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Commentary

Reference range of serum prostate-specific antigen levels in Indian men

The subject of this study by Gupta and colleagues[1] is fundamentally interesting, important and of high relevance to public health. It provides an opportunity to know the age specific serum PSA (prostate specific antigen) distribution in healthy men and its comparison with worldwide studies. This study is important to establish reference range of PSA in north Indian men since PSA is one of the valuable tools for the diagnosis of the most common non-dermatological malignancy known as prostate cancer (PC) in men[2,3]. The results suggested that the PSA levels were associated with increasing age groups. Literature review reports serum PSA as 4ng/ml that has been accepted as the reference range of serum PSA for all age groups[4]. However, the incidence rate of prostate cancer is low among Indians in comparison to other populations of the world. There is a need to set a reference range for PSA in healthy individuals in India.

With the increase in age the susceptibility towards the disease (PC) also increases[3,4]. In the present study[1], the subjects were divided into six age groups: <40, 40-49, 50-59, 60-69, 70-79 and above 80 yr. There are two important findings of this study: *(i)* the 95th percentile of serum PSA level in healthy men was 1.17ng/ml, that was lower than those reported by others and *(ii)* there was a progressive increase in mean value and 95% CI with advancing age group from below 40 to above 80 yr. The reference range of serum PSA level increased from 0.71 to 2.35 ng/ml with advancing age group.

The authors suggested that the variations of serum PSA level could be either due to inherited susceptibility associated with genetic factors or other factors that influence serum PSA level. The increase in serum PSA level with advancing age group is well established. Age is a major risk factor for prostate cancer. Age specific reference ranges have the possibility to make serum PSA as a good serum tumour biomarker for prostate cancer in older men and early detection of cancer in younger men.

The authors have indicated that the PSA value varies in different geographical areas and have a discrepancy with age and ethnicity. Black & White men have the highest PSA values in the world, while the PSA values are lower in Asian and Arabian men and higher in European men[5]. In India, it is the third commonest male cancer in Delhi, fourth in Mumbai, fifth in Bangalore and ninth in Chennai[6].

The authors have rightly mentioned about the discrepancy of standard reference intervals of serum PSA level in Indian men without prostate disease and the values in use are the reference range reported in world literature. Thus, the standard reference range (4ng/ml) for serum PSA may not be applicable for Indian men. It has also been established by several studies that the effect of race and ethnicity, environmental factors, lifestyles, metabolic and physiological changes with advancing age can lead to changes in serum PSA levels[7]. However, there is no specific normal or abnormal levels of PSA in the blood. In the past, most urologists considered PSA levels of 4.0 ng/ml and lower as normal. Therefore, if a man had a PSA level above 4.0 ng/ml doctors would often recommend a prostate biopsy to determine whether prostate cancer was present.

It has been shown that some men with PSA levels below 4.0 ng/ml have prostate cancer and that many men with higher levels do not have prostate cancer[7]. For example, a man's PSA level often rises if he has prostatitis or a urinary tract infection. Prostate biopsies and prostate surgery may also change the PSA level. Conversely, some drugs including finasteride and dutasteride, which are used to treat benign prostate hyperplasia (BPH) lowers the PSA level. PSA level may also vary somewhat across testing laboratories[7,8].

Another factor is that studies to establish the normal range of PSA levels have been conducted primarily in populations of white men. Although experts' opinions vary, there is no clear consensus regarding the optimal PSA threshold for recommending a prostate biopsy for men of any racial or ethnic group. However, a continuous rise in the PSA level over time may be a sign of prostate cancer. There are hardly any reports providing reference interval of serum PSA for healthy men. Therefore, it is commendable that the authors have generated PSA reference values in healthy adult men categorized on the basis of age.

It is true that India being a socio-culturally and ethnically diverse country, there is a need to have separate reference range of serum PSA. Additionally, age specific reference ranges have the possibility to make serum PSA a more specific tumour marker for detecting clinically significant cancer in older men and to find more potentially curable cancer in younger men. The age specific PSA range for healthy Indian men in their study was on lower side and the serum PSA was associated with advancing ages. However, the stratifications done for different age groups lowered the power of the study and increased numbers in each group could have reflected more convincing results especially for the age group >80 yr.

Regarding limitations of the study, there is no information of TRUS (transrectal/ultrasound) findings about prostate size or abnormality and no prostate biopsy done to prove that the participants were cancer free. The authors should have discussed the PSA dynamics, namely PSA velocity (PSAV), doubling time (PSADT) and free to total PSA ratio (F/T ratio), that have more prognostic value than PSA itself[9]. PSAV is defined as the change in PSA concentration per year and PSADT is defined as the time necessary for the serum PSA level to double. Information on factors like lifestyle such as smoking and tobacco, alcohol consumption, dietary habit and BMI is missing which could have potentially confounded their conclusions.

Nevertheless, the study by Gupta and colleagues[1] provides the reference range for PSA level in context with Indian men and direct relationship between serum PSA level and age. With the incorporation of data for confounding factors and with larger sample size, multi-centric study is warranted for more convincing conclusions.

Rama Devi Mittal
Department of Urology, Sanjay Gandhi Postgraduate Institute of Medical Sciences
Raebareli Road, Lucknow 226 014, India
ramamittal@gmail.com

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