadi et al [19], Cullmann et al [27], and Usama S. Al-Nasiri et al [22] which were 97.5%, 92%, 99%, 95% respectively. The false negative result of the current study was 2.5% of total negative cases which was much lower than the result of studies Cho M et al [24], and Saleh AFM et al [23], which were 11% and 3.12% respectively.

CONCLUSION:

Transperineal aspiration of prostate under ultrasound used in the current study is an easy cost effective and an outpatient procedure with high sensitivity, specificity and diagnostic accuracy. The results were as good as those of Iraqi and international studies obtained by aspiration through the rectum. It does not need prior bowel preparation and anal and perianal lesions does not interfere with the procedure. Complications are very little or unknown apart from slight swelling and tenderness at site of aspiration in comparison with complication of transrectal aspiration that may results in local inflammation or even peritonitis.

RECOMMENDATION:

Further studies on transperineal percutaneous aspiration of prostate under ultrasound are recommended.

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