

# Age-specific reference range for serum prostate-specific antigen in Sudanese men

Abdelkarim A. Abd rabo, MSc, PhD, Adil I. Fadlalla, MD, MCS, Imad M. Fadl-Elmula, MD, PhD.

## ABSTRACT

**الأهداف:** تحديد القيم المرجعية العمرية للمستضد الكلي الخاص بالبروستاتا في عينة مجتمعية من الرجال السودانيين الأصحاء والذين تتراوح أعمارهم ما بين 40-90 عاماً.

**الطريقة:** أُجريت هذه الدراسة الحالية خلال الفترة من يناير 2008م إلى مايو 2010م بقسم جراحة المسالك البولية، مستشفى سوبا الجامعي، الخرطوم، السودان. لقد تم قياس المستضد الكلي الخاص بالبروستاتا باستخدام تقنية القياس المناعي الإنزيمي، فيما فُحص البول العام باستخدام أشرطة الاختبار. شملت الدراسة 3475 رجل ممن لم تظهر عليهم أية أعراض من أمراض المسالك البولية، واختير منهم بعد ذلك 1051 فقط لأن المستضد الكلي الخاص بالبروستاتا كان لديهم أقل من 10 نانوغرام/مل، ولم تظهر عليهم أيضاً أي أمراض المسالك البولية. تم تحليل البيانات باستخدام برنامج التحليل الإحصائي (SPSS) لنظام ويندوز وذلك من أجل تحديد القيم المرجعية للمستضد الكلي الخاص بالبروستاتا.

**النتائج:** أظهرت النتائج أن المتوسط الهندسي للمستضد الكلي الخاص بالبروستاتا في مجموعة الدراسة التي شملت 1051 من الرجال السودانيين قد بلغ 1.48 نانوغرام/مل. كما بينت النتائج كذلك أن المستويات في الفئة العمرية 40-49 عاماً كانت 0-3 نانوغرام/مل، وفي الفئة 50-59 عاماً كانت 0-3.02 نانوغرام/مل، وفي الفئة 60-69 عاماً كانت 0-3.8 نانوغرام/مل، وفي الفئة 70-90 عاماً 0-8.7 نانوغرام/مل.

**خاتمة:** تشير نتائج الدراسة الحالية إلى أن القيم المرجعية المعتمدة حالياً للمستضد الكلي الخاص بالبروستاتا ليست مناسبة للسودانيين. كما تشير الدراسة إلى أن النطاقات المرجعية لهذه الدراسة قد تكون أكثر ملائمة للسودانيين.

**Objectives:** To determine age-specific prostate-specific antigen (PSA) reference values in a community-based sample of Sudanese men, aged 40-90 years.

**Methods:** This study was conducted in the Central Laboratory Services, Soba University Hospital, Khartoum, Sudan from January 2008 to May 2010. Total serum PSA in 3475 Sudanese men with no clinical

evidence of lower urinary tract symptoms were measured using immunoenzymetric assay. Out of the 3475, only 1051 men met the inclusion criteria. Those with total PSA <10 ng/ml and no recent urinary tract infection were included in this study. The data were analyzed using SPSS for Windows to define age-specific reference ranges of PSA.

**Results:** The geometric mean of total serum PSA in the study group of Sudanese men was 1.48 ng/ml. The 95th percentile total serum PSA ranges in the age groups was 0-3 ng/ml for 40-49 years, 0-3.02 ng/ml for 50-59 years, 0-3.8 ng/ml for 60-69 years and 0-8.7 ng/ml for 70-90 years.

**Conclusion:** The currently adopted age-specific total PSA reference ranges are not appropriate for Sudanese men. Accordingly, our study indicates that the reference ranges of this study may be more suitable.

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*From the Department of Clinical Chemistry, Faculty of Medical, Laboratory Sciences, Al-Neelain University, Khartoum, Sudan.*

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*Address correspondence and reprint request to: Dr. Abdelkarim A. Abd rabo, Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, Al-Neelain University, PO Box 12702, Postal Code 11121, Khartoum, Sudan. Tel. +249 912905847. Fax +249 183796532. E-mail: Abd rabokarim@hotmail.com*

Prostate cancer (PC) is now recognized as one of the principal medical problems faced by the male population all over the world and has already gained increased attention from Sudanese urologists owing to its rapidly increasing incidence as recent reports have indicated.<sup>1</sup> However, the incidence rates of PC are generally higher in Western countries compared with African countries, perhaps due to the extensive use of prostate-specific antigen (PSA) as screening tool.<sup>2</sup> In addition to the post-mortem studies, PC is underdiagnosed since many men die with it rather

than die from it and most of elderly men have been observed to have histological evidence of the disease, a much smaller proportion develop clinical evidence of the disease. Although the natural history of PC is poorly understood, prognosis is clearly related to the stage and grade of tumor.<sup>3</sup> Despite the growing awareness of the importance of PSA test for early PC screening, optimal reference values of serum PSA for PC screening in Sudanese men have still not been determined. The age-specific reference ranges for any population is one such approach suggested to increase PSA specificity.<sup>4</sup> Some investigators have suggested that there are differences between African and Caucasian men in age-specific serum PSA concentrations; and that the cut-off points required for ensuring optimal sensitivity and specificity should be adjusted for race.<sup>5</sup> The aim of this study is to identify the reference ranges of each age group in Sudanese men, which may increase the diagnostic accuracy of PSA in the target population.

**Methods.** Between January 2008 and May 2010, 1051 men (age range between 40 and 90 years) had a total PSA tests at the Central Laboratory Services, Soba University Hospital, Khartoum, Sudan as part of their general health examinations. Each individual have signed a written informed consent following the approval of ethical clearance from Al-Neelain-University Ethical Committee (Based on Helsinki Declaration). Data on men's PSA values, ages, and race or ethnic group were kept in the computer form predesigned questionnaire. Individuals were clinically and laboratory checked to exclude persons with recent urinary tract infection, prostate symptoms, and urine retention.

**Specimen processing and sample collection.** Serum sample were used for the assay of total PSA using an automated immunoenzymometric system. Blood specimens collected was stored at 18-25°C until a clot had formed (usually 15-45 minutes) then centrifuged to obtain the serum sample for assay. Samples were stored at 2-8°C for up to 24 hours prior to analysis. If the analysis could not be carried out within 24 hours, the samples were stored at -20°C or below for up to the suitable day (not more than 60 days). Repeated freeze-thaw cycles were avoided. Turbid serum samples or samples containing particulate matter were centrifuged prior to testing.<sup>5</sup> Mid-stream urine samples were collected to perform urine analysis using dipsticks test.

The data was analyzed using SPSS for Windows® and express in mean and standard deviation. Descriptive statistical analysis was carried out and the quartile of 95th percentile were identified for each age group. Normal distribution and descriptive statistics for numerical variables of age, total PSA had being carried out using Kolmogorov-Smirnov. According

to the recommendations of Oesterling et al<sup>6</sup> the data were analyzed by age groups (40-49, 50-59, 60-69, and 70-90).<sup>6,7</sup> The quartiles and 95th percentiles were calculated for each age group.

**Results.** The upper and lower level of total PSA in any of the age groups was considered the 95th percentile, and 0 ng/ml, respectively. The analysis of the 4 age groups showed that the number of individual in each group ranged between 189 and 360 individual and the total PSA mean was 0.96±0.63. The highest total-PSA-range (8.70 ng/ml) seen in older age group was 70-90 years (Table 1).

Table 2 compares the upper values of age groups with the study of Oesterling et al,<sup>6</sup> the annual increase of total PSA levels in this study was 14.8%.

Table 3 compares the upper value of each age group in this study with data from Korean, Japanese, Asian-Americans and Chinese population.<sup>8</sup> It is found that age-specific PSA reference ranges for 40-49-year-old Asian Americans were similar to those of other groups except Sudanese, but generally it appears that Asian-Americans have higher values than other populations.

**Table 1 -** Age-specific 95<sup>th</sup> percentile ranges for prostate-specific antigen (PSA).

Age (years)	N	Total PSA Mean ± SD	PSA range (ng/ml)
40-49	189	0.76 ± 0.54	0.00 - 3.00
50-59	311	0.88 ± 0.51	0.00 - 3.02
60-69	361	1.00 ± 0.54	0.00 - 3.80
70-90	190	1.20 ± 0.9	0.00 - 8.70
Total	1051	0.96 ± 0.63	

**Table 2 -** Comparison between age-specific reference ranges of Sudanese men (present study) and the age-specific reference ranges reported by Oesterling et al.<sup>6</sup>

Age (years)	Prostate-specific antigen range (ng/ml)	
	Present study	Oesterling's study
40-49	0.00 - 3.00	0.00-2.50
50-59	0.00 - 3.02	0.00-3.50
60-69	0.00 - 3.80	0.00-4.60
70-90	0.00 - 8.70	0.00-6.50

**Table 3 -** Comparison between age-specific reference range of Sudanese men (present study) and other studies carried out in Asian populations.<sup>8</sup>

Age (years)	Recent study	Korean	Japanese	Asian American	Chinese
40-49	3.0	2.00	2.00	2.00	2.15
50-59	3.02	2.40	3.00	4.50	3.20
60-69	3.8	3.90	4.00	5.50	4.10
70-90	8.7	6.30	5.00	6.80	5.37

**Table 4** - Comparison between age-specific reference range of Sudanese (Black races) and white races.<sup>6</sup>

Age (years)	Prostate-specific antigen range (ng/ml)	
	Sudanese (Black race)	White race
40-49	0.00 - 3.00	0.00 - 2.50
50-59	0.00 - 3.02	0.00 - 3.50
60-69	0.00 - 3.80	0.00 - 3.50
70-90	0.00 - 8.70	0.00 - 3.50

Table 4 shows comparison between Sudanese men (black race) with American and Europeans (White race),<sup>9</sup> it appears clearly that black races have higher PSA values than white.

**Discussion.** Despite the growing awareness of the importance of PSA for early PC diagnosis, optimal reference values of serum PSA for PC screening in Sudanese men have not been determined. Studies from Asian countries such as Korea and China suggested that serum PSA levels in Asian people are lower than in other ethnic groups.<sup>8,10</sup> Therefore, the known age-specific PSA reference ranges may not be applicable for Sudanese males.<sup>7</sup> The current study sought to determine optimal age-specific PSA reference ranges for Sudanese men. We observed that the 95th percentiles of serum PSA levels in Sudanese men increased with age. The average annual increase was 14.8%, which was higher than the average annual increase of 3.2% observed by Oesterling et al.<sup>6</sup> The age-specific PSA reference range for each age group in this study was also lower than those observed in previous study<sup>6</sup> (Table 1). This difference was relatively higher in 40-49 years age group (3.0 versus 2.0), but gradually increased with age and was the highest in 70-90 years age group (8.7 versus 6.5). It is therefore likely that the use of age-specific reference ranges reported by Oesterling et al<sup>6</sup> to screen for PC in Sudanese men may increase specificity and decrease sensitivity. This was observed in the 70-79 years age group when serum PSA >8.7 ng/ml was used as a cut-off for prostate biopsy. Previous studies have observed higher age-specific serum PSA values in African men without PC compared with Caucasian.<sup>11</sup> This finding is in agreement with our results where we demonstrate a marked high level of total PSA in Sudanese men at age groups 40-49 years and 70-90 years without PC. The reason for the higher PSA values in black men is unknown. In previous investigations of men with newly diagnosed PC, black patients had higher PSA values compared to white men even when adjusted for age, tumor grade, and the clinical stage of disease. Tumor volume, which was greater in black men, accounted for some, but not all, of the racial difference in PSA levels.<sup>12</sup>

The study was limited by the fact that reference range studies require a larger sample size to ensure a representative distribution of the population and to be considered representative of groups of people to whom results will be generalized or transferred. Thus, other studies with larger sample size should be conducted to include all people in large country such as Sudan.

In conclusion, the results of this study may help clinician to increase the sensitivity and specificity in detection of PC using total PSA levels in different age groups.

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