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CORRELATION STUDY BETWEEN LEVELS OF SERUM PROSTATE-SPECIFIC ANTIGEN LEVELS WITH PROSTATE NEEDLE BIOPSY RESULTS IN DETECTING PROSTATE CARCINOMA

General Surgery

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ABSTRACT

Background And Objective: Other causes of increased blood PSA levels besides cancer include prostate gland manipulation, BPH, prostatitis, prostate massage, and after needle biopsy. The present study's purpose is to discover a relationship between blood prostate-specific antigen levels and prostate needle biopsy findings in prostate cancer diagnosis. **Methods:** Individuals with abnormal DRE and/or increased serum PSA levels were enrolled in this study and underwent TRUS guided needle biopsy. TRUS guided needle biopsy was performed to get 12 cores, which were subsequently histologically examined. **Results:** The degree of prostatomegaly has no substantial link with the development of cancer unless it is accompanied by other DRE outcomes. PSA levels and adenocarcinoma Gleason score show a small positive relationship that is not statistically significant. Abnormal DRE results (hard nodular prostate) should be evaluated in connection to blood PSA levels in situations where cancer is suspected. **Conclusion:** This study shows that in patients with prostatic adenocarcinoma, there is a weak positive correlation that is not statistically significant between serum PSA levels

KEYWORDS

Adenocarcinoma, Prostate-specific Antigen, Gleason, Prostatomegaly And Prostate Needle Biopsy.

INTRODUCTION:

Prostate adenocarcinoma is the second most common malignant tumor in men over the age of 65. Around 10-15% of younger men with prostate cancer have a family history of the disease. [1]

Adenocarcinoma is the histological pattern of malignancy in the prostate gland because it has a glandular shape. The first change associated with cancer is the loss of basement membrane with the confluence of glandular cells. Because prostate cancer typically develops in the prostate's periphery, surgery for benign gland enlargement offers minimal cancer prevention. Prostate cancer accounts for around 9.7 percent of all male cancers, rising to 15.3 percent in developed nations and accounting for just 4.3 percent in undeveloped countries. [2]

GLEASON recommends classifying the histological pattern based on glandular differentiation and its relationship to the stroma. Prostate adenocarcinoma is the world's sixth greatest cause of cancer death. As a result, the value of having a reliable prostate cancer detection tool is obvious. A digital rectal examination, a prostate biopsy, and blood PSA levels are among them. [3]

Although the diagnostic effectiveness of any of these approaches is debatable. Although it is a subjective opinion, DRE is the most straightforward method of examining the prostate. Despite the fact that palpable tumors are considered clinically significant, 50% of suspicious nodules are benign. [4]

Although PSA readings are objective and highly reproducible, they might be difficult to interpret due to false positive results caused by prostatic hyperplasia. PSA measurements in serum are the most therapeutically useful for detecting early-stage, curable prostate cancer. Serum PSA is tissue-specific, not cancer-specific. PSA testing can uncover males who are asymptomatic. Serum PSA levels are beneficial for monitoring the evolution of advanced disease, but they lack sensitivity and specificity for detecting early-stage cancer..[5]

PSA levels in normal blood vary from 0 to 3.9 ng/ml, with levels between 4.0 and 10 ng/ml having predictive value for prostate cancer identification. PSA levels more than 10ng/ml are suggestive of cancer, while levels greater than 35ng/ml are symptomatic of advanced prostate cancer. [6]

Serum PSA testing is one of numerous markers that can be used to identify high-risk tumors. Other factors to consider include Gleason score, clinical stage, and patient life expectancy. When normal architecture is disrupted, as in prostate cancer or BPH, PSA diffuses into the surrounding stroma and tiny blood capillaries, enters the circulation, and manifests as elevated levels. The half-life of PSA is 2.2 days. Although PSA levels in the blood are widely used to detect prostate cancer, they have a low specificity and positive predictive value. Serum PSA levels rise in proportion to the clinical stage of prostate adenocarcinoma, while serum PSA levels fall in proportion to the estimated volume of the tumor. [7]

Men are frequently asymptomatic. Only later in the illness did males describe lower urinary tract symptoms such as bladder outlet blockage, pelvic discomfort and hematuria, bone pain, malaise, anaemia, or pancytopenia. The goal of this study was to identify a connection between serum PSA (free+total) levels and prostate cancer identification utilizing TRUS guided biopsy findings.

MATERIALS AND METHODS:

STUDY AREA AND DESIGN

After approval from the ethical committee and obtaining written and informed consent from the affected patient or his relatives, this proposed study was conducted in cases who presented with raised levels of serum PSA or abnormal Digital Rectal Examination in the urology unit of the Department of General Surgery, SRN Hospital, MLN Medical College, Prayagraj over a one-year period from September 2020 to August 2021.

SAMPLE SIZE CALCULATION:

Calculated using the formula,
N=4PQ/E2
The minimum sample size thus obtained was 32.

Inclusion Criteria

- All patients with LUTS with abnormal digital rectal examination or raised serum PSA levels.

Exclusion Criteria

- Patient having active urinary tract infection or deranged coagulation profile
- Patient having prostatitis or prostatic abscess.

- Patients who were not willing to participate in the study.

METHODOLOGY:
Our study comprises of patients who were having abnormal DRE and/ or raised values of serum PSA values and underwent TRUS-guided needle biopsy.

12 core obtained by TRUS guided needle biopsy and send for histological evaluation.

INTERNATIONAL PROSTATE SYMPTOM SCORE (IPSS):
It consists of eight questions, Inadequate emptying, Intermittency, Frequency, Immediacy, weak stream, Constraint, and Nocturia.

DIGITAL RECTAL EXAMINATION:
1. Shape
2. Consistency-Firm/Hard
3. Surrounding mucosa-free/fixed
4. Grade of Prostatomegaly

Radiological investigation:
1. TRUS-guided prostate needle biopsy- determine the location and characteristics of any lesions (i.e., hypoechoic, hyperechoic, calcifications, contour abnormalities, cystic structures). A spring-driven 18-gauge needle core biopsy device or biopsy gun that can be passed through the needle guide attached to the ultrasound probe and 12 core biopsy was obtained.
2. X ray KUB region

Analgesia:
TRUS guided biopsy performed under local anesthesia

Post Procedure Complications:
1. UTI-the most prevalent organism causing UTI is E.Coli, which is treated with preprocedural antibiotic prophylaxis with third-generation cephalosporins.
2. Rectal bleeding- Rectal bleeding is usually minimal and easily managed with direct ultrasound probe pressure or digitally.
3. Urine Retention- A patient with an enlarged prostate experiences urinary retention, necessitating catheterization.

RESULTS:
From September 2020 to August 2021, 50 patients with LUTS and either increased serum PSA and/or abnormal DRE came to the urology OPD or were admitted to the P.G. Department of surgery at Swaroop Rani Nehru Hospital. The patients were first examined by a skilled urologist, who then performed blood tests for GBP and serum PSA, as well as TRUS guided biopsies. Out of 50 patients, 7 had blood PSA levels less than 4ng/ml, 14 have levels between 4 and 10ng/ml, and the remaining 29 have levels greater than 10ng/ml.

PSA readings up to 4ng/ml with no evidence of adenocarcinoma in these individuals with abnormal DRE, 4-10ng/ml 7 instances had adenocarcinoma, 4 of which have abnormal DRE results, >10ng/ml, out of 29 cases with biopsy proved adenocarcinoma, i.e. 79.3 percent of which have aberrant DRE findings. [Table: 1]

Table 1: Post hoc table (adjusted p value)

S.No.	Serum PSA value	Adenocarcinoma (+)	Adenocarcinoma (-)
01	Up to 4	0.0009	0.0009
02	4-10	>0.999	>0.999
03	>10	0.0007	0.0007

Calculated $\chi 2$ value 19.84 > critical $\chi 2$ value 5.99 ($p<0.0001$). Hence there is a relationship between serum PSA level and adenocarcinoma. Probability of occurrence of adenocarcinoma increases with the rise in serum PSA level.

From the table it is clear that at 4-10 serum PSA level, it is non-significant i.e. occurrence of adenocarcinoma is independent of serum PSA value.

Calculated $\chi 2$ value 28.12 > critical $\chi 2$ value 3.82 ($p<0.0001$). Hence consistency and occurrence of adenocarcinoma are not independent i.e. related. There is probability of adenocarcinoma even on firm consistency , firm consistency associated with nodularity on DRE. Out of 25 cases with firm consistency only 6 have adenocarcinoma but all these having serum PSA values >4ng/ml and nodularity on DRE. Hard consistency is being more associated with cancer risk in prostate with higher values of serum PSA. [Table: 2]

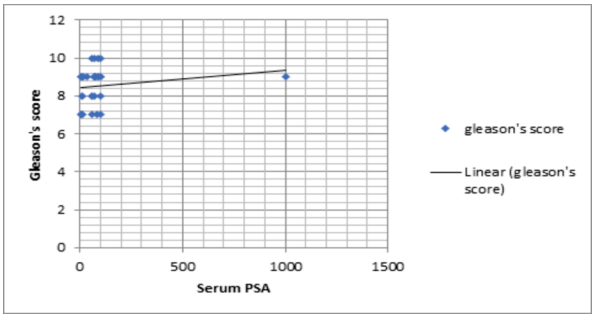
Table 2: Distribution on basis of consistency of prostate on DRE

Consistency	S. PSA level			Calculated $\chi 2$ value	Critical $\chi 2$ value	p- value	Statistical outcome
	Up to 4	4-10	>10				
Firm	7	13	5	2.40	5.99	0.301	Non significant
Hard	0	1	24	20.26	5.99	<0.0001	Significant

Calculated $\chi 2$ value 21.31 > critical $\chi 2$ value 5.99 ($p<0.0001$). Hence grade and adenocarcinoma are not independent i.e. related. Probability of occurrence of adenocarcinoma increases as grade rises along with higher values of serum PSA Grade/ serum PSA. [Table: 3]

Table-3: Relation between grade of prostatomegaly on DRE and Adenocarcinoma

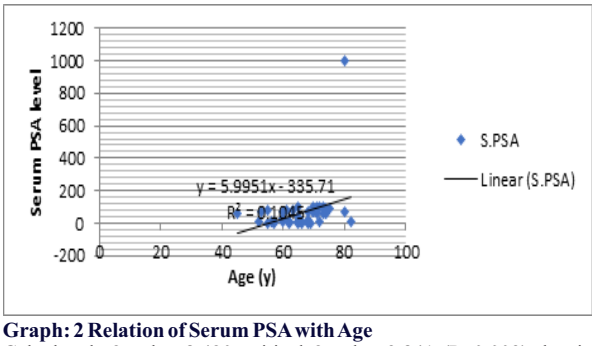
Grade	S. PSA level			Calculated $\chi 2$ value	Critical $\chi 2$ value	p-value	Statistical outcome
	Up to 4	4-10	>10				
II	3	0	1	2.33	5.99	0.311	Non significant
III	4	13	6	2.88	5.99	0.236	Non significant
IV	0	1	22	18.02	5.99	0.0001	Significant



Graph: 1 Relation Between serum PSA and GLEASON SCORE:

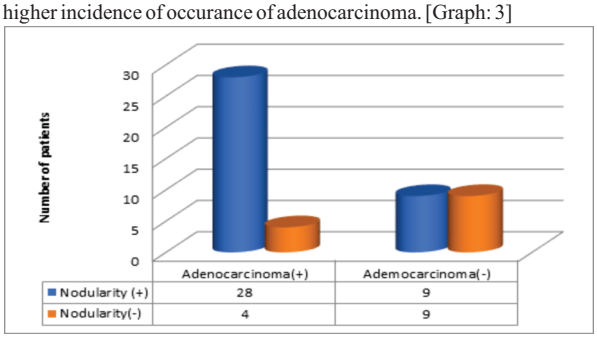
Pearson's correlation coefficient (r) for Serum PSA value and Gleason's score is 0.164 (p= 0.369) i.e. non-significant correlation. It means that Gleason's score vary with respect to serum PSA value insignificantly. [Graph: 1]

Relation of serum PSA with age
Pearson's correlation coefficient (r) for Serum PSA value and age (y) is 0.323 (p= 0.012) i.e. significant correlation. It means that serum PSA varies with respect to age significantly. Value of serum PSA increases with age. [Graph: 2]



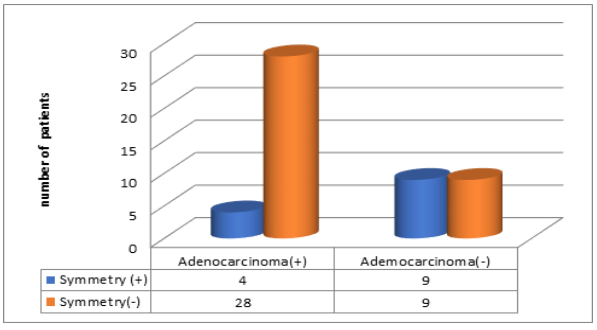
Graph: 2 Relation of Serum PSA with Age
Calculated $\chi 2$ value 8.420>critical$\chi 2$ value 3.841 (P=0.003) that is nodularity is related to occurrence of adenocarcinoma. In case of nodularity with no evidence of adenocarcinoma all cases having serum PSA values <4ng/ml. In all 4 cases with adenocarcinoma with no nodularity and symmetry on DRE have serum PSA values >4ng/ml. Hence nodularity with abnormal value of serum PSA is associated with

higher incidence of occurance of adenocarcinoma. [Graph: 3]



Graph: 3 Relation of Nodularity

Calculated $\chi 2$ value 8.420> critical $\chi 2$ value 3.841 (P=0.003) that is symmetry is related to occurrence of adenocarcinoma. Asymmetry of lobe along with nodularity associated with adenocarcinoma in case of higher serum PSA values (>4ng/ml). [Graph: 4]



Graph: 4 Relation of Symmetry

DISCUSSION:

Prior to the emergence of serum PSA and TRUS, the only test for prostate cancer that was widely available was DRE. In clinical practice, 40-50 percent of all palpable abnormalities were believed to be prostate cancer and were subsequently shown to be malignant after being subjected to biopsy testing. Because the DRE is a very subjective exam. The DRE and blood PSA are now widely used to diagnose prostate cancer. PSA testing has been used in clinical practice since 1986, 8 and has resulted in changes in prostate cancer screening, early detection, and therapy. Overall survival has risen as a result of the widespread adoption of PSA screening. An increasing number of people are being diagnosed with early-stage prostate cancer.

PSA testing has been shown to be useful in identifying tumor progression, evaluating therapeutic response, and detecting early diagnosis. The benefits and drawbacks of PSA testing have also been highlighted. A restriction of PSA testing is the possibility of overdiagnosis and subsequent negative biopsies due to insufficient specificity. PSA levels can be influenced by a number of diseases; PSA is prostate-specific but not prostate-cancer-specific. Significant benign prostatic hyperplasia, prostatitis, prostate manipulations, and recent ejaculation within 24 hours are all possible causes of PSA increases. In clinical practice, the average PSA cut off is 4.0 ng/mL. A lower cut off increases sensitivity but reduces specificity, allowing the detection of clinically insignificant prostate cancer..9

In this study patient was divided into three groups according to levels of serum PSA levels 0-4ng/ml,4-10ng/ml,>10 ng/ml. This is consistent with Hamid Janbaziroudsari et.al. 2016 10 who reported increased incidence of adenocarcinoma in s.PSA levels >10ng/ml. In his study among 139 cases 45 have adenocarcinoma (32.4%). Among 45, 35 have PSA values >10ng/ml (71.8%)

In our study of 50 patients, 30 had adenocarcinoma (60%) and 23 had s.PSA levels over 10ng/ml. Catalona et al. 1994 11 examined blood PSA levels in 1653 healthy men aged 50 and more; 22% had cancer, with a range of 4-10, and 67% had serum PSA levels greater than 10ng/ml.

In the current study, the incidence of adenocarcinoma increases as S.PSA levels rise; values more than 10ng/ml on prostate biopsy are more consistent with adenocarcinoma. This was also reported in a 2016 study by Hamid et al.,10 Levels in the 4-10ng/ml range exhibited no discernible connection with biopsy outcomes.

In a study conducted by Russelle et al.,12 33 of 45 patients had firm consistency with histological evidence of adenocarcinoma (p>.05).

Irekpita et al. (2014) investigated 131 males, 64 of whom had a diagnostic finding of hard nodular prostate, 51 (79.7 percent) of whom had adenocarcinoma. In his analysis, the most prevalent result indicating the likelihood of adenocarcinoma was hard nodular prostate.13

In our study, 50% of participants had hard consistency, which was related with nodularity and the occurrence of adenocarcinoma. As a result, they are statistically significant (p = 0.0001).

In a 2022 research by Russelle et al, 23 patients (51.1 percent) had nodular prostate, and 15 had adenocarcinoma prostate (65 percent), with a p value of 0.46.12 The most prevalent anomaly was hard prostate, followed by nodularity (51.1). According to Ojewola et al. (2013), the most prevalent finding on DRE is nodularity (53.8 percent), followed by hard prostate. There is a substantial connection (p=.005) between DRE detection and cancer histology.14

In our study, 37 of the 50 participants had nodularity as well as asymmetry (74 percent). 28 of the 37 have adenocarcinoma (75.68 percent). Nodularity and the occurrence of adenocarcinoma have a statistically significant relationship (p-value = 0.003).

In 2016, 1495 individuals were investigated, with 192 (12.84 percent) having asymmetrical lobes and 67 having adenocarcinoma (34.89 percent). While benign and asymmetry had the same chance of detecting cancer (p value=0.105), nodularity is more important (p=.001).15 This study found a modest positive connection that is not statistically significant between serum PSA levels and the recently announced (2016) Gleason group grade of prostatic carcinoma in patients with prostatic adenocarcinoma. This is consistent with prior research by Mohammad et al.16

CONCLUSION:

Although no PSA level was associated with a 100 percent positive predictive value, increasing blood PSA levels increased the probability of adenocarcinoma. PSA values above 10ng/ml are associated with an increased risk of adenocarcinoma. Among the DRE results, hard nodular prostate is the most useful for cancer diagnosis. Unless it is accompanied by other DRE events, the degree of prostatomegaly has no significant connection with the development of cancer. PSA levels and adenocarcinoma gleason score show a small but statistically significant positive connection. In cases when cancer is suspected, abnormal DRE results (hard nodular prostate) should be assessed in conjunction with blood PSA values.

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