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Analysis of Prostate-Specific Antigen Levels in a Population-Based Prostate Cancer Screening Program at Hiwa Hospital, Sulaymaniyah, Iraq

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Abstract

Background: Prostate cancer is the third most frequently diagnosed cancer worldwide with a significant public health burden. ***Objective***: To investigate the effect of prostate-specific antigen (PSA) testing in the early detection of prostate cancer and to highlight age and body mass index as the associated risk factors in a screening program at Hiwa Cancer Hospital in Sulaymaniyah City in Iraq. ***Methods***: This was a population-based screening study that enrolled 958 men aged between 30 and 75 years. A questionnaire was designed to collect demographic data, and serum PSA concentrations were measured for all participants. ***Results***: PSA values exceeding 4.0ng/mL were referred for further urological evaluation. Most of the participants (94.6%) exhibited PSA levels within the normal range (≤4 ng/mL), whereas 52(5.42%) of them demonstrated PSA levels exceeding 4.0ng/mL. Among those with abnormal PSA levels, 41(4.3%) participants had PSA values ranging from 4.1 to 10ng/mL, while 11(1.1%) participants had levels above 10 ng/mL. Prostate cancer was confirmed in five individuals, which accounts for 9.61% of participants with elevated PSA levels (>4.0ng/ml). Patients diagnosed with prostate cancer showed a substantially higher PSA level (median: 43ng/mL) compared with non-cancer participants (median: 5.5ng/mL). No statistically significant associations were observed between PSA levels and either body mass index or age, although PSA demonstrated a moderate positive correlation with increasing age. ***Conclusions***: The study indicates a low prevalence of prostate cancer within the screened population while emphasizing the importance of PSA screening programs for early detection.

Keyword: Cancer; Prostate; Population; PSA; Screening.

تحليل مستويات المستضدات الخاصة بالبروستات في برنامج فحص سرطان البروستات القائم على السكان في مستشفى هيوا، السليمانية، العراق

الخلاصة

الخلفية: سرطان البروستات هو ثالث أكثر أنواع السرطان تشخيصا على مستوى العالم، وله عبء صحي عام كبير. **الهدف**: دراسة تأثير اختبار المستضد الخاص بالبروستات (PSA) في الكشف المبكر عن سرطان البروستات وتسليط الضوء على العمر ومؤشر كتلة الجسم كعوامل خطر مرتبطة في برنامج فحص في مستشفى هيوا للسرطان في مدينة السليمانية/العراق. **الطرائق**: كانت هذه دراسة فحص قائمة على السكان شملت 958 رجلا تتراوح أعمارهم بين 30 و75 عاما. تم تصميم استبيان لجمع بيانات ديموغرافية، وتم قياس تراكيز PSA في المصل لجميع المشاركين. **النتائج**: تم إحالة قيم PSA التي تجاوزت 4 نانوغرام/مل لتقييم مسالك بولية إضافي. أظهر معظم المشاركين (94.6٪) مستويات PSA ضمن النطاق الطبيعي (≤4.0 نانوغرام/مل)، بينما أظهر 52 منهم (5.42٪) مستويات PSA تجاوزت 4.0ng/mL. من بين الذين لديهم مستويات PSA غير طبيعية، كان لدى 41 (4.3٪) مشاركين قيم PSA تتراوح بين 4.1 إلى 10ng/mL، بينما 11 (1.1٪) من المشاركين كانت مستويات أعلى من 10 ng/mL. تم تأكيد سرطان البروستات لدى خمسة أشخاص، وهو ما يشكل 9.61٪ من المشاركين الذين لديهم مستويات PSA مرتفعة (>4.0ng/ml). أظهر المرضى الذين تم تشخيصهم بسرطان البروستات مستوى PSA أعلى بكثير (الوسيط: 43ng/mL) مقارنة بالمشاركين غير المصابين بالسرطان (الوسيط: 5.5ng/mL). لم تلاحظ أي ارتباطات ذات دلالة إحصائية بين مستويات PSA ومؤشر كتلة الجسم أو العمر، رغم أن PSA أظهر ارتباطا إيجابيا معتدلا مع زيادة العمر. **الاستنتاجات**: تشير الدراسة إلى انخفاض انتشار سرطان البروستات بين السكان الذين خضعوا للفحص مع التأكيد على أهمية برامج فحص PSA للكشف المبكر.

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INTRODUCTION

Prostate cancer is one of the most frequently diagnosed cancers among men worldwide, and it is considered a major global public health challenge. It ranks as the third most frequently diagnosed cancer worldwide, following breast cancer (12%) and lung cancer (11%); it accounts for approximately 7% of all newly reported cancer cases [1]. In 2022, an estimated 1.46 million new cases were reported globally, with approximately 396,000 deaths attributed to the disease [2]. The global burden of prostate cancer, as stated by the Lancet Commission on Prostate Cancer, projects it will rise to approximately three million cases, and mortality is expected to increase to about 85% in 2040 [3]. This increase will result in an estimated loss of 7.5 million life-years, with the most pronounced rises expected in Africa, Asia, and the Latin America and Caribbean regions [4]. The incidence has been rising in many countries among men younger than 50 years [5]. Furthermore, prostate cancer exerts significant burdens on national economies through loss of productivity and the increasing cost of treatment. It has been estimated that the cumulative global

economic cost of prostate cancer between 2020 and 2050 will reach approximately USD 624 billion [6]. The most utilized tumor biomarkers in the clinical evaluation of prostate cancer are prostate-specific antigen (PSA) [7]. PSA is produced by normal prostate epithelial cells; malignant prostate tissue releases approximately tenfold higher concentrations of PSA into the circulation compared with normal prostate tissue or benign prostatic hyperplasia [8]. Although PSA is one of the most widely used biomarkers for the early detection and monitoring of prostate cancer [7,9]. However, PSA is not cancer-specific, as its serum concentration may rise with several benign conditions, including prostatitis, benign prostatic hyperplasia, urinary tract infections, urinary retention, and recent urological manipulation. Consequently, elevated PSA levels do not necessarily indicate malignancy and may result in unnecessary diagnostic procedures [10]. Nowadays, additional PSA-derived parameters, particularly PSA density and the free-to-total PSA ratio, have been incorporated into clinical assessment algorithms [10,11]. These indices provide better risk stratification and improve the diagnostic performance of PSA in differentiating prostate cancer from benign prostatic conditions. Despite considerable biological variability of PSA levels within the general population, no specific PSA concentration can definitively exclude the presence of prostate cancer. Nevertheless, a total serum PSA level of 4.0 ng/mL is conventionally regarded as the upper limit of normal and is widely used as a threshold to prompt further diagnostic evaluation, including prostate biopsy. There is increasing agreement that routine PSA screening leads to the detection and treatment of prostate cancer in many men who would otherwise remain undiagnosed throughout their lifetime. Despite widespread use, the survival benefit of routine PSA screening, particularly its impact on reducing prostate cancer-specific mortality, remains uncertain. Available evidence suggests that PSA testing is associated with only modest reductions in prostate cancer mortality, while simultaneously leading to substantial increases in the overdiagnosis and overtreatment of prostate cancer [12]. The accelerated increase in prostate cancer incidence, accompanied by rising mortality, represents a serious and unacceptable public health concern. Coordinated and sustained efforts are urgently required to reduce this burden and ultimately reverse the current pattern. For this purpose, a population-based screening program was conducted to assess PSA levels for the early detection of prostate cancer and to identify the associated risk factors among participants at Hiwa Cancer Hospital in Sulaymaniyah City, Iraq.

METHODS

Study design and setting

This study was designed as a cross-sectional screening study using voluntary community-based recruitment with both descriptive and analytical components. The study was conducted at Hiwa Cancer Hospital in Sulaymaniyah, Iraq. The study included over 900 male participants. Eligible individuals were adult men who attended the screening program from October 2022 to October 2023.

Inclusion and exclusion criteria

A non-probability sampling method based on voluntary participation was employed. Men were invited to participate voluntarily in a screening program for prostate cancer conducted at Hiwa Cancer Hospital in Sulaymaniyah, Iraq. Individuals who expressed interest and willingness to undergo screening were considered eligible for inclusion. The participants were recruited through both preregistration and through opportunistic hospital-based recruitment. Those who provided written informed consent were subsequently enrolled in the study cohort. Men with a previously confirmed diagnosis of prostate cancer who were currently receiving treatment were excluded from the survey.

Data collection

Prospective data collection was carried out between October 2022 and October 2023 using a non-probability sampling method based on voluntary participation. A structured questionnaire was developed and organized into two main parts. The first part collected participants' demographic and personal characteristics, including age, height, and body weight for body mass index (BMI) calculation [BMI=Weight (kg)/Height (m^2)], blood group, educational level, marital status, cigarette smoking status, history of alcohol consumption, and personal history of cancer. The second part recorded prostate cancer screening outcomes, specifically the measurement of serum PSA levels for the assessment of prostate cancer. A PSA level >4.0 ng/mL was used as the cut-off value for referral to a consultant urologist. Participants with elevated PSA levels underwent further clinical evaluation by the urologist. Based on the clinical assessment, the urologist determined whether MRI and/or prostate biopsy was indicated according to standard clinical practice. The definitive diagnosis of prostate cancer was confirmed by histopathological examination of prostate biopsy specimens.

Blood sampling

Five milliliters of blood were collected from each participant. Serum was separated from the samples for the assessment of PSA.

Ethical considerations

All procedures for diagnosis and blood sampling were performed in accordance with established ethical standards and the principles of the Declaration of Helsinki. The Scientific Research Unit at Hiwa Cancer Hospital-Sulaymaniyah Directorate of Health (DOH) approved the study protocol on October 1st, 2022, with reference number 70. Written informed consent was provided by all participants prior to blood

sample collection, and verbal informed consent was obtained before completion of the questionnaire.

Data analysis

Data were analyzed using GraphPad Prism version 10.4.1 for macOS. Categorical variables were summarized as frequencies and percentages. Comparisons between the prostate cancer group and the non-cancer group were performed using the Mann-Whitney test. The association between PSA level and the related factors was assessed using the Pearson correlation test. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 958 male participants, aged 30 to 75 years, were included in the study. The largest age group was 50-59 years, comprising 65.38% of the sample (Table 1).

Table 1: Sociodemographic characteristics of the participants (n=958)

Variables		Result n(%)	
Age (year)			
30-39		22(2.3)	
40-49		166(17.3)	
50-59		391(40.8)	
60-69		272(28.4)	
≥70		107(11.2)	
Marital status			
Single		16(1.7)	
Married		931(97.2)	
Divorced		4.0(0.4)	
Widow		7.0(0.7)	
Educational level			
No formal schooling		105(11)	
Primary		271(28.2)	
Secondary		169(17.6)	
High school		104(10.9)	
University Undergraduate		245(25.6)	
Postgraduate		64(6.7)	
Smoking status	Current	Ex-smoker/drinker	No smoker/drinker
	197(20.6)	249(26)	512(53.4)
Alcohol consumption	77(8)	76(7.9)	805(84)
		Yes	No
Personal cancer history		70(7.3)	888(92.7)

Values are presented as frequency and percentage.

Most of the participants were married (931, or 97.2%), and only 16 (1.7%) of them were single. Serum PSA levels were measured for all individuals who participated in this survey (n= 958). Within the overall cohort, most participants, 906 (94.6%), exhibited PSA values within the normal range (≤4.0 ng/mL). However, 52 men (5.42%) had PSA levels exceeding 4 ng/mL and were selected for further clinical analysis (Figure 1). In this subgroup, the PSA level of 41 (4.3%) of them were in the range of 4.1-10 ng/mL, and 11(1.1%) were > 10. Out of the 52 men with a PSA more than 4.0 ng/ml, five individuals were confirmed to have prostate cancer, corresponding to a prevalence of 9.61%. All cancer-positive (CA) cases exhibited markedly elevated PSA values (>20 to 113.3 ng/mL) compared with the non-cancer (NCA) group (4.1-20 ng/mL) (Table 2). However, age and BMI were comparable in both groups, and the difference was not significant between the CA and NCA groups (p= 0.59 and 0.16, respectively). PSA levels among the 52 individuals demonstrated considerable variability and a skewed distribution; therefore, they were expressed as the median with the interquartile range (IQR). The NC-PSA group (n= 47) showed relatively consistent values, with a median of 5.5 ng/mL (IQR= 4.7-7.6).

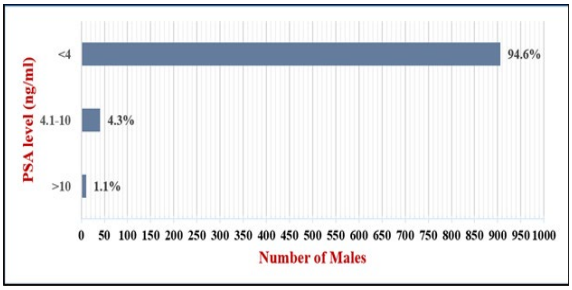

Figure 1: Prostate-specific antigen level among the surveyed population.

Table 2: Main characteristics of prostate cancer and non-cancer patients with PSA >4

Parameters	CA	NCA)	*p*-value
Age (year)	67.0±7.31	63.74±11.12	0.59
BMI (kg/m^2)	28.55±2.07	26.59±4.28	0.16
PSA			
Median (ng/mL)	43.0	5.5	<0.0001
Interquartile range (IQR) (ng/mL)	21.3-79.35	4.7-7.6	<0.0001

Values are presented as mean±SD, median, and interquartile range. Data were analyzed using Mann-Whitney test for comparison of age and BMI. A p-value of < 0.05 was considered SD: Standard Deviation.

In contrast, the CA-PSA group (n= 5) demonstrated markedly higher PSA levels, with a median of 43.0 ng/mL (IQR 21.3-79.35); this difference was statistically significant ($p< 0.0001$) indicating higher PSA and greater variability among participants in this group as shown in Table 2. In order to evaluate the relationship between PSA levels and the continuous variables, BMI and age, among the participants with elevated PSA, the correlation analysis was performed as summarized in Table 3.

Table 3: Correlation between Body Mass Index (BMI) and Age with Prostate-Specific Antigen (PSA) level in Prostate Cancer Patients (n=5)

Correlation	PSA level *vs*. BMI	PSA level *vs*. Age
Correlation coefficient		
r	-0.08621	0.5685
95% confidence interval	-0.900 to 0.862	-0.63 to 0.966
R squared (R^2)	0.007	0.323
p-value		
p (two-tailed)	0.89	0.317

Pearson's correlation test was used to assess the correlation between age, BMI, and serum PSA levels. PSA: Prostate-Specific Antigen.

No significant correlation between PSA level and BMI was observed, as indicated by a very low Pearson correlation coefficient (r= - 0.086). The association was not statistically significant ($p= 0.89$), which confirms the absence of a relationship between PSA and BMI. On the other hand, the correlation between PSA and age showed a moderate positive correlation, with Pearson's r = 0.569. Although this finding suggests that PSA level tends to increase with advancing age, the 95% confidence interval (-0.63 to 0.966) remained expansive, which indicates a degree of uncertainty associated with the relatively small sample size. The R^2 value of 0.323 indicates that age accounts for approximately 32% of the variation in PSA, but the relationship did not reach statistical significance ($p= 0.317$); therefore, the correlation observed in the studies' sample cannot be regarded as a reliable finding. Age and BMI did not significantly correlate with PSA levels in the present sample, although a moderate positive relationship was observed with age.

DISCUSSION

The findings of the present study demonstrate that only a small number of participants were diagnosed with prostate cancer. The PSA levels among the non-cancer group showed a relatively narrow interquartile range, suggesting limited variability in this group. Meanwhile, participants diagnosed with prostate cancer showed higher PSA levels and greater variability, which is evidenced by both a higher median value and a wider interquartile range. This outcome is consistent with the well-established relationship between elevated PSA levels and the presence of prostate cancer. The profound differences of PSA levels observed in the cancer group may reflect variability in the severity of the disease or stage of the disease at the time of diagnosis. These findings highlight the importance of reporting PSA data using the median and interquartile range, particularly in screening populations where values are often not normally distributed and influenced by heterogeneous clinical characteristics. Although only a small number of prostate cancer cases were identified in the present study, the findings point out the potential value of population-based PSA screening for the early detection of prostate cancer. These results support the feasibility of implementing organized PSA screening and suggest that such programs may facilitate the identification of prostate cancer at an earlier stage. However, further longitudinal studies with appropriate comparison groups are required to evaluate the effectiveness of population-based PSA screening in improving clinical outcomes. Large-scale randomized studies support the role of screening programs, as evidenced by the European Randomized Study of Screening for Prostate Cancer, which was conducted between 2009 and 2025; it reported that PSA-based screening was associated with a meaningful reduction in prostate cancer mortality, and extended follow-up data demonstrated a relative decrease in prostate cancer deaths ranging from approximately 13% to 21% over follow-up periods of 13 to 23 years [13]. Previous studies have suggested that organized PSA screening programs, through regular PSA testing and appropriate follow-up of individuals with elevated PSA levels, may facilitate the earlier detection of prostate cancer and reduce missed or delayed diagnoses. In contrast, opportunistic screening often depends on individuals seeking medical care and may therefore be associated with delayed diagnosis. However, the present study did not evaluate the diagnostic accuracy or effectiveness of PSA screening, and these observations are based on evidence reported in the literature. Other randomized trials, as demonstrated by the findings from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, have highlighted some of the limitations associated with weak screening approaches, where inconsistencies in screening practices may diminish their overall impact on cancer detection and outcomes [14]. Additionally, an organized screening program supports the generation of reliable health records, which are essential for monitoring disease and evaluating healthcare performance. The role of structured screening programs has been recognized by the World Health Organization, which encourages the implementation of organized cancer screening programs as a means of improving clinical outcomes [15], as combining screening programs with clinical assessment may strengthen patient management by providing appropriate follow-up, integrated care, and more data collection. Another study conducted by previous researchers [16] stated that an organized and systematic long-term screening approach positively enhances early detection of prostate cancer and

addresses the limitations of unorganized diagnostic practices. Additionally, in the present study, correlation analyses were performed to investigate the factors associated with cancer. No statistically significant associations were observed between PSA levels and either body mass index or age, although PSA demonstrated a moderate positive correlation with increasing age. In contrast to our study, evidence from a systematic review and meta-analysis revealed a significant inverse non-linear relationship between BMI and PSA levels [17], suggesting that increased body mass index is associated with lower circulating PSA concentrations. Despite this observation, BMI appeared to have minimal influence on the overall risk of prostate cancer, although a modest increase in the risk of advanced prostate cancer was reported among individuals with higher BMIs. The lower PSA levels detected in overweight and obese individuals may reduce the sensitivity of PSA-based screening and consequently delay prostate cancer diagnosis. This may result in an underestimation of the actual relationship between obesity and prostate cancer risk. Furthermore, advancing age is an important determinant of PSA levels, as PSA concentrations tend to rise with age due to physiological changes in the prostate gland [17]. These studies have also suggested that age and BMI may influence PSA levels and should therefore be considered when interpreting PSA results and evaluating screening outcomes. Taking these factors into account may improve clinical decision-making and reduce the potential for misinterpretation of PSA values. Although the screening of PSA levels has an important clinical role, PSA-based screening has many limitations, particularly due to its relatively low specificity. Increased PSA levels can arise from conditions other than prostate cancer, which may result in unnecessary biopsy procedures. Based on these concerns, the U.S. Preventive Services Task Force has emphasized the need for individualized screening decisions based on patient-specific risk factors, preferences, and a careful consideration of the potential benefits and harms associated with PSA testing [18]**.** In addition to the advantage of PSA levels in the detection of prostate cancer, the findings of the studies should be interpreted while considering the known limitations of total PSA as a sole biomarker. Several non-malignant factors, including benign prostatic hyperplasia, prostatic inflammation, and urinary tract pathology, can increase PSA levels and reduce its specificity for prostate cancer detection. Therefore, depending solely on total PSA may lead to false-positive results and unnecessary biopsies. The existing literature has demonstrated that PSA-derived parameters, particularly PSA density and the free-to-total PSA ratio, provide superior diagnostic ability compared with total PSA alone [10]. The combination of these parameters may therefore enhance the sensitivity and specificity of prostate cancer detection and support more accurate clinical decision-making [19].

Conclusion

The study demonstrated a low prevalence of prostate cancer within the screened population and emphasized the importance of population-based PSA screening programs for early detection. Further studies are recommended to evaluate the clinical outcomes, cost-effectiveness, and optimization of screening strategies.

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Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

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