Section: Pathology

Original Research Article

CORRELATION OF SERUM ADENOSINE DEAMINASE LEVELS IN BENIGN PROSTATIC HYPERPLASIA AND PROSTATIC CARCINOMA ALONG WITH THEIR RESPECTIVE HISTOPATHOLOGY: - A TERTIARY CARE CENTRE EXPERIENCE

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Abstract

Background: Prostate cancer is not uncommon malignancy in India, being third most common cancer in males. Unfortunately they are diagnosed late. For screening as well as for diagnosis most used tumor marker is Prostate specific antigen (PSA). But PSA being a costly test, there is a need of alternate tumor marker which should be cheaper and in combination can increase the sensitivity of PSA. The aim and objective were to estimate the level of serum ADA in benign prostatic hyperplasia and prostatic carcinoma along with their histopathology. **Materials and Methods:** Serum of cases and controls was used for ADA estimation. **Result:** ADA Levels were significantly higher in BPH patients than normal patients. ADA Levels were significantly higher in CA prostate patients than normal patients. But the difference between BPH and CA prostate was not statistically significant. **Conclusion:** ADA levels can be useful in determining high cell proliferetion rate ie. BPH and CA prostate, however no significant difference in levels was observed between BPH and CA prostate.

INTRODUCTION

In India prostate cancer is the third most common cancer in males.[1] Approximately 75% of prostate cancer cases are diagnosed at a later stage since the patient manifest symptoms, such as bone pain or other orthopedic complaints which are ignored. Prostate cancer is slow growing cancer and is mostly curable when detected early. The main obstacle in the way to diagnosis is the silent nature of disease. Therefore early detection at curable stage remains the prime object of all persons concerned with the management of this disease.

Digital rectal examination (DRE), transrectal ultrasonographic imaging (TRUS), tumour markers, random biopsies and many more techniques have been evaluated for the diagnosis at an early yet clinically significant stage.[2] The treatment and follow-up were revolutionized by the introduction of the tumour marker prostate specific antigen.[3] Tumor markers help in deciding benign and malignant conditions of prostate.[4]

Among these serum prostate specific antigen appears the most promising tool(A). Serum PSA is the most commonly used tumour marker available for differentiating between benign and malignant conditions and management.[5] The substantial number of false positive and false negative results has led to search for other tumor marker for improving sensitivity and specificity. And also the cost for this PSA test is high, so we need a cheaper tumour marker for screening.

Altered level of adenosine deaminase (ADA) in serum of men with prostatic disease has opened a view that serum ADA can be helpful as tumour marker as PSA in screening/diagnosis/management of prostatic disease.[6] It is also cheaper than PSA.

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MATERIALS AND METHODS

Case Selection: The present study was carried out in the Department of Pathology and department of Surgery of GSVM Medical College, Kanpur in between Jan 2007 to Sep 2008. This was an observational cross-sectional study. These cases were selected on clinical ground on the basis of history, sign & symptoms along with DRE with consent of patients.

Total three groups were formed. First GROUP was Control group of patients having age between 50-90 yrs. Precautions have been taken to ensure that weight of prostate is below 20 gm on USG and patient is free from prostatic symptoms. Second GROUP was having patients with BPH which was confirmed by histopathology. Third GROUP was having patients with CA prostate, Confirmed by histopathology. Patients having history of tuberculosis, nephrotic syndrome, autoimmune disease and allergy, history of recent septic infections and any other carcinoma and those who were not willing to participate in the study were excluded from the study.

Specimen Collection and Preparation: Serum of cases and controls was used. The blood was allowed to clot completely before centrifugation and tubes were kept stoppered at all times. Samples were centrifuged to separate serum. Within two hours after centrifugation serum was transferred to a storage tube. Fresh as well as refrigerated serum at 2-8°C for maximum period of 5 days were used. If the assay couldn't be done within this time, the samples were stored at temperature of -20°C for upto 30 days. Repetitive thawing and freezing were avoided.

Aims of study was to estimate a level of serum ADA in benign prostatic hyperplasia and prostatic carcinoma along with their histopathology.

RESULTS

Table 1: Distribution of cases under study (Total 105 Cases)

Type of patients	No. of cases	Percentage
Normal	33	31.42
BPH	42	40
CA	30	28.57

Table 2: Distribution of cases by Age groups

Age (Yrs)	Normal		BPH		CA	
	No.	%	No.	%	No.	%
50-59	11	33	9	21.42	6	20
60-69	12	36.36	18	42.85	7	23.33
70-79	7	21.14	9	21.42	14	46.66
>80	3	9.5	6	14.28	3	10
Total	33		42		30	
Range	50-84 yrs		52-87 yrs		55-81 yrs	
Mean	65.36 yrs		67.52 yrs		69.36 yrs	
±SD	9.18		9.11		8.90	

Table 3: ADA(IU/L) in control, BPH and CA-prostate cases: Mean and SD

	Mean	SD
Cases of control	14.46	4.11
Cases of BPH	31.90	26.60
Cases of CA prostate	27.59	18.96

Table 4: ADA levels in cases, whose respective histopathology was done

Range of ADA	No. of Cases	BPH	Cancer prostate
0-15	20	12	8
15.01-30	25	12	13
30.01-45	14	9	5
45.01-60	7	5	2
60.01-75	1	1	0
75.01-90	2	1	1
90.01-120	1	0	1
>120.01	2	2	0
Total	72	42	30

Maximum cases (25) were in the range of 15.01-30 IU/L

Maximum cases (12) of BPH were in the range of 15.01-30 IU/L

Maximum cases (13) of cancer prostate were in the range of 15.01-30 IU/L

Table 5: Distribution of cancer prostate cases according to Gleason grading

Grade	No. of cases	Percentage
I	02	6.6
II	05	16.7
III	05	16.7

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IV	12	40
V	06	20

Table 6: Comparison of levels of ADA in control and patient with BPH and Statistical analysis

Groups	Total no. of cases	ADA levels in U/L		
		Range	Mean	SD
BPH	42	5.5-122.77	31.90	26.60
Control (normal)	33	6.92-22.87	14.46	4.11
Statistical analysis				
T	P		Interference	
T(cal)=3.78	P<0.001		Highly significant	

ADA levels in BPH cases showed a range of 5.5-122.77 U/L
Mean was 31.90U/L ±26.60.
ADA levels in control cases showed a range of 6.92-22.87 U/L
Mean was 14.46 U/L ±4.11
The difference between ADA levels in these two groups (normal and BPH) was statistically highly significant.

Table 7: Comparison of Levels of ADA in control and patient with CA-Prostate and Statistical analysis

Groups	Total no. of Cases		ADA levels in U/L	
		Range	Mean	±SD
CA-Prostate	30	5.56-78.13	27.59	±18.96
Control (Normal)	33	6.92-22.87	14.46	±4.11
Statistical analysis				
T	P		Interference	
T(call)=3.94	P<0.001		Highly significant	

ADA levels in CA-prostate cases showed a range of 5.56-78.13 U/L
Mean was 27.59 U/L±18.96
ADA levels in control cases showed a range of 6.92-22.87U/L
Mean was 14.46U/L ±4.11
The difference between ADA levels in these two groups (normal and CA prostate) was statistically highly significant.

Table 8: Comparison of levels of ADA in patients with BPH and CA-Prostate

Groups	Total no. of cases	ADA levels in U/L		
		Range	Mean	±SD
BPH	42	5.5-122.77	31.90	±26.60
CA-Prostate	30	5.56-78.13	27.59	±18.96
Statistical analysis				
T	P		Interference	
T(call)=0.77	P>0.05		No significance	

ADA levels in BPH cases showed a range of 5.5-122.77 U/L
Mean was 31.90 U/L±26.60
ADA levels in CA-prostate cases showed a range of 5.56-78.13U/L
Mean was 27.59U/L±18.96
The difference between ADA levels in these two groups (BPH and CA prostate) was not statistically significant.

DISCUSSION

A total of 105 cases were taken for the present study. The cases were divided into 3 groups- Control, BPH and CA-prostate.

Age

In the present study maximum number of case of carcinoma were in the age group of 70 to 79 years. The next common age group was 50 to 59 years. Mean age for cancer was 69.36±8.9 (range 55-81 years). Peak incidence in BPH was found in the age group 60-69 years the mean of 67.52±9.11 (range 52-87 years). Hence cancer prostate was found in slightly older population in all studies, including the present one, as compared to other prostatic problems.

Histopathological Grading

According to Gleason score in present study, the most common grade was grade IV, followed by grade V, then II and III and lastly grade I the most common score was 6 followed by 7, 8-10 finally 5 and 3.

Our study was in concordance to the study done by Tritsch and Murphy, 1990,[6] for ADA specific activity in normal, benign hypertrophied and neoplastic human prostate tissue. They found ADA activity in normal tissue, 037 mumol/subturned over /h/mg protein, carcinoma, 0.33; BPH 1.22 thus there may be a cellular level of immunostimulation in BPH relative to normal prostatic tissue which is no longer detectable in carcinoma.

In our present study serum ADA level for men with prostate cancer were between 50.56 to 78.13 U/L

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with mean of 27.59 U/L ±18.96, whereas for BPH serum ADA levels were between 5.50 to 122.77 U/L with mean of 31.90 U/L±26.60. In the control the levels of serum ADA were between 6.92 to 22.82 U/L with mean of 14.46±4.11 U/L.

In the present study the maximum cases that were proven benign or malignant on the basis of histopathology were in the range of 15.01-30U/L.

Thus there may a cellular level of immunostimulation, which may be related to enlargement of prostatic glands but not related to the benignity or malignancy.

Review Of Literature

ADA in Cancer

A very few studies have done of ADA in prostatic lesions so small literature is available on the same topic.

It has been studied that there is variation on serum ADA level and ADA expression in tissues either benign or malignant. It has been observed that there is an increase in serum A.D.A. levels in patient with hepatomas, (≈2 times) and adenocarcinomas, like gall bladder adenocarcinomas, (≈ 3 times), colon adenocarcinomas, (≈ 2 times), prostatic adenocarcinomas, (≈ 2 times). In pancreatic head (≈ 2 times), lung cancer (≈ 1.5 times) and mild increase in cancer of breast, esophagus and stomach (Koehler and Benz, 1966).[7]

ADA activity in tumor tissues was significantly higher in patients whose clinical course remained stable than in those with recurrent diseases.

In a study by Durak et al (1997),[8] the activity of some of the key enzymes participating in purine metabolism was measured in cancerous and noncancerous human kidney tissues from 18 patients with renal cell carcinoma. Adenosine deaminase (ADA) and guanase (GUA) activity was increased and xanthine oxidase (XO) activity decreased in cancerous tissues compared to noncancerous ones. Results suggest that the changes observed in the activity of the enzymes participating in purine metabolism result from accelerated DNA turnover in the cancerous tissues and cells, and these changes might provide selective advantage, possibly by causing acceleration of salvage pathway activity, to the cancer cells to grow and develop more rapidly.

Iker Durak, Hasan Biri et al,[9] studied effect of tomato juice on adenosine deaminase activity in human prostate tissue from patient with prostate cancer. And they found that tomato juice causes significant inhibition on ADA activity in the prostate tissues. Protective effect proposed for tomato against prostate cancer may result from its inhibition potential on ADA.

A study was done by Tritsch GL, Murphy GP (1990),[10] for ADA specific activity in normal, benign hypertrophied and neoplastic human prostate tissue. They found that deficiency in the purine salvage pathway enzyme, adenosine deaminase (ADA) is associated with immunodeficiency suggests that this enzyme may be crucial for normal function of immunocompetent cells in men. They found ADA activity in normal tissue, 0.37 mμmol/subturned over /h/mg protein, carcinoma, 0.33; BPH 1.22. Thus there may be a cellular level of immunostimulation in BPH relative to normal prostatic tissue which is no longer detectable in carcinoma.

CONCLUSION

However being a time bound study and having small sample size significance of all these parameters and association with diagnosis need to be explored by more studies having larger sample size and good follow up with a more time period.

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