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Assessment of Prostate-Specific Antigen Expression Among Sudanese Prostate Cancer Patients

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Abstract

Background: Prostate cancer (P.C), an international health issue affecting men from various socioeconomic classes, is caused by an uncontrolled proliferation of prostatic gland cells. **Objective:** The study aims to estimate the importance of PSA markers in differentiating between patients with prostate malignancy. Methods: A retrospective study was conducted in Khartoum State from August to December 2011. The study included 113 paraffin wax blocks from histopathology centers in Khartoum state on males diagnosed with P.C., which were gathered with prior ethical authorization. **Results:** PSA expression varied across histological grades, indicating significant relationships (p-value = 0.00). Seventy-one cases were categorized as high, 23 as moderate, and 20 as low. PSA positive was found in 47.8% of patients, including a wide range of histological diagnoses, including well-differentiated, moderately differentiated, and poorly differentiated adenocarcinoma, prostatic intraepithelial neoplasia (PINH), and adenocarcinoma in situ. **Conclusion:** Higher-grade tumors are the most prevalent histological grade, with a strong correlation between PSA expression and histological grade. The study also discovered that PSA is not an ideal prognostic indicator since its expression is lost in the advanced stages of P.C.

Keywords: PSA, Prostate Cancer, Sudan

Introduction:

Prostate cancer (P.C), a worldwide health problem that affects men from various socioeconomic groups, is caused by an unregulated proliferation of prostatic gland cells [1]. (P.C) is one of the greatest threats to the system of healthcare in several countries worldwide, and it notably causes a more significant number of deaths among men. It is the second most prevalent cancer in men and the sixth-leading cause of malignancies internationally [2-5]. Annually, 20.7 out of every 100,000 males die. P.C. was identified in around 180.000 new cases annually in the United States. Europe has the highest frequency; approximately 450,000 new cases and 107,000 deaths were recorded in 2018.

Prostate cancer causes 4.4% of deaths related to cancer. [6,7]. According to the most recent WHO data published in 2020, prostate cancer deaths in Albania reached 203, or 0.83% of all recorded mortality cases [8]. The risk of prostate cancer remains significant in patients having prostatectomy for assumed benign tumors of the prostate. A national awareness program, along with a focused screening of patients over 40, might increase early diagnosis of prostate cancer, thereby lowering morbidity as well as mortality [9-11]. Prostate cancer is associated with several risk factors. Serum levels of early prostate-specific antigen (PSA) were considerably elevated in prostate cancer patients [12]. PSA is frequently called a tumor marker. PSA test, first used in the second decade of the twentieth century, provides a rapid and inexpensive approach to detecting asymptomatic men who may have prostate cancer at an earlier stage [13, 14]. However, it does not adequately assess the biological properties of prostate cancer cells, so still, it is uncertain to predict whether high PSA levels alone in the blood will always lead to prostate cancer. Therefore, there is a need to create more biological markers to determine the improvement of prostate cancer, including prostate biopsy for histology, regardless of the PSA level required [15-21]. The use of PSA testing is essential not only because it assists in recognizing individuals for whom a prostate biopsy would be sufficient but also because it helps to review the response to treatments and monitor tumor development [22, 23]. This study aimed to investigate the correlation between the grading of prostatic adenocarcinoma and the expression of PSA markers in Sudanese men diagnosed with prostate cancer. Also, this article can provide a comprehensive and critical evaluation of the use of PSA in prostate cancer, risk categorization, monitoring, and follow-up therapy.

Objectives

The study aims to estimate the importance of PSA markers in differentiating between patients with prostate malignancy.

Literature Review

The primary purpose of any screening exam is to detect the early stages of a pathological condition, enabling timely intervention and preventing unnecessary morbidity or mortality before clinical signs or symptoms develop. In prostate cancer screening, an elevated serum prostate-specific antigen (PSA) level is the most common initial laboratory finding, as the vast majority of men with early prostate cancer are asymptomatic. PSA is a highly sensitive but relatively nonspecific and imprecise screening tool, as both benign and malignant conditions elevate the serum marker.[1] The use of PSA screening has become controversial, with differing guidelines and recommendations regarding its application across various age groups. Despite the risks associated with serum PSA screening, including the potential for unnecessary biopsies and overdiagnosis, it remains the single most useful tool for the early detection of prostate cancer, offering patients the best chance for a cure. Although the use of PSA for prostate cancer screening is somewhat controversial, its effectiveness in determining the extent of malignancy, monitoring disease progression, identifying biochemical recurrences, and evaluating treatment response is unquestionable. PSA decreases seminal viscosity by chemically breaking down the proteins semenogelin and fibronectin, which are responsible for the initial gel-like consistency of normal semen. This reduced viscosity allows for easier sperm migration into the cervix and promotes overall fertility.[9] As men age, spermatozoa production is altered, with a resultant adverse effect on sperm count and quality, which impairs reproductive function.[10] PSA levels also increase with age, which is believed to be an evolutionary adaptation that confers genetic fitness and promotes fertility over other competing males. This adaptation may partly explain the increasing prevalence of conditions such as benign prostatic hyperplasia in the general population and the need for age-specific normal ranges for serum PSA levels. Prostate cancer cells do not produce more PSA than benign cells; in fact, they tend to manufacture less. However, malignant cells more easily allow PSA to pass through the cell wall into the surrounding extracellular fluid and eventually reach the bloodstream. This process occurs because these malignant prostate cells lack a basal layer that otherwise restricts the passage of PSA outside the cell. Very high Gleason score cancer cells that are highly undifferentiated may not produce PSA. Serum prostate-specific antigen is still a somewhat controversial screening tool for healthy, asymptomatic males because elevated levels of serum PSA can be

associated with various benign prostatic conditions. Infection, trauma, inflammation, and benign prostatic hyperplasia can elevate serum PSA levels, reducing the specificity of the biomarker for use in predicting prostate cancer. Studies show that up to 86% of individuals with benign prostatic hyperplasia may have elevated levels of serum PSA.[11] The decision to screen an asymptomatic male using serum PSA should involve shared decision-making. Such discussions involve risks and benefits, such as a falsely elevated PSA value that may lead to an unnecessary biopsy of a benign condition or the discovery of indolent prostate cancer that can lead to the treatment of a condition that has remained totally asymptomatic and clinically inactive. The United States Preventative Task Force recommends selectively offering serum PSA screening individually according to professional judgment and patient preference in males aged 55 to 69 (grade C).[12] The patient's general health is an important factor in the decision to screen, as guidelines recommend against screening individuals with a life expectancy of fewer than 10 years. Current guidelines recommend against routine prostate cancer screening with serum PSA in healthy asymptomatic individuals aged 70 to 75.

Materials & Methods:

Subjects:

This retrospective study was conducted in Khartoum state, Sudan, from August to December 2011. The study enrolled 113 paraffin wax blocks collected from histopathology centers in Khartoum state. All the samples belong to Sudanese males diagnosed with prostatic cancer, aged between (39-95 years). The study excluded any other disorders that affect the prostate than prostate cancer.

Sample Processing:

According to Mayer's method, all tissue blocks were prepared, cut by microtome into sections, and stained with hematoxylin and eosin for detection of PAS by immunohistochemistry stain according to (Leica Biosystems-21440 W. Lake Cook Road. Floor 5-Deer Park, IL 60010 United States.

Ethical Issues:

The research ethics committee at the College of Medical Laboratory Science, Alzaiem Alazhari University, Khartoum, Sudan, authorized the current research.

Statistical Analysis:

SPSS version 20 software for Windows was used to analyze the data. The data has been expressed as numbers and percentages, and the findings were displayed as tables and pictures. A P value of less than 0.05 was deemed significant.

Results

The present study involved 113 cases of prostate cancer. According to the Grade of disease, the research population's age ranged from 39 to 95 years, with an estimated mean of 67 years. PSA Expression frequency according to histologic Grade based on histological examinations: 71 of the 113 prostate cancer patients involved in the study were classified as high Grade, 23 as moderate Grade and 20 as low Grade.

Table (1, 2) shows the prevalence of differential histological diagnoses; after evaluating 113 prostatic cancer specimens, it was discovered that 59 cases (52.2%) had negative PSA expression, whereas the remaining 54 cases (47.8%) had positive PSA. Positive cases included 18 (33.33%) well-differentiated adenocarcinomas, 18 (33.33%) moderately differentiated adenocarcinomas, 11 (20.37%) poorly differentiated adenocarcinomas, and 6 (11.11%) prostatic intraepithelial neoplasia (PINH). Furthermore, one (1.86% positive) was classified as adenocarcinoma in situ.

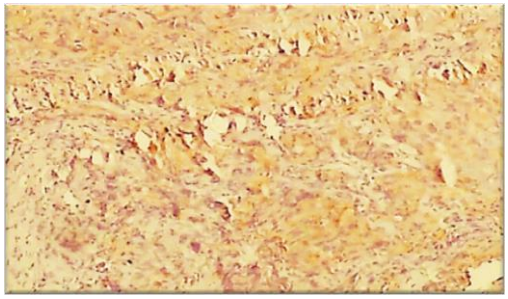
Regarding PSA expression and histological Grade, this study's outcomes demonstrate a statistically significant relationship between prostatic adenocarcinoma grades and PSA expression (P-value = 0.00).

Table 1: Distribution of the study sample according to PSA expression in different histological grades of Prostatic adenocarcinoma.

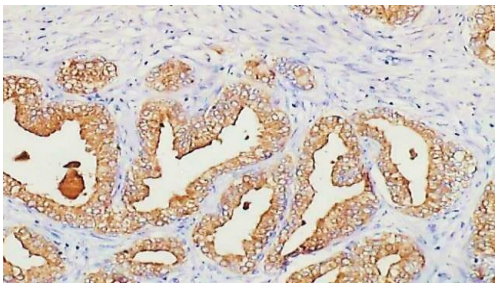
Tissue PSA detection	Histological diagnosis										Total
	Poorly differentiation		Moderately differentiation		Well differentiation		PINH		Intraepithelial law grade		
	N	%	N	%	N	%	N	%	N	%	
Positive	11	17.18	18	78.26	18	100	6	100	1	50	54
Negative	53	82.82	5	21.74	0	00	0	00	1	50	59
Total	64	100	23	100	18	100	6	100	2	00	113

Table 2: Histological grade * PSA expression Cross tabulation

		PSA expression		Total
		Positive	**Negative**	
Tumor type	Well-differentiated	18	0	18
	Moderately differentiated	18	5	23
	Poorly differentiated	11	53	64
	Prostatic intraepithelial neoplasia high-grade	6	0	6
	Intraepithelial neoplasia low-grade	1	1	2
Total		**54**	**59**	**113**

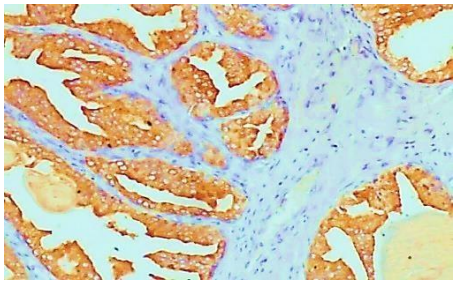


A



B

A: PSA expression in high-grade prostatic intraepithelial neoplasia.
B: PSA expression in prostatic intraepithelial neoplasia law grade.



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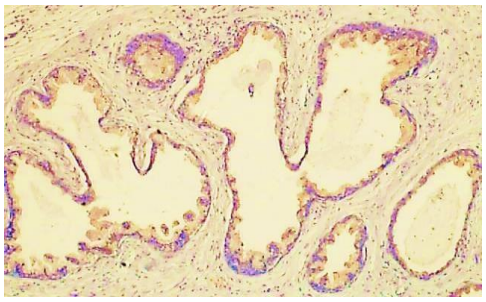
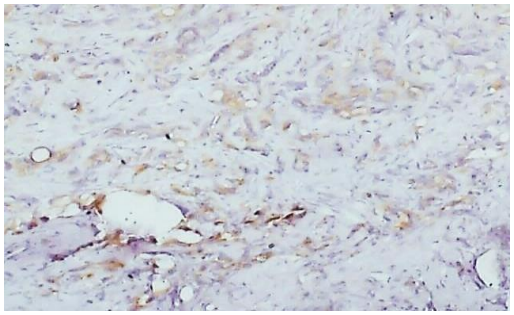
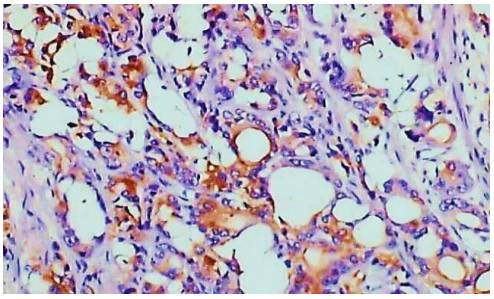


D

C: PSA expression in adenocarcinoma in situ
D: PSA expression in well-differentiated adenocarcinoma



E



F

E: PSA Expression in moderately differentiated prostatic adenocarcinoma.
F: PSA expression in poorly differentiated prostatic adenocarcinoma.

Discussion

This study examined various features of prostate cancer in a cohort of 113 cases. Few previous studies have explored the frequency and association of PSA in prostate cancer patients in Sudan, even though it is the most common malignancy in men, according to Hamad and Abuidris,20110 [24]. In the current study, the age distribution of our patient cohort was expansive, ranging from 39 to 95 years, with an estimated mean of 67 years. This proves the need for prostate cancer screening and diagnosis in the elderly. It also matched Taha et al.'s (2020) [25] study, which indicated that the incidence has increased dramatically in the last decade, and the median age of individuals presented with the disease is 72 years. It also agreed with Chao et al.'s (2009) [26] study, which found that the chance of prostate cancer rises with age, and the patients' average age was 63.3 years old. Therefore, the probability of prostate cancer increases with age. According to the current study, the expression of PSA in prostatic cancer patients was 54 (47.8%) positive, and 59 (52.2%) were negative. The 54 (47.8%) positive PSA expression, including 11 (17.18%) were poorly differentiated adenocarcinoma, 18 (78.26%) were moderately differentiated adenocarcinoma, 18 (100%) were well-differentiated adenocarcinoma, 6 (100%) were intra epithelial adenocarcinoma high grade, and 2 (50%) were in situ adenocarcinoma. These findings agreed with the study by Abrahamsson PA et al. (1995) [27]. Their analysis revealed that well-differentiated prostatic carcinomas have shown increased PSA immuno-reactive cells.

In contrast, poorly differentiated prostate adenocarcinoma tissues revealed considerable variation, with a lower incidence of immune-reactive cells within and among tumors, thus indicating that PSA-labeling occurs in a small percentage of the poorly differentiated adenocarcinoma. The current study also agrees with Van Hecke. D et al. (2002) [28] observed that PSA may not be expressed in all adenocarcinomas or metastatic tumors but that most prostate cancers express PSA and concluded that the immunohistochemically defined expression level is widely accepted to correlate inversely with tumor grade. More research should be conducted to identify other markers for the diagnosis of prostate malignancies. Molecular investigations in urine should be performed for PSA detection, early tumor identification, and the detection of mutations in various genes that may result in malignancy.

Conclusion:

This study concluded that higher-grade tumors are the most common histological grade, and there is a substantial relationship between PSA expression and histological grade. The study also found that PSA is not an excellent prognostic diagnostic; hence, its expression is lost in the advanced stages of prostatic cancer.

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