

## Age Related Prostate-Specific Antigen Reference Range among Men in South-East Caspian Sea

<sup>1</sup>A.R. Mansourian, <sup>2</sup>E.O. Ghaemi, <sup>3</sup>A.R. Ahmadi, <sup>1</sup>A. Marjani, <sup>2</sup>A. Moradi and <sup>4</sup>A. Saifi

<sup>1</sup>Department of Biochemistry,

<sup>2</sup>Department of Microbiology,

<sup>3</sup>Department of Medical Laboratory Sciences,

<sup>4</sup>Department of Pharmacology, Golestan University of Medical Sciences, Gorgan, Iran

**Abstract:** The purpose of this study was to describe the distribution of serum prostate specific antigen (PSA) and to determine age-specific reference range in a population of Persian men. Venous blood samples were taken from 287 men, from Gorgan located in the North of Iran, South-East of Caspian Sea, aged 15≥80 year. The serum PSA levels was measured using Enzyme-linked Immunosorbant-Assay (ELISA) technique and age-specific range for PSA level was determined. The serum prostate-specific antigen level for six age group of 15-40 years, 41-50 years, 51-60 years, 61-70 years, 71-80 years and >80 years were mainly in the range of 0-2.5 ng mL<sup>-1</sup>, for 76.6%, 2.6-4 ng mL<sup>-1</sup> for 9.1% and as whole 85.7% of all men in this study had ≤4 ng mL<sup>-1</sup>, 8.7 and 5.6% all men of six age group had PSA level of 4.1-10 ng mL<sup>-1</sup> and >10 ng mL<sup>-1</sup>, respectively. The findings of present study indicated that a large proportion (76.6%) men in this region have a lower PSA level of 0-2.5 ng mL<sup>-1</sup> and only 9.1% of men have PSA level of 2.6-4 ng mL<sup>-1</sup>. It is therefore concluded that acceptable reference range of 0-4 ng mL<sup>-1</sup> for PSA level require further reassessment.

**Key words:** Prostate-specific Antigen (PSA), reference range, men, distribution, age group

### INTRODUCTION

Prostate cancer has the highest incidence among male malignancies. Since the introduction of Prostate-Specific Antigen (PSA) testing in the late 1980s, the incidence of prostate cancer has increased, with a change toward detecting it an early stage (Jemal *et al.*, 2004; Mettin and Murphy, 1996). Age-specific reference ranges for serum PSA levels is established to improve it's sensitivity in younger men and to increase it's specificity in older men (Oesterling *et al.*, 1993), this later researcher suggested upper range reference value of 2.5, 3.5, 4.5 and 6.5 ng mL<sup>-1</sup> for the age decades of 40-49, 50-60, 60-69 and 70-79 years in asymptomatic men with no clinical evidence of prostate cancer. In spit of these findings, recent investigations emphasize the limitation of these PSA threshold value to discriminate between prostate cancer and benign disease, in asymptomatic men (Thompson *et al.*, 2004; Loeb *et al.*, 2005; Kundu *et al.*, 2005).

It is reported that the prostate cancer was detected in 15.2% of men whose total PSA level was <4 ng mL<sup>-1</sup>, which is the threshold for diagnosing prostate cancer (Thompson *et al.*, 2004), also it has been reported that, despite very low level PSA levels of 0.1-1.0 ng mL<sup>-1</sup> as many as 16.7% of those men had prostate cancer on biopsy (Thompson *et al.*, 2004). These later data indicate

that a normal PSA level can not exclude the presence of prostate on biopsy. In an another study it has been reported that men below 60 years of age with base line PSA level of 0.6-2.5 ng mL<sup>-1</sup> are at greater risk of having prostate than those men with a baseline PSA level <0.6 ng mL<sup>-1</sup> (Loeb *et al.*, 2005).

In a further study, it was also shown that a base line PSA level above the age-adjusted (40-49, 50-59, >60 years) median levels of 0.7, 0.9, 1.4 ng mL<sup>-1</sup> represents a significant risk factor for developing prostate cancer (Kundu *et al.*, 2005).

Several studies have also demonstrated that a substantial number of men have microscopic evidence of prostate cancer despite having a prostatic specific antigen (PSA) level below 4 ng mL<sup>-1</sup> the standard threshold used to define abnormal.

The findings from such investigation have led some physicians to look more carefully at a lower PSA threshold of 2.5 ng mL<sup>-1</sup> (Thompson *et al.*, 2004; Raaijmakers *et al.*, 2004; Catalona *et al.*, 1997), using this PSA level means that more men than before would be labeled as a abnormal and therefore are being looked more deeply and tested for prostate cancer. In this study it was tried to establish the PSA level in a various age groups of men, in Gorgan the capital city of Golestan Province in the South-east Caspian Sea of northern Iran.

The aim of this study was to determine age-specific reference ranges for serum PSA levels in men aged 15-≥80 years of age in this region.

**MATERIALS AND METHODS**

This study was carried out on 287 men whom referred to Danesh medical diagnostic laboratory, for Prostate-Specific Antigen (PSA) testing for a period of one year September 2005-October 2006. Data on the distribution of PSA level for the above sample population were obtained, using venous blood samples which were taken from the above number of men, whom mainly were resided in this cosmopolitan region which is the Capital city of Golestan Province in the north of Iran, located in the South-East of Caspian Sea. Total serum PSA levels were measured using Enzyme-Linked Immunosorbant Assay (ELISA) technique. The basis for this procedure was a sandwich method using monoclonal, antibodies against the PSA molecules specific antigenic part. The samples serum were placed into wells which was covered by the PSA antibodies. After incubation and subsequent washing the chromagen was added. The reaction was stopped afterward and the colored solution absorbance in the wells, were read using an ELISA reader (Belanger *et al.*, 1996; Zhov *et al.*, 1993), serum samples were aliquoted in 2 mL batches in freezer, in the early morning and stored until analysis of PSA determination was carried out in few hours time.

**RESULTS**

In this study, the PSA determination was carried out on the six age groups as follow: 15-40 years, 41-50 years, 51-60 years, 61-70 years, 71-80 years and more than 80 years. The results of PSA determination for the above age group were presented in Table 1. The PSA determination for each group were subdivided the following range of PSA concentration 0-2.5 nanogram per milliliter (ng mL<sup>-1</sup>), 2.6-4, 4.1-10 and >10 ng mL<sup>-1</sup>.

The men in 15-40 years, 41-50 years, 51-60 years, 61-70 years, 71-80 years and more than 80 years age groups had the following ratio of distribution 5.2, 20.6, 26.1, 27.8, 16.7 and 3.5%, respectively. The results from

Table 1 was also indicated that 76.6, 9.1, 8.7 and 5.5% of all the sample population in the above age groups in this study had the following PSA level ≤ 2.5, ≥ 2.6-4 ≤, ≥ 4.1-10 and >10 ng mL<sup>-1</sup>, respectively. The result in Table 1 showed that in 15-40 years age group, 100% of men having serum PSA level 0-2.5 ng mL<sup>-1</sup>, in 41-50 years age group 91.5, 6.7 and 1.7% of all men in this group had the PSA level, of 0-2.5, 2.6-4 and >10 ng mL<sup>-1</sup>, respectively. In 51-60 years age group, 74.6, 10.6, 9.3 and 5.3% of all men. In this age group had, the PSA level of 0-2.5, 2.6-4, 4.1-10 and >10 ng mL<sup>-1</sup>, respectively. In 61-70 years age group 72.5, 10, 12.5 and 5% of all men in this age group had the PSA level of 0-2.5, 2.6-4, 4.1-10 and >10 ng mL<sup>-1</sup>, respectively.

In 71-80 years age group, 62.5, 10.4, 12.5 and 14.5% of all men in this age group had the PSA level of 0-2.5 ng mL<sup>-1</sup>, 2.6-4 ng mL<sup>-1</sup>, 4.1-10 ng mL<sup>-1</sup> and >10 ng mL<sup>-1</sup>, respectively and finally in >80 years age group, 70, 10 and 20% of all men in this age group had the PSA level of 0-2.5, 2.6-4 ng mL<sup>-1</sup> and 4.1-10 ng mL<sup>-1</sup>, respectively.

In this study 85.7% all sample population in all of the six age groups had the serum PSA level ≤ 4 ng mL<sup>-1</sup> which is an permissible threshold for the excluding prostate abnormalities by the present PSA reference range. 8.7% of all men in this study had the PSA level of 4.1-10 ng mL<sup>-1</sup> and also 5.6% of all men in this study had the PSA level more than 10 ng mL<sup>-1</sup> which in both cases further medical investigation were required, by the present standard (Table 2).

Also in the Table 2 subjects with ≤ 2.5 ng mL<sup>-1</sup> of PSA level shown to be 76.6% of all men in this present study.

In this study, we also arranged the results for all six age groups of 15-40, 41-50, 51-60, 61-70, 71-80 and >80 years of age individually on the basis of 0.5, 1, 1.51, up to 9.5 ng mL<sup>-1</sup>, 10 ng mL<sup>-1</sup> and >10 was presented in Table 3, which showed the distribution of Prostate-Specific Antigen (PSA) level among the sample population in this study, by 0.5 ng mL<sup>-1</sup> PSA level increase.

According to present findings it is indicated that 76.6% of all men in this investigation had PSA level up to 2.5 ng mL<sup>-1</sup> and 9.1% of men had PSA level of 2.6-4 ng mL<sup>-1</sup> which is still considered to be normal (i.e., ≤ 4 ng mL<sup>-1</sup>) but further, it can be seen from the above

**Table 1: PSA level distribution among men subjects in different age group**

Age group (year)	PSA 0-2.5 (ng mL <sup>-1</sup> )	PSA 2.6-4 (ng mL <sup>-1</sup> )	PSA 4.1-10 (ng mL <sup>-1</sup> )	PSA >10 (ng mL <sup>-1</sup> )	Total No.
15-40	15 (100%)	-	-	-	15 (5.2%)
41-50	54 (91.5%)	4 (6.7%)	-	1 (1.7%)	59 (20.6%)
51-60	56 (74.6%)	8 (10.6%)	7 (9.3%)	4 (5.3%)	75 (26.1%)
61-70	58 (72.5%)	8 (10%)	10 (12.5%)	4 (5%)	80 (27.9%)
71-80	30 (62.5%)	5 (10.4%)	6 (12.5%)	7 (14.5%)	48 (16.7%)
>80	7 (70%)	1 (10%)	2 (20%)	-	10 (3.5%)
Total	220 (76.6%)	26 (9.1%)	25 (8.7%)	16 (5.5%)	287

**Table 2: PSA level distribution among men subjects regardless of age group**

PSA level (ng mL <sup>-1</sup> )	Number (men)	Percentage
≤ 2.5	220	76.6
≤ 4	246	85.7
4.1-10	25	8.7
>10	16	5.6

**Table 3: Distribution of serum Prostate-Specific Antigen (PSA) level by 0.5 ng mL<sup>-1</sup> increase among men undergone in this study**

Age group (year)	Total men	Prostate-Specific Antigen (PSA) ng mL <sup>-1</sup>																					
		0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6	6.5	7	7.5	8	8.5	9	9.5	10	≥10	
15-40	15	53%	27%	7%	-	13%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
41-50	59	27.5%	32.7%	25.8%	6.8%	-	5%	1.7%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.7%
51-60	75	25.3%	24%	16%	12%	2.6%	2.6%	4%	4%	2.6%	1.3%	2.6%	-	-	-	-	-	-	-	-	-	-	2.6%
61-70	80	19.2%	20.5%	17.9%	10.2%	6.4%	5.1%	1.2%	3.8%	3.8%	1.2%	1.2%	1.2%	1.2%	1.2%	-	-	-	-	-	-	-	5%
71-80	48	8.3%	18.7%	14.5%	14.5%	6.3%	4%	4%	2%	6.3%	-	2.1%	-	-	2.1%	-	-	-	-	-	-	-	14.5%
>80	10	40%	30%	-	-	-	-	10%	-	-	10%	10%	-	-	-	-	-	-	-	-	-	-	-

datas that only 8.7% of all men had PSA level of 4.1-10 ng mL<sup>-1</sup> and 5.5% of all men had PSA level of >10 ng mL<sup>-1</sup> which in both cases considered to be abnormal and needed further medical following-up.

**DISCUSSION**

Most men have a serum PSA level of ≤ 4 ng mL<sup>-1</sup> and this value rise steadily with age, which had been reported in number of studies including (Gilbert Welch *et al.*, 2005; Elijah *et al.*, 2005), which indicated that there is a significant correlation between men age and total PSA level. In the era of predominantly impalpable prostate cancer, PSA represents the main indicator of the likelihood of harboring prostate cancer, however the best threshold value has been disputed and revised by several investigator, some showed an identical prostate cancer detection rate in men with PSA level of 2.5-4 ng mL<sup>-1</sup>, as in those with levels of 4-10 ng mL<sup>-1</sup> (Catalona *et al.*, 1991; Schroder *et al.*, 2000; Lodding *et al.*, 1998). However a universal threshold value dose not represent a valid risk stratification for all men, regardless of age (Catalona *et al.*, 1991; Schrooder *et al.*, 2000; Lodding *et al.*, 1998) therefore, efforts were made to improve the sensitivity and specificity of PSA level threshold.

Age-specific PSA reference ranges of 0-2.5, 0-3.5, 0-4.5 and 0-6.5 ng mL<sup>-1</sup> for age categories. 40-49, 50-59, 60-69 and 70-79 years in asymptomatic healthy men at risk were proposed (Oesterling *et al.*, 1993).

The correlation between men subjects with age and total PSA level is also reported in other reviews (Dalkine *et al.*, 1993; Oesterling *et al.*, 1993; Collins *et al.*, 1993).

However, recent findings indicate that these reference range might need to be revised due to limited sensitivity and to an excessive proportion of false-negative results (Thompson *et al.*, 2004; Loeb *et al.*, 2005; Kundu *et al.*, 2005).

As far as there was not any report on the reference range limited value of prostate specific antigen in this area, we decided to explore PSA levels in this region which is mainly a cosmoplitant society, in the north of Iran, South-east of Caspian Sea.

Present finding in Table 1 indicated that the threshold of 100, 91.5, 75.6, 72.5, 62.5 and 70% of all men for the following age groups of 15-40, 41-50, 51-60, 61-70, 71-80 and >80 years had PSA level of ≤2.5 ng mL<sup>-1</sup>, which was partly similar to a separate study in USA (Gilbert Welch *et al.*, 2005), where it was reported that Prostate-Specific Antigen (PSA) level of <4 ng mL<sup>-1</sup>, nonetheless have microscopic evidence of prostate cancer has led to some investigations that the threshold defining abnormal should be lowered to 2.5 ng mL<sup>-1</sup>. In USA study it was concluded that, lowering the PSA threshold to 2.5 ng mL<sup>-1</sup> would double the number of men defined as abnormal (Gilbert Welch *et al.*, 2005). In this study the proportion of population affected by different thresholds would vary with age, among men of 15-40 years of age non of the men had PSA level more than 2.5 ng mL<sup>-1</sup>. 91.5, 6.7 and 1.7% of men in their 40s had PSA level ≤2.5, >2.5-4 and >10 ng mL<sup>-1</sup>, 74.6, 10.6, 9.3 and 5.3% of men in their 50s had PSA level of ≤ 2.5, >2.5-4 ≤ and >10 ng mol<sup>-1</sup>, 72.5, 10, 12.5 and 5% of men in their 60s had PSA level of ≤2.5, >2.5-4 ≤, >4.1-10 ≤ and >10 ng mL<sup>-1</sup>, 62.5, 10.4, 12.5 and 14.5% of men in their 70s had PSA level of ≤2.5 ng mL<sup>-1</sup>, >2.5-4 ≤ ng mL<sup>-1</sup>, 4.1-10 ≤ ng mL<sup>-1</sup> and

>10 ng mL<sup>-1</sup> and finally, 70, 10 and 20% in their 80s had PSA level of ≤2.5 ng mL<sup>-1</sup> >2.5-4 ≤ ng mL<sup>-1</sup>, >4.1-10 ≤ ng mL<sup>-1</sup>. In another study (Porter *et al.*, 2006) the men for example in their 60s, 17% of men had PSA level over 2.5 ng mL<sup>-1</sup> 5.7% had PSA level of 4 ng mL<sup>-1</sup> and 1.7% had a PSA level over 10 ng mL<sup>-1</sup> which was partly similar to present study. Present study about the correlation of age and total PSA level are also confirmed by other studies (Oesterling *et al.*, 1993; Daklin *et al.*, 1993; Collins *et al.*, 1993).

In this study, 85.7% of all men had the PSA level ≤4 ng mL<sup>-1</sup> which is normal level according to the definition for the PSA level it means that in our study 85.6% of all men have normal PSA level and only 14.4% of men have PSA level more than 4 ng mL<sup>-1</sup> and these men considered to be at risk and needed to be followed up for further investigation but there are some report which indicated that a large number of prevalent cases of biopsy detectable prostate cancer exist in men with a normal PSA level (Porter *et al.*, 2006), therefore for the men with normal PSA level in our study it should be a necessity to look for any clinical indication of prostate abnormality.

There is a study which was reported that 15.2% of 449 men with PSA level of <4 ng mL<sup>-1</sup> were found to have prostate cancer (Thompson *et al.*, 2004), with an even distribution across age groups. The mean PSA in our study was 1.72 ng mL<sup>-1</sup> which was little more than above study. In the above study (Thompson *et al.*, 2004) it was reported that the trial data showed that all patients with detected prostate cancer, 337 men (67.8%) had base line PSA levels above the mean PSA level of 1.34 ng mL<sup>-1</sup>. In a recently reported large screening population of 14000 men aged <60 years an initial base line PSA level of 0.6-2.5 ng mL<sup>-1</sup> was associated with a greater risk of developing prostate cancer (Loeb *et al.*, 2005). In another study it was indicated that a PSA level is directly correlated with age and showed that PSA level of 2.6-4 ng mL<sup>-1</sup> increased the risk of prostate cancer for each of the studied age group of 40-49, 50-59 and >60 years, but this effect was most pronounced in younger men aged 40-49 years (Kundu *et al.*, 2005). In another study (Oesterling *et al.*, 1993) it was showed that the PSA level increase by age. In this study we did have PSA level maximum of up to 2.5 and 3.5 ng mL<sup>-1</sup> for the aged group of 15-40 and 41-50 years. The PSA level increase for the age group of 51-60 year to about 5.5 ng mL<sup>-1</sup> also 1.7% of men in this age group had PSA level of >10 ng mL<sup>-1</sup>. In the age group of 61-70 years of age, the PSA level raised up to 7 ng mL<sup>-1</sup> also we had 2.6% of men in this age group to have the PSA level >10 ng mL<sup>-1</sup>. In the age group 71-80 years the PSA level increased up to 8 ng mL<sup>-1</sup> in here also we had 5% of men in this age group with PSA >10 ng mL<sup>-1</sup>.

In this study in age group of >80 years also we had PSA level >10 ng mL<sup>-1</sup> for 14.5% of men in this group, but 70% of men of >80 year had PSA level of up to 1 ng mL<sup>-1</sup>, but it should be mentioned that the number men in this a group was only 10 men: (Table 3). The data from this present study indicated that as in the earlier reports in various part of the world the serum PSA levels are age dependent, there are numerous studies in this regard. (Oesterling *et al.*, 1993; Loeb *et al.*, 2005; Gilbert Welch *et al.*, 2005; Elijah *et al.*, 2005; Lodding *et al.*, 1998; Veltri *et al.*, 2002).

In conclusion the present study is unique in the origin of the population and among the conflicting reports of the PSA level which are considered for the detection of prostate cancer, the PSA level require reassessment for the different countries and even in one country with different ethnic groups where the detection of prostate cancer and its genetic make-up may differ from one another.

The present study confirms earlier reports that serum PSA level are age-dependent, but also a big majority of men having PSA level of ≤ 2.5 ng mL<sup>-1</sup>. Therefore, it is appropriate to have age specific reference ranges for the age variable in various communities, this will enhance the positive predictive value of PSA estimation in the diagnosis of prostate cancer in each society. Further investigations in this region is required to obtain some data about the correlation between serum PSA levels, prostate volume and race-dependency in this community, which is a unique multi-racial society, in the north of Iran.

## REFERENCES

- Belanger, A. and H. van Harbeek *et al.*, 1996. Molecular mass and carbohydrate structure of prostate specific antigen. Studies for establishment of an int. PSA. *Prostate*, 27: 187-197.
- Catalona, W.J., D.S. Smith and T.L. Ratliff *et al.*, 1991. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. *N. Engl. J. Med.*, 324: 1156-1161.
- Catalona, W.J., D.S. Smith and D.K. Ornstein, 1997. Prostate cancer detection in men with serum PSA concentrations of 2.6 to 4.0 ng mL<sup>-1</sup> and benign prostate examination. Enhancement of specificity with free PSA Measurements. *JAMA.*, 277: 1452-145.
- Collins, G.N., R.J. Lee, G.B. Mckelvie, A.C. Rogers and M. Hehir, 1993. Relationship between prostate specific antigen, prostate volume and age in the benign prostate. *Br. J. Urol.*, 71: 445-450.

- Dalkin, B.L., F.R. Ahmann and J.B. Kopp, 1993. Prostate specific antigen levels in men older than 50 years without clinical evidence of prostatic carcinoma. *J. Urol.*, 150: 1837-1839.
- Elijah, O.K., O.A. Mojiminiyi, M. Sheikh, K.A. Al-Awadi, A.S. Daar, A. Al-Hunaya, J.T. and A.A. Al-Sumait, 2005. Age-specific reference levels of serum prostate-specific antigen and prostate volume in healthy Arab men. *BJU Int.*, 96: 308.
- Gilbert Welch, H., M. Lisa schwarts and steven woloshin, 2005. Prostate-specific antigen levels in the united states: Implications of various definitions for abnormal. *J. Nat. Cancer Inst.*, 97: 1132-1137.
- Jemal, A., R.C. Tiwari and T. Murray *et al.*, 2004. Cancer statistics. *CA Cancer J. Clin.*, 54: 8-29.
- Kundu, S.D., K.A. Roehl, J.A.V. Antenor, W.J. Catalona and R.B. Nadler, 2005. Age-Specific risk of prostate cancer if PSA is between the median value and commonly used biopsy thresholds. *AUA, Abstract*, pp: 953.
- Lodding, P., G. Aus and S. Berdahl *et al.*, 1998. Characteristics of screening detected prostate cancer in men 50-66 years old with 3-4 ng mL<sup>-1</sup>. Prostate specific antigen. *J. Urol.*, 159: 903.
- Loeb, S., K.A. Roehl, J.A.V. Antenor, W.J. Catalona, B.K. Suarez and R.B. Nadler, 2005. Baseline PSA compared with median PSA for age group as predictor of pathologic tumor features in men <60 years of age. *AUA Proceedings, Abstract*, pp: 533.
- Mettin, C.J., G.P. Murphy and R. Ho, 1996. The National CancerDatabase report on longitudinal observations on prostate cancer. *Cancer*, 77: 2162-2166.
- Oesterling, J.E., S.J. Jacobsen and C.G. Chute *et al.*, 1993. Serum prostate-specific antigen in a community-based population of healthy men. Establishment of age-specific reference ranges. *JAMA.*, 270: 860-864.
- Porter, M.P., J.L. Stanford and P.H. Lange, 2006. The distribution of serum prostate-specific antigen levels among American men: Implication for prostate cancer prevalence and screening. *Prostate*, 1: 1044-1051.
- Raaijmakers, R., B.G. Blijenberg, J.A. Finlay, H.G. Rittenhouse, M.F. Wildhagen and M.J. Roobol *et al.*, 2004. Prostate cancer detection in the prostate specific antigen range of 2.0 to 3.9 ng mL<sup>-1</sup>: Value of percent free prostate specific antigen on tumor detection and tumor aggressiveness. *J. Urol.* [CrossRef][ISI][Medline], 171: 2245-2249.
- Schroder, F.H., I. van der Crujisen-kOoeter, H.J. de Koning, A.N. Vis, R.F. Hoedemaeker and R. Krase, 2000. Prostate cancer detection at low prostate specific antigen. *J. Urol.*, 163: 806-812.
- Thompson, I.M., D.K. Pauler, P.J. Goodman, C.M. Tangen, M.S. Lucia and H.L. Parnes *et al.*, 2004. Prevalence of prostate cancer among men with a prostate-specific antigen level 4.0 ng per milliliter. *N. Engl. J. Med.*, 350: 2239-2246.
- Veltri, R.W., M.C. Miller, G.J.O.' Dowd and A.W. Partin, 2002. Impact of age total complexed Prostate-Specific Antigen cutoffs in a contemporary referral series of men with prostate cancer. *Urol.*, 60: 47-52.
- Zhov, A.M., P.C. Tewari and G.W. Card Weu, 1993. Multiple forms of PSA in serum; differences in immunorecognition by monoclonal and polyclonal assay. *Clin. Chem.*, 39: 2483.