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Significance of Prostate Specific Antigen for the Diagnosis and Treatment of Prostate Cancer

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Abstract: A prospective study has been planned to ascertain the most common form of cancer in adult males. Ninety six blood samples were taken from the patients attending KIRAN Hospital, The Lab., in which 41 were confirmed cases of prostate cancer and 55 individuals having unknown diseases of prostate gland (prostatitis etc). Their age and bone scan results have been recorded. IRMA estimated tumor marker PSA by using PSA kit supplied by immunotech, a Beckman coulter company. RIA technique was used to detect prostate specific antigens. Serum alkaline phosphatase was detected in Selectra automated analyzer. All tests were performed as described by the manufacturer. In case of malignancy, 53.6 cases showed the abnormal PSA level (>4 ng dL^{-1}). While 46.34% individuals had normal PSA level (0-4 ng dL^{-1}). There was a greater elevation in PSA level in the patients with prostate cancer as compare to bone scan and alkaline phosphatase. PSA has significant correlation with alkaline phosphatase, prostate cancer was easily diagnosed when PSA level was above 100 ng dL^{-1}. Bone scan has the importance when PSA level is above 100 ng dL^{-1}. Hemoglobin is greatly affected and showed less than normal values and nearly same effect was observed on lymphocytes, PSA level increases in cancer patients also in non cancerous patients.

Key words: Prostate cancer, PSA (Prostate Specific Antigens), alkaline phosphatase, bone scan, RIA (Radio Immunoassay)

INTRODUCTION

Adenocarcinoma of the prostate represents the most common form of cancer in adult males. Prostate carcinoma now surpasses the incidence of lung cancer and represents the second cause of death in male[1]. Increase in incidence is more pronounced in the United States, Canada, Australia, France and the Asian countries while mortality rates increasing more rapidly in Asian countries than in high-risk countries[2]. It is the most common diagnosed neoplasm and it is second cause of cancer death after lung cancer in America now. The incidence of prostate cancer is low in Pakistan, only 3.8% of male population, whereas it is also the number one in USA. The most likely explanation for this is lower life expectancy and no screening[3]. PSA (Prostate Specific Antigens)was identified in 1971 and called semino protein[4]. In 1978 this protein was purified from seminal plasma and characterized as a potential semen marker. PSA is not only useful for marking the progress of prostatic carcinoma but additionally has a potential role for screening and diagnosis of this disease[5]. It is responsible for seminal liquefaction it has been found to be prostate specific but not prostate cancer specific, it is under evaluation as a screening tool a staging tool AND as a monitor after therapy as a screening tool[6]. Bone scan is used for the detection and localization of metastasis[7]. Serial alkaline phosphatase estimation is essential in the follow up of patients with prostate cancer and bone metastasis[8]. Prostate specific antigen has a direct correlation with the incidence of a positive bone scan finding[9]. PSA is also widely used to monitor responses to therapy and is under investigation as a therapeutic target. It indicates that PSA has additional role in the pathogenesis of prostate cancer[10]. The objective of this study was to establish a relationship between prostate specific antigens with other clinical parameters and to evaluate the specificity of PSA in the diagnosis and treatment of prostate cancer and other prostatic diseases. PSA level also increases with increasing age, so effect of increasing age on PSA level was also studied.

MATERIALS AND METHODS

Present study was conducted from June 2003 to January 2004. For this 41 blood samples collected from prostate cancer patients, referred to KIRAN Hospital for monitoring the treatment and 55 blood samples have been collected from the patients with different prostatic diseases and referred to the Lab for the detection of PSA.

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PSA was determined by immuno radiometric assay (IRMA technique), in which two monoclonal antibodies against two different epitopes of PSA molecules are used. The sample and standards are incubated in monoclonal antibody coated tubes with the Iodine(^{125}I) labeled antibody. After incubation, aspirate the content of tubes, wash with wash solution and radioactivity is measured in a gamma counter. Normal PSA level was 0-4 ng dL^{-1}. Selectra E, an automated analyzer, detected alkaline phosphatase by using para nitro phenyl as Substrate. The serum is stored at 2-8°C. The normal value of alkaline Phosphatase was 98-279 μ L^{-1}.

The data of bone scan was available in the hospital which is detected by radiograph method by using dimethyl diphosphate (MDP) and a radio labeled tracer Tcm-99 and radioactivity was measured by gamma counter. Sysmex, a fully automated analyzer, did complete blood count. It provides complete blood picture including WBCs (White blood cells), RBCs (Red blood cells), platelets, hemoglobin (Hb) and their variations.

RESULTS

All serum samples were analyzed for the Prostate Specific Antigen (PSA) by Immunoradiometric Assay (IRMA) technique. Distinguishable difference between PSA values of Group A and non Cancerous Patients of Group B were observed (Fig.1 and 2, Table 1). After determining the PSA level of 41 cases their other clinical and biochemical tests like alkaline phosphatase, Bone scan and Complete Blood Count (CBC) have been performed and compared.

In Group A, 22 cases (53.65 %) were found to have PSA level above than normal range i.e., >4 ng dL^{-1}, rest of the 19 cases (46.34%) have the PSA within normal range 0-4 ng dL^{-1}, while in Group B 10.90% patients showed PSA values above then normal and 90% showed normal PSA level which indicate that PSA mostly increases in cancer condition because only smaller percentage of non cancerous patients showed abnormal PSA values (Table 1 and Fig. 2).

Arithmetic mean values of 41 Group A cases were found to be 63.7195 ng dL^{-1} while of Group B 55 cases 12.256 ng dL^{-1} (Table 1).

Table 2 showed the different categories of PSA level and these categories has been compared with bone scan and alkaline phosphatase in order to establish a correlation of these parameters for the early detection of Prostate Cancer. So in case of 0-4 ng dL^{-1} which is a normal range bone scan results in such cases were 32% +ve while alkaline phosphatase which is also a diagnostic tool for prostate cancer, was elevated in 42% cases.

Table 1: Comparison of PSA level between prostates cancer (Group A) and other prostatic disease (Group B)

Study group	Elevated PSA level (>4 ng dL^{-1})	Normal PSA level (0-4 ng dL^{-1})	Arithmetic mean values of PSA (ng dL^{-1})
Group: A Known prostate cancer cases (n = 41)	22(53.65%)	19(46.34%)	63.7195
Group: B Other prostatic disease Cases (n = 55)	6(10.90%)	49(89%)	12.256

Table 2: Correlation of increased PSA level with alkaline phosphatase and bone scan in prostate cancer patients

PSA level (ng dL^{-1})	No. of patients with +ve bone scan	%	No. of patients with elevated alkaline phosphatase	%
0-5	6(19)	31.51	8(19)	42.10
5-50	4(10)	40	3(10)	30
50-100	0(2)	0	2(2)	100
100-200	6(6)	100	4(6)	66.6
>200	3(4)	75	0(4)	0

Total No. of patients: 41, Normal PSA level: 0-5 ng dL^{-1}
Normal alkaline phosphatase: 98-279 uL^{-1}

Table 3: Percentages of normal values of different parameters in heamatology of 41 persons with prostate cancer

Parameters	No. of persons with normal values	%
Heamoglobin (g dL^{-1})	4	9.75
RBCs (mm^{-3})	31	75.60
Lymphocytes (%)	5	12.19
Platelets (mm^{-3})	39	95.12
Total leucocyte Count (mm^{-3})	30	73.17

Normal value of Hb: 14-18 gm dL^{-1}, Normal value of RBCs: 4-6x10^{6} mL^{-1}, Normal value of lymphocytes: 25-45%, Normal value of platelets: 150-450 mm^{-3}, Normal value of TLC: 5000-12000 mm^{-3}

Table 4: Correlation of increasing age of 41 patients with abnormal PSA level and +ve bone scan

Age (years)	Abnormal PSA (ng dL^{-1})	%	Bone scan +ve	%
40-49	2(2)	100	1(2)	50
50-59	4(7)	57.14	4(7)	57.14
60-69	9(20)	45	9(20)	45
70-79	8(2)	25	4(8)	50
80-90	2(4)	50	0(4)	0

Total case: 41, Abnormal PSA: 25(60.97%), +ve bone scan: 18(43.90%)

While in case of PSA values between 5 -50 ng dL^{-1}, 40% cases had +ve bone scan 30% had elevated Alkaline Phosphatase. When PSA values were in between 50-100 ng dL^{-1}, 0% bone scan +ve while 100% elevated alkaline phosphatase which indicate that bone scan can not be used as diagnostic tool in association with PSA while alkaline phosphatase can be used when PSA values are in between 50-100 ng dL^{-1}, when PSA values are in between 100-200 ng dL^{-1}, bone scan results are significant for the detection of prostate

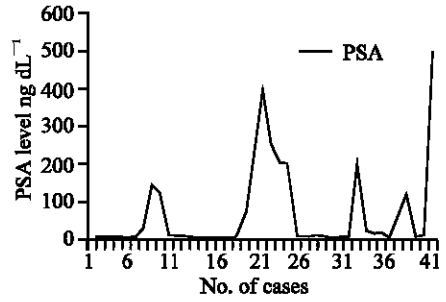

Fig. 1: PSA level in 41 cases with prostate cancer

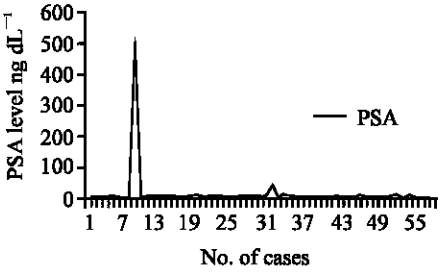

Fig. 2: PSA level in 55 cases with other prostatic diseases

cancer while alkaline phosphates can not be used in association of these PSA values as diagnostic marker. In case of more then 200 ng dL^{-1} PSA values bone scan can be used as diagnostic tool (Table 2).

Table 1 explained the CBC values of Group A patients. It was observed that Heamoglobin (Hb) and lymphocytes are adversely affected in these patients i.e., only 9.75% cases showed normal Hb level while rest about 90% showed Hb values below then normal while in case of lymphocytes only 12% cases showed normal count i.e., 25-45 and 82% showed below then normal range while RBCs and platelets and total leucocytes were not that much affected (Table 3).

In Table 4 PSA values have been compared with different age groups in order to establish a definite correlation of increasing PSA values with age. In Pakistan maximum age limit is in between 50-60 years and abnormal PSA was observed in between 50-59 years of age, 57% patients showed abnormal PSA level while in rest of the age group no significant correlation can be established. A significant correlation of PSA level with increasing age were observed in patients of age group 50-59 years as compare to other age group (Table 4). Another reason for maximum frequency in this age group is that average age in our country is 50-60 years.

DISCUSSION

The area of this study was based on over all 96 patients, 41 from KIRAN Hospital and 55 from The Lab. All of them were under different treatments like. 46.34% patients of Group A were found to observe a fall in PSA values within normal range, as a result of different types of treatment like chemotherapy, radiotherapy etc. And their reports showed a decrease in PSA up to 80% of its initial baseline values. Out of 41 patients Group A 19 cases have PSA within normal range (Fig. 1 and 2, Table 1 and 2), (0-4 ng dL^{-1}) as a result of different types of treatment as so it can be taken as a good prognostic indicator within 4 weeks. Therefore PSA can be used to monitor the effect of treatment. While in 53.65% patients of Group A, abnormal PSA level was observed[11]. Out of 55 cases 89% cases showed the normal PSA level while only 10.9% cases showed elevation in PSA level and this showed that PSA level increases in prostate cancer but also in other prostatic diseases[12]. Oesterling in 1993 also reported that PSA is an accurate tumor marker for the diagnosis of prostate adenocarcinoma. Beside PSA other methods are also available for evaluating the patients with prostate neoplasia like prostate acid phosphatase, alkaline phosphatase, ultrasonography and bone scan[13].

This investigation showed a significant correlation of PSA and Bone Scan for the detection of metastasis as compare to alkaline phosphatase (Table 2). Some metastatic cancer had negative bone scan. According to the survey by American collage of surgeons that 40% of prostate cancer has already spread beyond the prostate at the time of diagnosis[14].

Most of the patients with prostate cancer has the age range of 50-59 years (Table 4) which is similar to the report[15] that carcinoma of prostate is strongly age dependent tumor as 57.14% of patients were found between 50-59 years of age. It was observed that PSA (Tumour marker) test has significant role for monitoring the affectivity of treatment but as a diagnostic marker it has low specificity because it also increases in other prostatic diseases like prostatitis, benign prostatic hyperplasia etc.

Immunoradiometric assay (IRMA) is a very sensitive and specific technique for the quantitative analysis of prostate specific antigen in serum. Prostate specific antigen has low specificity as a diagnostic marker of prostate cancer. PSA can be used to monitor the effect of treatment. PSA level also increases in some patients with benign prostatic diseases. PSA has more significant correlation with bone scan for the detection of metastasis as compared to alkaline phosphatase.

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REFERENCES

1. Silverberg, E., C.C. Boring and T.S. Squires, 1990. Cancer statistics. CA, 40: 9.
2. Hsing, A.W., L. Tsao and S.S. Devesa, 2000. International trend and patterns of prostate cancer incid ence and mortality. Intl. Cancer, 85: 60-65.
3. Gillatt, D. and J.M. Reynard, 1995. What is normal range for prostate specific antigen use of a receiver operating charecteristic curve to evaluate a serum marker. Br. J. Urol., 75: 341-346.
4. Fried, R.M., N.S. Davis and G.H. Weiss, 1997, Prostate cancer screening and management. Med. Clin. North Am., 81: 801.
5. Wang, M.C., L.A. Velenzuelae and G.A. Murphy, 1979. Purification of a human serum prostate specific antigen. Invest. Urol., 17: 159.
6. Catalona,W.J. and F.R, Richie Ahmed, 1994. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer. J. Urol., 151: 1283.
7. Wahner, H.W. and M.L. Brown, 1988. Role of Bone Scanning. In Diagnosis and Management of Metatstatic Bone Diseases. Sim, F.H. (Eds.), New York, Reven Press, Chap. 8, pp: 51-67.
8. Bishop, M.C., J.G. Hardy, M.C.M. L. Taylor Wastie and R.J. Lemberger, 1985. Bone imaging and serum phosphatases in prostatic carcinoma. Br. J. Urol., 57: 317-324.
9. Chybowski, F.M., J.J. Keller, E.J. Bergstralh and J.E. Oesterling, 1991. Predicting radionuclide bone scan findings in patients with newly diagnosed, untreated prostate cancer: Prostate specific antigen is superior to all other clinical parameters. J. Urol., 145: 313-8.
10. Balk, S.P. and G.J. Bubley Ko, 2003. Biology of prostate-specific antigen. J. Clin. Oncol., 21: 383-91.
11. Saima, N., A. Sarah, G. Farkhanda, S.B. Nadeem and A. Waheed, 2004. Free and total Prostate specific antigen in benign prostatic hyperplasia and prostate cancer, J. Coll. Physicians. Surg. Pak., 14: 69-71.
12. Oesterling, J.E., 1991. Prostate specific antigen: A critical assessment of most useful tumor marker for adenocarcinoma of the prostate. J. Urol., 145: 907-923.
13. Javaid, M.S., M. Tariq, I.A. Bajwa, A. Mubashir and K.A. Shamim *et al.*, 1996. Prostate specific antigen and bone scan correlation in the staging of patients with carcinoma prostate. Ann. King Edward Med. Coll., pp: 35-37.
14. Donoghue, O., E.P.N. Constable, A.R. Sherwood, T. Stevenson and Chisholm, 1978. Bone scanning and plasma phosphates in Carcinoma of prostate. Br. J. Urol., 50: 172.
15. Osterling, J.E., S.J. Jacobes, C.X. Hute, C.G. Guess, A. Girmanh and C.J. Panser, 1993. Serum Prostate specific antigen in a community based population of healthy men Establishment of age-specific ranges. JAMA., 270: 860.