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Effect of ageing and body mass index on prostate-specific antigen levels among Chinese men in Singapore from a community-based study

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OBJECTIVE

To assess the effect of ageing and body mass index (BMI) on prostate-specific antigen (PSA) among Chinese men from the results of the 2005 Prostate Awareness Week in Singapore.

SUBJECTS AND METHODS

In all, 2714 men participated in the programme, consisting of 2431 Chinese, 114 Malays, 117 Indians and 52 'others'. Of these, 2410 Chinese men who had a PSA level of <20 ng/mL and were aged >50 years but <80 years were included in the analysis. Height and weight were used to calculate the BMI. The relationship between age and PSA levels was analysed using linear regression and bivariate correlation, and the associations among different groups of BMI and PSA levels were analysed using analysis of variance and covariance.

RESULTS

PSA levels were significantly correlated with age (correlation coefficient, $r = 0.27$, $P < 0.001$). Analyses showed a significant inverse association between PSA level and BMI; mean PSA levels decreased with increasing BMI for both standards (standard classification; geometric mean, GM, PSA of 1.08, 1.06, 0.96, 0.83 ng/mL for a BMI of <18.5, 18.5–24.9, 25–29.9 and ≥30 kg/m^2, respectively, P trend <0.01; and for Asian classification, GM PSA 1.08, 1.09, 0.96, 0.91 ng/mL for a BMI of <18.5, 18.5–22.9, 23–27.5 and ≥27.5, respectively, P trend <0.001). There were significant differences ($P < 0.05$) in the age-adjusted GM PSA levels for the groups with BMI <25 (1.05 ng/mL) and BMI ≥25 kg/m^2 (0.97 ng/mL). Similarly, there were significant differences ($P < 0.05$) in the age-adjusted GM PSA levels in those with a BMI of <30 (1.03 ng/mL) and ≥30 kg/m^2 (0.85 ng/mL).

CONCLUSION

These data suggest that the BMI in Chinese men in Singapore is significantly associated with PSA levels, especially among the obese men aged 70–79 years.

KEYWORDS

body mass index, prostate-specific antigen, Chinese, obesity

INTRODUCTION

PSA was first identified by researchers attempting to find a substance in seminal fluid that would aid in the investigation of rape cases [1]. It was subsequently found to be able to identify prostate cancer in men not known to have the cancer [2]. Men with prostate cancer generally have elevated PSA levels in their serum; this tumour marker is now frequently used for prostate cancer screening, diagnosis and monitoring of response to therapy [3]. Since then, PSA screening was been widely adopted in many countries even before there was any evidence of its effectiveness in reducing prostate cancer mortality. Controversies still surround PSA screening. There is limited specificity of the test, as most men referred for biopsy for elevated PSA levels are not diagnosed with prostate cancer [4]. Although the widespread use of PSA testing in North America has led to increased detection of cancer and a migration to lower stage and lower-volume tumours, it is still unknown whether PSA screening significantly reduces mortality from prostate cancer [5]. PSA levels can be affected by many factors that might be unrelated to prostate disease, e.g. age and race [6]. Recent studies also reported that healthy but obese men have lower PSA levels, among North Americans, even after adjusting for age and race/ethnicity (i.e. non-Hispanic White, Hispanic White, African-American, White, Mexican American) [7,8]. There have been reported concerns that if the body mass index (BMI) is not factored into determining the threshold PSA levels for biopsy, obese men 'undergo biopsy later in the course of the disease (prostate cancer), because it takes longer for their PSA levels to rise above a given threshold' [9]. However, one recent report found no association between BMI and PSA level among 616 men with no known prostate cancer who participated in an annual

prostate cancer-screening event in Montreal, Canada [10].

Although the incidence of prostate cancer in Singapore is not as high as that of the USA or the Nordic countries, it is increasing. Prostate cancer is now the fifth most common cancer among Singaporean men, and the incidence has been increasing steadily over the last 35 years. The mean annual rate of increase between 1968 and 2002 was 5.6%, with the last 10 years having seen a relatively steeper increase [6]. Like in developed countries, the prevalence of obesity (BMI ≥30 kg/m^2) among Singaporean men has also increased, from 4.0% in 1992 to 6.4% in 2004 [11]. In 2004, the WHO revised its recommendation for BMI thresholds for Asians [12] based on evidence that compared with Caucasians, the risks of type 2 diabetes and cardiovascular diseases among Asians is already substantial even at a BMI lower than the existing WHO threshold for 'overweight' (≥25 kg/m^2). WHO has recommended an Asian BMI classification as follows; <18.5, underweight; 18.5–22.9, normal, 23–<27.5, pre-obese; ≥27.5 kg/m^2, obese [12]. What is the relationship between BMI and PSA levels among Chinese men? Although there are a few reports of BMI and Asian men, these studies either involved Japanese subjects with diabetes [13], Japanese men with elevated PSA levels [14], or young Korean men (<50 years old) [15,16]. All these reported studies do not reflect the general population. To our knowledge, there are no reported studies on large populations involving Asians or Chinese of BMI and PSA levels. In the present study we aimed to assess the relationship between BMI and PSA levels among a large cohort of Chinese men who participated in the Singapore Prostate Awareness Week (PAW) 2005, and to compare the differences in the WHO standard BMI and Asian BMI, and PSA levels.

Variable	Mean (median, range) or *n* (%)
Age, years	59.1 (58, 50–75)
50–59	1454 (60.3)
60–69	799 (33.2)
70–79	157 (6.5)
WHO standard BMI, kg/m^2	24.1 (24.1, 14.8–63.5)
Underweight, <18.5	83 (3.4)
Normal, 18.5–24.9	1453 (60.3)
Obese, 25.0–29.9	768 (31.9)
Severely obese, ≥30.0	106 (4.4)
WHO Asian BMI, kg/m^2	
Underweight, <18.5	83 (3.4)
Normal, 18.5–22.9	1093 (45.4)
Pre-obese, 23.0–27.4	925 (38.4)
Obese, ≥27.5	309 (12.8)
PSA, ng/mL	1.52 (1.0)
0–1	1288 (53.4)
>1–2	633 (26.3)
>2–3	210 (8.7)
>3–4	115 (4.8)
>4–10	144 (6.0)
>10	20 (0.8)

TABLE 1
Descriptive characteristics of the 2410 Chinese men

SUBJECTS AND METHODS

This study was carried out as part of the Singapore PAW from 26 to 30 April 2005, which was organized by the Singapore Urological Association. Men aged >50 years were invited to go to any of four public hospitals to participate in the study. Participants were asked to complete a questionnaire and provide a 5-mL blood sample to measure their PSA level. Participants were weighed (wearing their clothing but without shoes, and with emptied pockets). Standing height was measured using a fixed stadiometer with a vertical backboard and a moveable headboard; the BMI was calculated as usual.

Signed informed consent was obtained from all participants and the relevant Institutional Ethical Review Boards approved the study. Men with known prostate conditions who were previously under treatment were excluded from the study.

In all 2714 men participated in the programme, consisting of 2431 Chinese, 114 Malays, 117 Indians and 52 'others'. Of these, 2410 Chinese men who had a PSA level of <20 ng/mL and were aged >50 but <80 years were included in the analysis. The other ethnic groups were excluded from further analysis as there were too few to attain the necessary power for statistical analysis.

All serum samples from the four institutions were delivered by courier to a designated laboratory to prevent interlaboratory variation in measurements of PSA levels. The total PSA level was assayed using an immunometric assay (IMx Total PSA assay kit, Abbott Laboratories, Abbot park IL, USA).

The relationship between serum PSA level and age was assessed and tested using Pearson correlation. Subjects were divided into four BMI categories of <18.5, 18.5–24.9, 25.0–29.9 and ≥30.0 kg/m^2 according to the WHO standard classification [17], and four BMI categories using the new Asian classification [12] of <18.5, 18.5–22.9, 23–<27.5 and ≥27.5, to assess the influence of BMI on serum PSA levels and to compare any differences between the standard and Asian BMI classifications and serum PSA levels. PSA levels were logarithmically transformed to obtain a normal distribution. ANOVA was used to test for differences in the means of PSA levels among the different BMI categories, and analysis of covariance to adjust for the effect of age on PSA levels among the different BMI categories.

RESULTS

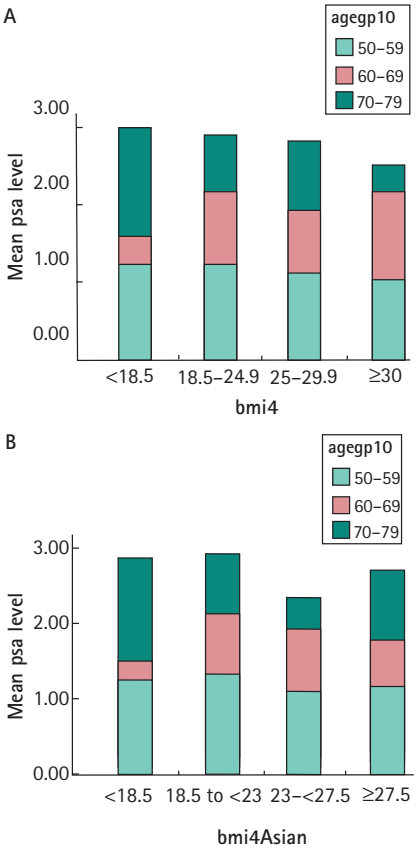
Of the Chinese men, >60% were aged 50–59 years; ≈60% of men were in the normal (standard) BMI range, with 36.7% classed as obese or severely obese and 3.4% who were underweight. Based on the WHO Asian classification, only 45.4% would be considered to have a normal weight, with 51.2% being pre-obese and obese (Table 1). Of the Chinese men, 93.3% had a PSA level of ≤4 ng/mL. There were no clinical differences in the mean age across the two BMI classifications (Table 2). The mean PSA levels

TABLE 2 Relationship of BMI categories with age and PSA levels among the Chinese study population

Variable	BMI categories, kg/m^2			
	<18.5	18.5–24.9	25–29.9	≥30
Sample size	83	1452	769	106
Mean (SD) age, years	60.9 (7.0)	59.4 (6.3)	58.5 (5.8)	58.5 (6.1)
Range	50.6–74.6	50.0–75.0	50.0–74.8	50.1–73.8
PSA level, ng/mL				
Mean	1.53	1.60	1.38	1.39*
Geometric mean	1.08	1.06	0.96	0.83†
Median	1.02	0.98	0.90	0.68
Mode	1.75	0.61	0.40	0.25
Percentiles				
25	0.62	0.59	0.57	0.39
50	1.02	0.98	0.90	0.68
75	1.80	1.83	1.61	1.52
BMI categories	<18.5	18.5–22.9	23–<27.5	≥27.5
Sample size	83	1092	925	310
Mean (SD) age, years	60.9 (7.0)	59.6 (6.3)	58.7 (6.0)	58.5 (6.1)
raNge	50.6–74.6	50.0–75.0	50.1–74.9	50.0–74.3
PSA level, ng/mL				
Mean	1.53	1.68	1.38	1.37†
Geometric mean	1.08	1.09	0.96	0.91†
Median	1.02	1.01	0.91	0.82
Mode	1.75	0.61	0.60	0.40
Percentiles				
25	0.62	0.59	0.59	0.48
50	1.02	1.01	0.91	0.82
75	1.80	1.88	1.59	1.49

P *for trend *<0.01; †<0.001.*

*FIG. 1. Distribution of mean PSA levels by (**A**), standard BMI and age groupings, and (**B**), Asian BMI and age groupings.*



decreased progressively across each of the BMI categories in both classification groups. These trends were significant ($P < 0.01$ to <0.001) for both the mean and geometric means of PSA levels (Table 2). The median PSA level for subjects with a BMI of ≥30 kg/m^2 (severely obese) was 30.6% lower than that of subjects with a BMI of 18.5–24.9 (normal weight); for the obese men (BMI 25.0–29.9) it was 9.2% lower than for those with a BMI of 18.5–24.9 (normal weight); for those with a BMI of 27.5 (obese) it was 18.8% lower than that for those with a BMI of 18.5–22.9 (normal weight); and for the pre-obese (BMI 23.0–<27.5) it was 8.9% lower than for subjects with a BMI of 18.5–22.9 (normal weight).

Figure 1 shows the distribution of mean PSA levels by standard BMI and age groupings (Fig. 1A), and Asian BMI and age groupings (Fig. 1B). Mean PSA levels increased with each 10-year age grouping and decreased with increasing BMI grouping. Within the 70–79-year age group, there was a reduction in the mean PSA level with each increasing BMI group. This trend was not as clear in the 50–59- and 60–69-year age groups (Fig. 1A). With the Asian BMI classification, there were no trends in mean PSA levels and BMI groups within each age grouping (Fig. 1B).

Age was significantly correlated with PSA level ($r = 0.27$; $P < 0.001$) but there was only a weak correlation with height, weight and BMI ($r = -0.19$, -0.17 and -0.08, respectively). Table 3 shows the mean and geometric mean PSA levels adjusted for age by two categories of BMI. There were significant differences in the BMI groupings for standard (<25 vs ≥25 and <30 vs ≥30) and Asian (<23 vs ≥23 and <27.5 vs ≥27.5) classifications even after adjusting for age.

DISCUSSION

The present study was conducted as part of the PAW programme, where the main aim of the campaign was to educate the public on prostate diseases that occur in ageing men, i.e. BPH, prostatitis and prostate cancer. The PAW campaign was announced in the local newspapers and men aged >50 years were invited to go to any of four public hospitals to participate in the study. There was no systematic sampling of the subjects and thus biases could be introduced. Some subjects included in the study could possibly have different types of prostate diseases. Although the subjects were asked about their medical conditions, we did not ascertain their conditions against medical records, as these were not available to us. Thus, the PSA levels in these subjects could reflect underlying prostate disease (e.g. BPH, prostate cancer, etc.). If this were so, then these men with prostate diseases would skew the PSA levels.

It is a well-documented phenomenon that health-conscious men are those who usually respond to any health education or disease-screening campaign, while the reverse is true

for those who are not health conscious. To the best of our knowledge, there are no definite lifestyle/habits that are correlated strongly with PSA levels. As such, the health consciousness of men who participated in this study is unlikely to significantly affect PSA levels. Most prostate diseases, except for prostatitis, are unlikely to have any symptoms at the early stage, but it is possible that men with an underlying prostate disease (e.g. BPH, prostate cancer, etc.) could still be included in the study. The men who participated in the study were not aware that we were studying the relationship between BMI and PSA levels, so the weight of the men would not have affected the study findings through selection bias.

BMI	*N* subjects	PSA level, ng/mL		*P* for GM
		Mean	GM	
Standard				
<25	1535	1.57	1.05	0.023
≥25	875	1.43	0.97	
<30	2304	1.52	1.03	0.022
≥30	106	1.39	0.85	
Asian				
<23	1175	1.67	1.09	0.002
≥23	1235	1.38	0.97	
<27.5	2100	1.53	1.03	0.039
≥27.5	310	1.41	0.93	

TABLE 3
The mean and geometric mean (GM) PSA levels adjusted for age by WHO standard BMI and Asian BMI

The negative association between BMI groups and PSA levels found in the present study is consistent with other recent studies [8,18,19]. Werny *et al.* [8] analysed data from the USA 2001–2004 National Health and Nutrition Examination Survey involving 1476 White, 435 Black and 485 Mexican-American men. They reported that White and Mexican-American men had a trend of decreasing PSA levels with increasing BMI. The median PSA levels for BMI groups of <25 and 25–<30 kg/m^2 in the Whites (1.1; 0.8, respectively), Blacks (0.9; 0.8, respectively) and Mexican Americans (0.9; 0.9, respectively) were quite similar to that of the Chinese men in the present study (0.98; 0.9) (Table 2). Baillargeon *et al.* [7] examined the association between BMI and PSA levels in a population-based study of 2779 American men (with different ethnicity/race) without prostate cancer. They reported that the geometric mean PSA levels for a BMI of <24.9 and 25–29.9 kg/m^2 were 1.03 and 1.01 ng/mL, respectively. These results are quite similar to the mean PSA levels of Chinese men in the present study for a BMI of <24.9 and 25–29.9 (1.06 and 0.96 ng/mL, respectively).

There were no marked significant differences in the mean or median PSA levels between the WHO standard BMI and Asian BMI when compared within each grouping (Table 2). It might not be useful to adopt the Asian BMI when evaluating an individual PSA level. However, individuals with a BMI of ≥30 (severely obese) and who had their PSA levels assessed might deserve closer attention. Half of these men had PSA levels that were 30.6% lower than men with a BMI of 18.5–24.9 (normal weight). In those aged 70–79 years there was a significant reduction in the mean PSA level with each increasing WHO standard BMI group (Fig. 1A). This is also the age group that is more at risk of prostate cancer. For subjects aged >70 years who are obese (BMI ≥30) it would be pertinent to evaluate their PSA levels with added attention, and further investigation might be warranted if there are other grounds for suspicion.

There are reports of differences in the mean PSA levels among Caucasian, Japanese, Koreans, Chinese (from China and Singapore), Malays and Indians [6]. However, interestingly, when PSA levels from different race and ethnic groups are compared by BMI, the PSA levels are quite similar. Banez *et al.* [20] reported in their subjects who had a radical prostatectomy for prostate cancer that BMI was associated with higher plasma volume and lower PSA concentrations. They suggested that haemodilution might be responsible for the lower PSA levels among obese men. However, that these men had a radical prostatectomy would be a potential source of selection bias. Obese men have been reported to have lower testosterone levels [21]; a lower testosterone level could result in smaller prostates, which translates to lower PSA levels.

Obesity is becoming a growing health problem, especially among developed countries. It has reached epidemic proportions in the USA, with the prevalence of obesity reported to be up to 30% among the adult population. Likewise in Europe, the prevalence of obesity is increasing rapidly [22]. Clinicians have reported a poorer prognosis among obese men with prostate cancer. It was found that these obese men tended to have lower PSA levels than non-obese men in the same age group. Thus it might take longer for their PSA level to rise to a level for biopsy to be offered. When such biopsies are taken, the prostate cancer might have reached a more advanced stage. Patients with prostate cancer and a higher BMI might have more obesity-related comorbidity, e.g. diabetes mellitus, hypertension, ischaemic heart diseases, etc. These medical conditions could also influence their survival. Of course, obese men are at higher risk of having other obese-related comorbidity and dying from these diseases first, even before developing prostate cancer. Obesity is also associated with changes in levels of hormones, including testosterone, oestrogen, insulin, IGF-1 and leptin, which have all been linked to prostate cancer [22].

Akin to the developed countries, the prevalence of obesity (BMI ≥30 kg/m^2) among Singaporean men has increased from 4.0% in 1992 to 6.4% in 2004 [11]. Similarly, the prevalence of obesity among Chinese men, especially in China, is also increasing [23]. In the light of the present findings and the growing prevalence of obesity and prostate cancer in Singapore and other Chinese population groups, it would be pertinent to consider the BMI of individuals when evaluating PSA levels, to prevent late biopsies and a delayed diagnosis of prostate cancer.

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CONFLICT OF INTEREST

None declared.

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Abbreviations: **BMI**, body mass index; **PAW**, Prostate Awareness Week.