## Prostate specific antigen reference ranges in Saudi men

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## **ABSTRACT**

**Objectives:** The aim of this study is to find out the age-specific and population-specific values of prostate specific antigen (PSA) among Saudi men. Normal values for different age groups between 40 and 89 years will be obtained.

**Methods:** The study was conducted in King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia. The total free and percent free PSA were measured for Saudi men who were free of prostate cancer by digital rectal examination (DRE) and with PSA value of <4ng/ml. Transrectal ultrasonography and needle biopsy were performed in those with suspicious DRE or PSA >4ng/ml. A total of 567 cancer free Saudi men were included in this study. All men were divided into 5 groups; each 10 years interval starting from the age of 40 years.

**Results:** The mean values of total PSA were 0.87 for men 40-49 years, 1.36 for men 50-59 years, 1.81 for men 60-69 years, 2.32 for men 70-79 years and 2.36 for men 80-89 years. The percent free PSA was >30% in all age groups. When those with PSA <4ng/ml were considered, the percent free PSA was the same and only 16.6% of them had a ratio of 18%. The upper limit of normal PSA was near to that of Chinese and Korean.

**Conclusion:** Normal mean PSA values for Saudi men are lower than the reported values. The percent free PSA for men having PSA <4ng/ml is applicable. Racial variations of PSA values were observed.

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S erum prostate specific antigen (PSA) has now become a valuable tool for detecting unsuspected cases of prostate cancer.¹ The cutoff value of 4ng/ml is used to differentiate benign from malignant prostatic disease.² However, this cutoff value is not practical to generalize for all ages, and age-specific values should be considered.³ It is generally accepted that PSA levels increase in correspondence with age increase.³-5 Furthermore, many investigators stated that racial variations should be considered, and studies have been started to find out population specific ranges of PSA.³.6-11 The present study was carried out to define age and population specific reference ranges of PSA among Saudi men. To our knowledge, this is the first study in the Kingdom of Saudi Arabia (KSA).

Methods. The study included Saudi males presenting to outpatient department or admitted to King Fahd Hospital of the University, Al-Khobar, KSA, for different reasons. Digital rectal examination (DRE), total PSA and free PSA were performed (using microparticle enzyme immunoassay method) to all patients. Percent free PSA was calculated. Transrectal ultrasonography and needle biopsy of the prostate were carried out if there was an abnormality by DRE or serum levels of PSA >4ng/ml. Patients with prostate cancer were excluded from the study. Prostate cancer free men were divided into 5 age groups, each of 10 years interval starting from the age of 40 years. The means of PSA values for all groups were compared using the analysis

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of variance test. Correlation coefficient test was used to test the correlation between the age and PSA levels. The 95th percentile was used to define the upper limit of normal values of PSA. The derived values of PSA were compared with those reported in previous studies.

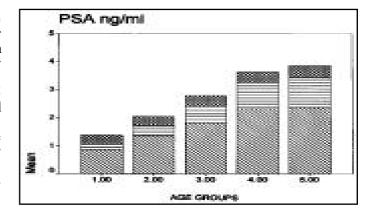
**Results.** Five hundred and sixty-seven Saudi males were studied and divided into 5 age groups, each of them has a 10 years interval starting from the age of 40 years and ending by the age of 89 years (Table 1). The mean values of total, free and percent free PSA were measured for all age groups (Figure 1). There was a positive correlation between age increase and increase in total PSA (r=0.263, P<0.01), free PSA (r= 0.351, P<0.01) and percent free PSA (r=0.236, P<0.01) (Figures 2, 3 & 4). The mean value of total PSA was 0.87 for the age 40-49 years, 1.36 for the age 50-59 years, 1.81 for the age 60-69 years, 2.32 for the age 70-79 years, and 2.36 for the age 80-89 years (Table 1). The mean value of free PSA was 0.22 for the age 40-49 years, 0.37 for the age 50-59 years, 0.61 for the age 60-69 years, 0.92 for the age 70-79 years, and 1.05 for the age 80-89 years (Table 2). The percent free PSA was between 30% and 45% for all groups (Table 2). The difference between the mean values of total PSA, free PSA and percent free PSA for all age groups was statistically significant (F=10.662, P<0.05, F=16.422, P<0.05, and F=7.142, P<0.05 respectively) (**Tables 1 & 2**). The mean values of total PSA were compared with those of published studies and they were lower than reported values except for one study<sup>12</sup> (**Table 3**). The 95th percentile was obtained for all men to define the upper limit of normal of total PSA. Comparison between our results and that in previous studies revealed levels almost near to that of the Chinese and Korean studies (Table 4).

**Discussion.** In the present study, normal PSA values for 567 Saudi men between the age of 40 years and 89 years have been established. Many studies found correlation between age increase and increase. 5,7-10,12-20 Some authors found only correlation between age increase and total PSA increase with no correlation regarding free PSA and percent free PSA.<sup>13</sup> In the present study, there was a significant correlation between age increase and the increase in total PSA, free PSA and percent free PSA. When the mean values of total PSA in the present study were compared with those in previous studies, they were lower than the suggested values, 18-20 except for one study, which recorded similar values.12 In the present study, the mean of percent free PSA was >30% in all age groups. Some authors proposed that the percent free PSA is valid only at a total PSA range from 4-10ng/ml.<sup>4,21</sup> The value of percent free PSA for screening for prostate cancer has not yet been assessed optimally especially in the PSA range <4ng/ml and a threshold should be established.<sup>22</sup> Reviewing the literature of published data for the upper limit of normal PSA values showed obvious variations among the

**Table 1** - The means of total PSA values for different age groups (N=567).

| Group | Age<br>intervals | n<br>of men | Mean (SD)    | 95% CI    |
|-------|------------------|-------------|--------------|-----------|
| 1     | 40-49            | 93          | 0.87 (0.735) | 0.71-1.03 |
| 2     | 50-59            | 157         | 1.36 (1.502) | 1.11-1.62 |
| 3     | 60-69            | 200         | 1.81 (1.783) | 1.53-2.09 |
| 4     | 70-79            | 86          | 2.32 (2.139) | 1.78-2.86 |
| 5     | 80-89            | 31          | 2.36 (1.924) | 1.55-3.17 |

F = 10.662, p <0.05, CI - confidence intervals, PSA - prostate specific analysis



**Figure 1 -** The means of total PSA, free PSA and percent free PSA. PSA - prostate specific analysis.

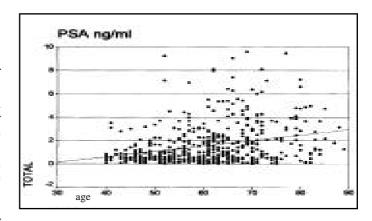


Figure 2 - Scatter gram for the total PSA values for all men. PSA -prostate specific analysis.

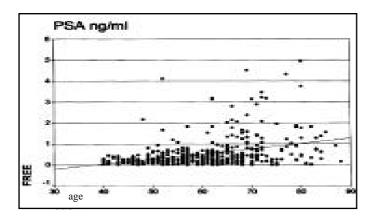
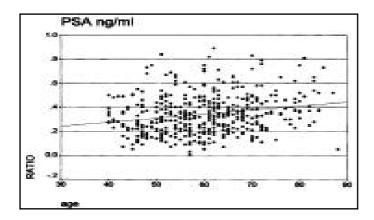


Figure 3 - Scatter gram for the free PSA values for all men. PSA -prostate specific analysis.



 $\begin{tabular}{ll} \textbf{Figure 4--} Scatter gram for the percent free PSA for all men. PSA-prostate specific analysis. \\ \end{tabular}$ 

**Table 2** - The means of free and percent free PSA of different age groups.

| Group | n<br>of men | Mean<br>free PSA (SD) | 95% CI    | Mean %<br>Free PSA (SD) | 95% CI    |
|-------|-------------|-----------------------|-----------|-------------------------|-----------|
| 1     | 81          | 0.22 (0.258)          | 0.17-0.28 | 0.30 (0.145)            | 0.26-0.33 |
| 2     | 136         | 0.37 (0.453)          | 0.29-0.44 | 0.31 (0.153)            | 0.29-0.34 |
| 3     | 156         | 0.61 (0.679)          | 0.50-0.72 | 0.36 (0.154)            | 0.34-0.39 |
| 4     | 63          | 0.92 (1.008)          | 0.67-1.18 | 0.38 (0.169)            | 0.34-0.42 |
| 5     | 24          | 1.05 (1.156)          | 0.57-1.54 | 0.45 (0.179)            | 0.37-0.52 |

 $F=16,422,\,p{<}0.05\ (for\ men\ free\ PSA),\,F=7.142,\,p{<}0.05\ (for\ men\ percent-free\ PSA)\, only\,\,460\, patients\, had\, free\ PSA\, value.\\ CI-confidence\ intervals,\,PSA-prostate\ specific\ analysis$ 

**Table 3** - Comparison of mean total PSA with previous studies.

| Studies                          |       | A     | age groups |       |       |
|----------------------------------|-------|-------|------------|-------|-------|
| Studies                          | 40-49 | 50-59 | 60-69      | 70-79 | 80-89 |
| Atalay et al <sup>18</sup>       | 1.7   | 2     | 2.9        | 3.5   |       |
| Lankford et al <sup>19</sup>     | 2.5   | 3.5   | 4.5        | 6.5   |       |
| Dalkin et al <sup>12</sup>       | -     | 1.32  | 1.91       | 2.36  |       |
| Oesterling et al <sup>20</sup>   | -     | -     | 4.5        | 6.5   |       |
| Present study                    | 0.87  | 1.36  | 1.81       | 2.32  | 2.36  |
| PSA - prostate specific analysis |       |       |            |       |       |

Table 4 - The upper limit of normal PSA in different population-based

| Studies                          |       |       | Age groups | 3     |       |  |
|----------------------------------|-------|-------|------------|-------|-------|--|
|                                  | 40-49 | 50-59 | 60-69      | 70-79 | 80-89 |  |
|                                  |       |       |            |       |       |  |
| American 12                      |       | 1.3   | 1.91       | 2.36  |       |  |
| American-Black11                 | 2.8   | 5.4   | 9.59       | 15.45 | 21.05 |  |
| American-White11                 | 2.01  | 4.19  | 7          | 9.4   | 18.25 |  |
| American <sup>13</sup>           | 2     | 3     | 4          | 5.5   |       |  |
| American <sup>14</sup>           | 2.5   | 3.5   | 4.5        | 6.5   |       |  |
| American 15                      | 1.5   | 2.6   | 4.4        | 7.5   |       |  |
| African-American <sup>7</sup>    |       | 2.36  |            |       | 5.59  |  |
| Japanese <sup>10</sup>           |       | 2.1   | 3.2        | 4.4   | 6.5   |  |
| Japanese <sup>16</sup>           | 2.6   | 5     | 7.5        | 10.1  | 12.4  |  |
| Chinese <sup>17</sup>            | 2.71  | 5.01  | 6.05       | 7.92  |       |  |
| Chinese8                         | 1.88  | 2.37  | 4.82       | 5.86  |       |  |
| Chinese9                         | 2.59  | 3.31  | 5.03       | 5.73  |       |  |
| Korean <sup>3</sup>              | 2.4   | 3.9   | 6.3        |       |       |  |
| Present study                    | 2.85  | 3.99  | 5.41       | 6.29  | 6.84  |  |
| PSA - prostate specific analysis |       |       |            |       |       |  |

American population.<sup>7,11-15</sup> This can be explained by the fact that the American population is a multiracial community. The same observation was noted on reviewing the Japanese and Chinese figures.<sup>8-10,16,17</sup> As a population based study, our upper limit of normal PSA (95th percentile) was near to those of Chinese and Korean studies.<sup>3,8,9,17</sup> Our study is in accordance with other studies proposing racial variations of PSA values.<sup>3,6-11</sup>

In conclusion, age-specific PSA values in Saudi men were lower than reported values. Percent free PSA can be applied in patients with PSA <4ng/ml. Racial variations for PSA values are suggested.

## References

- Miller JI, Ahmann FR, Drach GW, Emerson SS, Bottaccini MR. The clinical usefulness of serum prostate specific antigen after hormonal therapy of metastatic prostate cancer. *J Urol* 1992; 147: 956-960.
- Catalona WJ, Richie JP, Ahmann FK, Hudson MA, Scardino PT, Flanigan RC et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. *J Urol* 1994; 151: 1283-1286.
- 3. Lee SE, Kwak C, Park MS, Lee CH, Kang W, Oh SJ. Ethnic differences in the age-related distribution of serum prostate-specific antigen values: a study in a healthy Korean male population. *Urology* 2000; 56: 1007-1010.
- Luderer AA, Chen YT, Soriano TF, Kramp WJ, Cuny C, Sharp T et al. Measurement of the proportion of free to total prostate specific antigen improves diagnostic performance of prostate specific antigen in the diagnostic gray zone of total prostate specific antigen. *Urology* 1995; 46: 187-190.
  Partin AW, Catalona WJ, Southwick PC, Subong EN, Gasior
- Partin AW, Catalona WJ, Southwick PC, Subong EN, Gasior GH, Chan DW. Analysis of percent free prostate specific antigen PSA for prostate cancer detection: influence of total PSA, prostate volume, and age. *Urology* 1996; 48: 55-58.
- Jackson E, Fowler JR, Steven A, Paul BF, Shandra SW. Prostate cancer detection in black and white men with abnormal digital rectal examination and prostate specific antigen less than 4ng/ml. *J Urol* 2000; 164: 1961-1963.
- Cooney KA, Strawderman MS, Wojno KJ, Doerr KM, Taylor A Alcser KH et al. Age-specific distribution of serum prostate specific antigen in a community based study of African-American men. *Urology* 2001; 57: 91-96.
- 8. Kao CH. Age-related free PSA, total PSA and free PSA/total PSA ratios: establishment of reference ranges in Chinese males. *Anticancer Res* 1997; 17: 1361-1365.

- Lin WY, Gu CJ, Kao CH, Changlai SP, Wang SJ. Serum prostate specific antigen in healthy Chinese men: establishment of age-specific reference ranges. *Neoplasma* 1996; 43: 103-105.
- Nakanishi H, Nakao M, Nomoto T, Miki T, Nakagawa S, Kitmura K et al. The investigation of age specific PSA reference range as the cut-off values in the mass screening for prostatic cancer. *Nippon Hinyokika Gakkai Zasshi* 1999; 90: 853-858.
- Sawyer R, Berman JJ, Borkow A, Moore GW. Elevated prostate specific antigen levels in black men and white men. *Mod Pathol* 1996; 9: 1029-1032.
- 12. Dalkin BI, Ahmann FR, Kopp JB. Prostate specific antigen levels in men older than 50 years without clinical evidence of prostatic carcinoma. *J Urol* 1993; 150: 1837-1839.
- Oesterling JE, Jacobsen SJ, Klee GG, Petterson K, Piironen T, Abrahamsson PA, et al. Free, complexed and total serum prostate specific antigen: the establishment of appropriate reference ranges for their concentrations and ratios. *J Urol* 1995; 154: 1090-1095.
- 14. Oesterling JE, Jacobsen SJ, Chute CG, Girman CJ, Panser LA, Lieber MM. Serum prostate specific antigen in a community-based population of healthy men. Establishment of age-specific reference ranges. *JAMA* 1993; 270: 860-864.
- Anderson JR, Strickland D, Corbin D, Byrnes JA, Zweiback E. Age-specific reference ranges for serum prostate-specific antigen. *Urology* 1995; 46: 54-57.
- 16. Yamazaki H, Suzuki Y, Madarame A, Katoh N, Massuda F, Ohishi Y et al. Detection of prostate cancer in urological practice: clinical establishment of serum PSA reference values by age. Nippon Hinyokika Gakkai Zasshi 1996; 87: 702-709.
- Wang Z, Liu D, Zhau I. Influence of age on serum prostate specific antigen concentration. *Zhonghua Wai Ke Za Zhi* 1996; 34: 368-369.
- 18. Atalay AC, Karaman MI, Guney S, Dalkilic A, Muslumanoglu AY, Ergenekon E. Age-specific PSA reference ranges in a group of non-urologic patients. *Int Urol Nephrol* 1998; 30: 587-591.
- Lankford SP, Peters KI, Elser RC. Potential effects of age-specific ranges for serum prostate-specific antigen. *Eur Urol* 1995; 27: 182-186.
- Oesterling JE, Jacobsen SJ, Cooner WH. The use of age-specific reference ranges for serum prostate specific antigen in men 60 years old or older. *J Urol* 1995; 153: 1160-1163.
- Peter HG, Jing MA, William J, Meir JS. Strategies combining total and percent free prostate specific antigen for detecting prostate cancer: A prospective study. *J Urol* 2002; 167: 2427-2434.
- 22. Chris HB, Ries K, Bert G, Schroder FH. The value of screening tests in the detection of prostate cancer. Part II: retrospective analysis of free/total prostate specific analysis ratio, age-specific reference ranges, and PSA density. *Urology* 1995; 46: 779-784.