



Detection of Prostate Specific Antigen (PSA) in Prostates patients

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Abstract:

The current study was carried out in Al-Sader teaching Hospital in Al-Najaf province during the period from 2017/1/8 till 2017/7/18. The study was undertaken to estimate the importance of PSA marker in differentiated between patients with prostate diseases and patients with prostate cancer. The cases enrolled in this study included 210 patients with prostate diseases, their ages ranged from (21-89) years divided into sex group according to their ages. 60 apparently healthy male as a control subject, their age ranged from (20-80). All 210 prostate patients had different serum PSA values from ≤ 2.5 (ng/ml) to > 4.0 ng/ml. 94 (44.8%) had PSA > 4.0 ng/ml and 116 (55.2%) had PSA < 4.0 ng/ml. 38 (43.2%) of patients with 60-69 years old had PSA level higher than the (4.0 ng/ml) while 27 (46.6%) of patients with 70-79 years old had PSA level higher than the (4.0 ng/ml) and the patients who had ≥ 80 years appears 10 (76.9%) of them had PSA level higher than the (4.0 ng/ml). The results of this study revealed that Serum PSA level can be used as predictive and diagnostic marker for prostate cancer.

Background:

Benign prostatic hyperplasia (BPH) influenced all men in normal life. This hyperplasia increased about 70% in men older than 60 years, So this disease more prevalent than Asthma or diabetes (Meigs&Barry,2000). The prevalence of BPH increase with age, 90% of men with 80 years old have histologically demonstrable. (Berry *et al.*,2004). BPH will affect a large proportion of the people in the world. BPH is chronic condition characterized by gradually increase PSA concentration, Prostate volume, decreasing urinary flow rate, and inferior urinary tract signs such as urgency, frequency, and nocturia (Anderson *et al.*,2009) . there is an evidence confirm that PSA a marker used as a diagnostic test for prostate cancer, is also useful in prognosticating disease progress in BPH when examined in combination with other indicators. Particularly, data suggest that PSA patients have at least 4 ng/ml with lower urinary tract signs and an increased prostate size which causes progression of a prostate cancer. The early diagnosis of this disease depending on this marker may help in pharmacotherapy to treat the progression of this disease (Anderson *et al.*,2009).

Objectives:

To estimate the importance of PSA marker in differentiated between patients with prostate diseases and patients with prostate cancer

Material &method :

Patients:

The cases enrolled in this study included 210 patients with prostate disease over a period of seven months in Al-Sadar city medical in Al-Najaf provinces , their ages ranged from (21-89)



years divided into sex group , disease that occur in ageing men, namely, benign prostate hyperplasia , prostates and prostate cancer .

Controls:

This study included a control group . this group consist of 60 apparently healthy male as a control subject , their age ranged from (20-80) years subject with any disease .

Collection of sample:

The blood specimens collected by vein puncture and put in plain venipuncture tube without anti-coagulants, these samples obtained in morning as fasting. After this the blood is clotting and centrifuged to get the serum. The samples can store a -20 °C for up to 30 days if we do not need analysis it at a time. 0.050 ml is required to PSA test. The procedure depends on biomerieux kit.

Statistical analysis:

The statistical analysis of the samples involves z test of two proportions for the estimation between the various groups. For comparing the means, it used Student z- test and t- test of one proportion. The significant level was set at $p < 0.05$.

Results:

All 210 prostate patients had different serum PSA values from ≤ 2.5 (ng/ml) to > 4.0 ng/ml. 94 (44.8%) had $\text{PSA} > 4.0$ ng/ml and 116 (55.2%) had $\text{PSA} < 4.0$ ng/ml as shown in (Table 1).

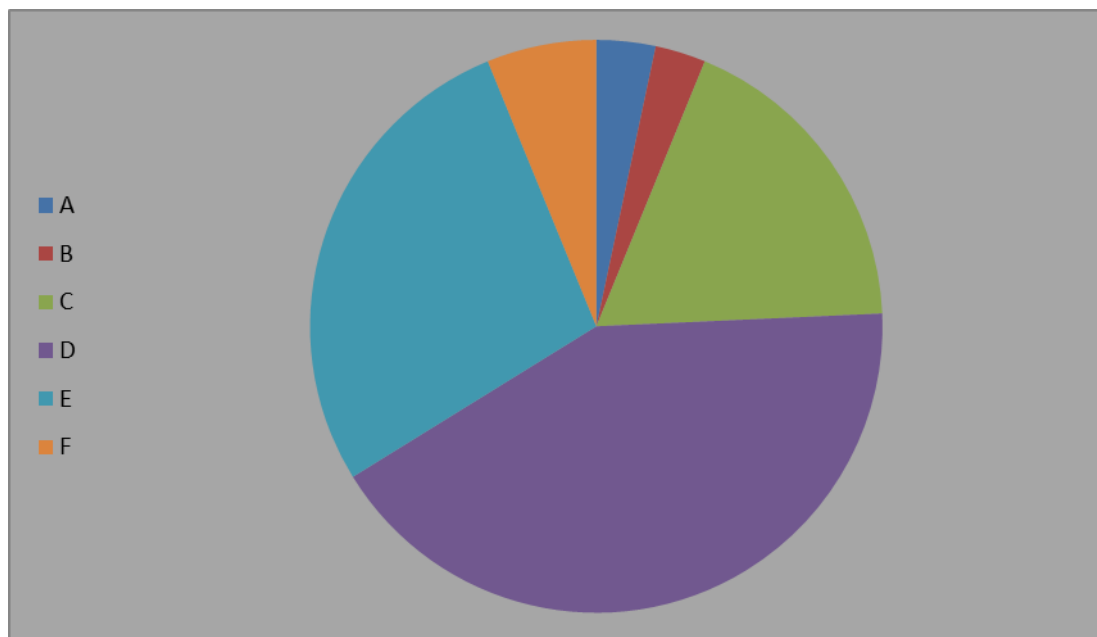
Table 1: Normal and elevated PSA in patients with prostate cancer and other prostate diseases:

Variable	Prostate cancer patients	Other prostate Diseases	Total
Elevated PSA	59 (62.7)	35(37.3)	94 (44.8%)
Normal PSA	19 (16.3)	97 (83.7)	116 (55.2%)
Total	78	132	210 (100%)

The 210 men with different prostate diseases divided into six groups according to age , the patients with (30-39) years was $n=7$ (3.3%) , (40-49) years was $n=6$ (2.9%) , (50-59) years was $n=38$ (18.2%) , (60-69) years was $n= 88$ (41.9%) , (70-79) years was $n=58$ (27.6%) , (80-89) years was $n=13$ (6.1%) as shown in (Table 2) and (Figure 1).

**Table 2: Prostates diseases patients according to Age groups:**

Age groups	Number (n)	Percentage (%)
A- (30-39)	7	3.3%
B- (40-49)	6	2.9%
C- (50-59)	38	18.2%
D- (60-69)	88	41.9%
E- (70-79)	58	27.6%
F- (80-89)	13	6.1%
Total	210	100%

**Figure 1: Serum PSA according to Age groups**

(Table 3) shown the men patients with multiple prostate diseases which have different PSA value classified into various ages. 38(43.2%) of patients with 60-69 years old had PSA level higher than the (4.0 ng/ml) while 27 (46.6%) of patients with 70-79 years old had PSA level higher than the (4.0 ng/ml) and the patients who had ≥ 80 years appears 10 (76.9%) of them had PSA level higher than the (4.0 ng/ml). There were only small differences in other age group.

**Table 3: Proportion of men with various serum PSA levels according to age.**

Age (yr)	N	<u>Serum PSA level in ng/ml</u>		
		≤ 2.5	2.51-4.0	> 4.0
30-39	7	5 (71%)	1 (14.5%)	1 (14.5%)
40-49	6	4 (66.6)	2 (33.3%)	1 (16.7%)
50-59	38	17 (44.8%)	2 (5.2%)	19 (50%)
60-69	88	33 (37.5%)	17 (19.3%)	38 (43.2%)
70-79	58	26 (44.8%)	5 (8.6%)	27 (46.6%)
≥ 80	13	1 (7.7%)	2 (15.4%)	(76.9%)

Abbreviation : PSA : Prostate -specific antigen . value are No.(%)

Discussion:

PSA is a serine protease produce predominately by a protease, it regarded as a biochemical marker for early detection of prostate cancer and also used for observation of therapy response (Partin & Oesterling, 2004). In the present study we performed PSA in 210 patients found 59 case positive for prostate cancer and found 44.8% of men who had PSA level more than 4.0 ng/ml as illustrated in (Table 1). Other researchers have the same estimated of specificity and sensitivity to the level of PSA more than 4.0 ng/ml (Jacobsen *et al.*, 2006). The importance of PSA marker is decreased in older patients who had a larger prostate gland in some patients with benign prostatic hyperplasia than those without it. Thus, the PSA marker is not considered as reliable in identifying benign prostatic hyperplasia but it is more specific in prostate cancer patients (Meigs *et al.*, 2006).

PSA is a specific marker in tissue but generally, it's not very specific due to its present in the malignant, normal, and benign prostate. Many patients with prostatic cancer, but patients with Benign prostatic hyperplasia (BPH) are much more. Some patients with BPH don't have asymptomatic, other show prostatism. Discriminatory prostatic cancer from BPH is decisive and regarded as a challenge (Brewer, 2000). PSA level was present with in normal range $< (4.0$ ng/ml) in 55.2 % among other prostatic disease patients . Our results supported by the study of each (Ercole *et al.*, 2003; Armitage *et al.*, 2005 ; Bernstein *et al.*, 2007; Palken *et al.*, 2008).

In the current study, it was clear the correlation between age of patients with serum PSA level, the patients' age between (30-89) years and the median age was 56 years, (41.9%) of patients were (60-69) years while (18.2%) of patients were (50-59) years old as shown in table 2. This study was accordance to the study of Dijkman&Debruyne (2006) that concluded prostate cancer is a well age-dependent as half of prostate cancer patients had age ranged from (61-70) years (Dijkman&Debruyne.,2006). This result is variated in some countries because of the dietary and environmental effects (De Antoni *et al.*, 2006).

Same studies accomplished in American, Korea , Japans and Chines men. The patient under 50 years had PSA level more than 4.0 ng/ml as shown in table 3 (Oesterling *et al.*, 2005 ; Liu *et al.* , 2009). So, it is very important to measure the PSA level in young men to make sure they don't effect with prostate cancer. In Japan, it has been used a lower PSA cutoff value of 2



ng/ml to predict prostate cancer in younger men. Some hospital in Japan already uses in screening for prostate cancer in younger men (Kuriyama et al., 2000; Gohjii et al., 2007). So, this marker can be used for detection of this type of cancer in young men and decrease the negative biopsies in old men who had PSA level more than 4.0 ng/ml (Polascik et al., 2009).

Conclusion:

Serum PSA level can be used as predictive and diagnostic marker for prostate cancer.

References :

- Anderson, J.B., Roehrborn, C.G., & Schalken, J.A., et al. (2009). The progression of benign prostatic hyperplasia: Examining the evidence and determining the risk. *Eur Uro*; 39:390-399.
- Armitage, T.G., Cooper, E.H., Newling, D.W., Robinson, M.R. (2005). The value of the measurement of serum prostate-specific antigen in patients with benign prostatic hyperplasia and untreated prostate cancer, *Br J Urol*; 62:584-9.
- Balk, S.P., Ko, Y., & Bubley, G.J. (2003). Biology of prostate-specific Antigen. *J. Clin Oncol*; 21:383-391.
- Bernstein, L.H., Rudolph, R.A., Pinto, M.M., Viner, N., Zuckerman, H. (2007). Medically significant concentrations of prostate-specific antigen in blood assessed. *Clin Chem*; 36:515-528.
- Berry, S., Coffey, D.S., & Walsh, P.C., et al. (2004). The development of human benign prostatic hyperplasia with age. *J. Urol*, 132:474-479.
- Brawer, M.K., Cheli, C.L., Leinonen, J., Stenmon, U.H., & Diamandis, E.P. (2000). Complexed Prostate Specific Antigen provides significant enhancement of specificity compared with total prostate specific antigen of prostate cancer. *Journal urology*; 163(5): 1476-1480.
- Brewer, M.K. (2000). Laboratory studies for the detection of carcinoma of the prostate. *Urol Clin North Am*; 17: 759-68.
- Brower, M.K., Cheli, C.D., Neaman, J.E., Goldblatt, J., Smith, C., Schwartz, M.K., et al. (2000). Complexed prostate specific Antigen provides significant enhancement of specificity compared with total prostate specific antigen for detecting of prostate cancer. *Journal Urology*; 163(5):1476-1480.
- Bunting, P.S., DeBoer, G., Choo, R., Danjoux, C., Klotz, L., & Fleshner, N. (2002). Intraindividual variation of PSA, free PSA and complexed PSA in a cohort of patients with prostate cancer managed with watchful observation. *Clinical Biochemistry*; 35(6): 471-475.
- Clements, J., & Mukhtar, A. (2004). Glandular kallikrein and prostate-specific Antigen are expressed in the human endometrium. *J Clin Endocrinol Metab*; 78:1536-1539.
- Cohen, P., Graves, H.C., Pechl, D.M., Kamarei, M., Giudice, L.C., & Rosenfeld, R.G. (2000). Prostatic-specific antigen is an insulin-like growth factor binding protein-3 protease found in seminal plasma. *J Clin Endocrinol Metab*; 75:1046-1053.
- Gohji, K., Nomi, M., Kizaki, T., Okamoto, M., & Fujii, A. (2007). An assessment of the usefulness of serum prostate-specific antigen level cancer volume in biopsy specimens to predict the extent of prostate cancer. *Br J Urol*; 79:602-7.
- De Antonice, E.P., Carwford, E.D., Oesterling, J.E., Ross, C.A., & Staggers, F. (2006). Age- and race-specific reference ranges for prostate-specific antigen from a large community-based study. *J Urology*; 48:234-9.



- Dijkman,G.A.,& Debruyne,F.M. (2006). Epidemiology of prostate cancer . *Eur Urol*; 30:281-95 .
- Ercole,C.J., Lange.P.H., Mathisen,M., Chiou,R.K., Reddy,P.K., Vessella,R.L. (2003) . Prostatic specific antigen and prostatic acid phosphates and staging of patients with prostatic cancer . *J Urol* ; 138:1181-4 .
- Flocks,R., Urich,V., Patel,C.,& Opitz,J.(1960). Studies on the antigenic properties of prostatic tissue .*Journal Urol*;84:134-143.
- Hara,M., Koyaanagi,V.,& Inove,T.(1971). Some physic-chemical characteristics of γ -seminoprotein , an antigenic component specific for human seminal plasma. Forensic immunological study of body fluids and secretion . *japans journal of legal medicine* ;25:322-324
- Jacobsen,S.J., Bergstralh,E.J., Guess,H.A., Katusic,S.K., Klee,G.G., et al. (2006). Predictive properties of serum prostate-specific antigen testing in a community- based setting , *Arch Intern Med* ; 156:2462-8 .
- Killian,C.S., Corral.D.A., Kaminski,E.,& Constantine,R.I. (2003). Mitogenic response of osteoblast cell to prostate- specific antigen suggest an activation of latent TGF- beta and a proteolytic modulation of cell adhesion receptor . *Biochem Biophys Res Common*;192:940-947 .
- Koloayashi,T., Kamato,T., Isogawa,Y., Kinoshita,H.,Terai,A.,& Habushi,T., et al. (2003). Ratio of prostate specific Antigen minor molecular form:. To total prostate specific Antigen Is constant regardless of the pathological condition of the prostate . *journal Urology*;169(1):121-124 .
- Kuriyama,M., Uno,H., Watanbe,H., Yamanaka,H.,& Shida,K.(2000). Determination of references value for total PSA, F/T and PSAD according to prostatic volume in japans prostate cancer patients with slightly elevated serum PSA levels ,*J Clin Oncol*; 29:617-22
- Liu,Z.Y., Sun,Y.H.,& Ren,S.C.(2009). Age specific PSA reference ranges in Chinese men without prostate cancer. *Asian J Androl*;11:100-3 .
- Loeb,S.,& Catolona,W.J.(2007). Prostate-Specific antigen in clinical practice .*cancer letters*;249(1):30-39 .
- Lundwall,A., & Lilja,H.(2007). Molecular cloning of human prostate specific antigen cDNA . *FEBC Letters* ; 214(2):317-322 .
- Magklaria,A., Scorilas,A., Catolona,W.J., & Diamonds,E.P. (2000). The combination of human glandular kallikerin and free prostate- specific Antigen (PSA) enhances discrimination between prostate cancer and benign prostatic hyperplasia in patients with moderately increased total PSA .*Clinical Chemistry*; 45:1960-1966 .
- Meigs,J.B., Barry,M.J., Oesterrling,J.E., Jacobsen,S.J. (2006) . Interpreting results of prostate – specific antigen testing for early detection of prostate cancer ,*J Gen Intern Med* ; 11:505-12 .
- Meigs,J.B., and Barry,M.I. (2000) . Natural history of benign prostatic hyperplasia. Text book of Benign Prostatic hyperplasia .Oxford , UK: *Lsis Medical media ltd*;139-148
- Mikolajczyk,S.D., Millar,L.S., Wang,T.J., Rittenhouse,H.G., Wolfer,R.L., Mark,L.S., et al . (2000) . "BPSA", a specific molecular form of free prostate- specific antigen, is found



predominantly in the transition zone of patients with nodular benign prostatic hyperplasia. *Journal Urology*;55(1):41-45 .

- Oesterling, J.E., Jacobsen, S.J., & Conner, W.H. (2005). The use of age- specific references ranges for serum prostate specific antigen in men 60 years old or older . *J Urol*;153:1160-1163 .
- Oesterling, J.E., Kumamoto, Y., Tsukamoto, T., & Girman, C.J. (2005). Serum prostate-specific antigen in a community-based population of healthy Japanese men : lower values than for similarly aged white men, *Br J Urol*;75:347-53 .
- Palken, M., Cooper, D.E., Warren, B.H., Hock, D.C. (2008) . Prostate cancer correlation of digital rectal examination , tranrectal ultrasound and prostate specific antigen level with tumor volume in radical prostatectomy specific, *J Urol* ;143:1155-62 .
- Papsidero, L.D., Wang, M.C., Valenzuela, L.A., Murphy, G.P., & Chu, T.M. (1980). A prostate specific Antigen in sera of prostatic cancer patients. *Cancer research* ; 40:2428-2432.
- Partin, A.W., & Oesterling, J.E. (2004). The clinical usefulness of prostate specific antigen : update, *J Urology*;152:1358-68 .
- Peracual, R., Tabores, G., Royle, L., Harvey, D.J., Dwek, R.A., Rudd, P.M., et al . (2003). Altered glycosylation pattern allow the distinction between prostate- specific antigen (PSA) from normal and tumor origins . *Glycobiology*;13:457-470 .
- Polascik, T.J., Oesterling, J.E., & Partin, A.W. (2009) . Prostate specific antigen : a decade of discovery : what we have learned and where we are going . *J Urol*; 162:293-306 .
- Rehault, S., Monget, P., Mazerbourg, S., Tremblaz, R., Gutman, N., & Cauthir, F. (2001). Insulin-like growth factor protein (IGFBP) as potential physiological substrate for human kallikreins hK2 and hK3 . *Eur J Biochem*; 268:2960-2968 .
- Stamey, T., Yang, N., Hay, A., McNeal, J., Freiha, F., & Redwine, E. (1987). Prostatic-specific antigen as a serum marker for adenocarcinoma of the prostate. *N.Engl.J.Med*; 317:909-916 .
- Thompson, I.M., Paller, D.K., Goodman, P.J., Tangen, C.M., & Parnes, H.L. (2004). Prevalence of prostate cancer among men with a prostate- specific antigen level ≤ 4.0 ng per milliliter . *N.Engl.J.Med*;2239 .
- Wang, T., Rettenhouse, H., Wolfer, R., Lynne, G., & Brackett, N. (2008). PSA concentration in seminal plasma . *Clin Chem.* ; 44:895-896 .
- Webber, M.M., Waghray, A., & Bello, D. (2005). Prostate- Specific antigen , aserin protease , Facilitates human prostate cancer cell invasion . *Clin Cancer Res*; 1:1089-1094
- Yu, H., Diamandis, E. (2005). Prostate-specific in milk of lactating women . *Clin Chem*;41:54-58 .