Baghdad Science Journal

Volume 22 | Issue 8 Article 2

8-15-2025

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How to Cite this Article

H.Al-Qazzaz, Ammar and F. Al-Taie, Anwar (2025) "Estimation of paraoxonase-1 and dipeptidyl peptidase in Iraqi prostatic cancer with hormones and chemotherapy drugs: a cross-sectional study," *Baghdad Science Journal*: Vol. 22: Iss. 8, Article 2.
DOI: https://doi.org/10.21123/2411-7986.5012

BAGHDAD SCIENCE JOURNAL 2025;22(8):2488–2499

RESEARCH ARTICLE

Estimation of Paraoxonase-1 and Dipeptidyl Peptidase in IRAQI Prostatic Cancer with Hormones and Chemotherapy Drugs: A Cross-Sectional Study

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ABSTRACT

Prostate cancer is a frequent masculine disease, especially when becoming older. Paraoxonase-1 (PON-1) is an enzyme present in the human body that plays an important function in preventing oxidative stress and inflammation. It is mostly linked to high-density lipoprotein (HDL). Dipeptidyl peptidase-4 (DPP-4) is an enzyme regulating blood sugar levels. It is found on many cells surfaces: immune cells, epithelial cells, and pancreatic cells. The aim of this cross-sectional study was to determine the biochemical role of PON-1 effect and DPP-4 enzymes with the anti-cancer ability of vitamin D. Research samples were collected from Iraqi prostate cancer patients (male aged 45–80 years) diagnosed after receiving chemotherapy (30 samples G2), and hormonal treatment (30 samples G3), compared to the healthy control (G1). ELISA technology was used to estimate serum levels of the enzymes with vitamin D. The results recorded an increase in PON-1 levels for G2 (115.33 ± 15.92) (p-value < 0.0001), and a slight increase for G3 (65.85 ± 6) (p-value > 0.05), compared to the G1 (61.99 ± 9.82). There was an increase in the effectiveness of the DPP-4 enzyme for patients after chemotherapy and hormonal treatment (22.79 ± 2.12) (p-value < 0.0001) and (10.93 ± 1.96) (p-value < 0.0001), respectively, compared to the G1 (8.51 ± 1.09). There was a severe loss of vitamin D for G2 (4.39 ± 0.69, p-value < 0.0001) and G3 (11.85 ± 1.61, p-value < 0.0001) compared to the G1 (18.92 ± 2.36). The results indicate the role of these enzymes as vital indicators for patients with prostate cancer and its development, and vitamin D deficiency is a risk factor for these patients.

Keywords: Dipeptidyl peptidase, Paraoxonase-1, Prostatic cancer, PSA, Vitamin D

Introduction

Prostate cancer (PCa.) is the second most common cancerous tumor worldwide and is the fifth leading cause of cancer-related mortality among men.[1] It begins when cells in the prostate gland start to grow out of control.[2] Cells in nearly any part of the body can become cancer cells, and later spread to other areas of the body. Some prostate cancers can grow and spread quickly, but mostly they grow slowly. In fact, autopsy studies show that many older men (and even some younger men) who died of other diseases also had prostate cancer which never affected them during their lives. In many cases, neither they nor their doctors even knew they had it.[3]

Symptoms and indicators that cancer has spread beyond the prostate gland include: Back, thighs, hips, shoulders, or other bones hurt, fluid accumulation or swelling in the legs or feet, unaccounted weight loss and exhaustion.

The majority of the tissue in the prostate gland produces a protein called Prostate-specific antigen

Received 24 September 2023; revised 22 April 2024; accepted 24 April 2024.
Available online 15 August 2025

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https://doi.org/10.21123/2411-7986.5012

(PSA). These proteins are found in tiny amounts in the blood flowing through the victims' bodies and in their semen as well. PSA is a 34-kDa single-chain glycoprotein secreted by the prostate gland.[4] The normal level of this protein in the serum is less than 4 ng/ml. A high PSA level suggests a possible prostate cancer. On the other hand, an irritated prostate also raises PSA levels. However, PSA testing is not 100 percent accurate, thus other confirmatory tests are necessary to establish the presence of cancer.[5]

Androgen suppression treatment is another name for hormone therapy. This treatment aims to lower androgen levels in the body or prevent them from promoting the development of prostate cancer cells. Prostate cancer cells are encouraged to proliferate by androgens.[6] Chemotherapy refers to any form of treatment that employs chemicals to eradicate or slow down the development of cancer cells. Cancer patients may benefit from chemotherapy, despite the fact that treatment is unlikely to completely cure prostate cancer. It might be used, for instance for lessening the impact of illness which in the turn delays disease.[7,8]

Paraoxonase-1 (PON1) is an enzyme that is largely connected with the high-density lipoprotein (HDL) particle, popularly known as (good cholesterol). It is mostly synthesized in the liver and is delivered into the bloodstream, where it interacts with HDL.[9,10] PON1 has received a lot of attention because of its potential to defend against oxidative damage and inflammation.[11] PON1 may help defend against plaque formation and minimize the risk of cardiovascular disease by reducing LDL oxidation. Changes in PON1 expression or activity have been linked to many cancers, including lung, breast, and prostate cancer, according to some studies.[12] An enzyme called dipeptidyl peptidase (DPP) is involved in the body's degradation of peptides. Particularly, it is a member of the group of proteases called peptidases or proteolytic enzymes. By hydrolyzing the peptide link between two amino acids, DPP breaks down dipeptides from the N-terminus (the amino-terminal end) of proteins or peptides.[13,14]

Vitamin D is a fat-soluble vitamin that is essential for many physiological functions in the body.[15–17] It is most known for its involvement in calcium and phosphate metabolism, as well as its significance in bone health.[18] Sunlight and food sources are the two main sources of Vitamin D.[19] This is crucial in immune cell function and immune response modulation. Adequate vitamin D levels are essential for immune system health.[20] According to studies, vitamin D may play further functions in a variety of physiological processes such as cardiovascular health, muscle function, cognitive function, and cancer prevention.[21] Several studies have reported a significant relationship between the indicated parameters with tumor.[22,23] The aim of this study is to determine the role of PON-1 and DPP in prostate cancer after chemotherapy and hormonal drugs, in addition to the anti-cancer ability of Vitamin D. and useful as markers for various cancer.

Materials and methods

Data collection: A cross-sectional study was carried out; ninety samples were collected between November 2022 to May 2023 at Imam Hussein Center, for the treatment of tumors and blood diseases (Al-Amal Building) in the Imam Hussein Medical City in the holy city of Karbala, and Teaching Oncology Hospital in Baghdad Medical City. Paraoxonase-1, Vitamin D, dipeptidyl peptidase, and PSA were estimated by ELISA kits: (SEA243Hu, CEA920Ge,) could-clone USA (E-EL-H6147) Elabscience USA & (REF 08791686 190) Roche Germany, respectively.

Ethical approval was obtained from the research committee in Karbala health directorate/ Ministry of health (Ref: 206 in 27/November 2022).

Inclusion criteria for cases and controls: The samples consist of 30 sera healthy control G1 were prostatic cancer patients, 30 serum G2 (prostatic cancer receiving either Cabazitaxel© or Taxotere© chemotherapy) and 30 samples of serum G3 (prostatic cancer receiving Zoladex© hormonal therapy); all samples were from 45–80 years old male. The body mass index BMI was less than 25 for all groups of patients and healthy group. For patients a high-grade cancer in Gleason scoring system was diagnosed by specialists in the oncology center.

Exclusion criteria for cases and controls: Prostatic cancer patients and healthy controls with other malignancy or diseases such as cardiovascular disease, thyroid disorder and diabetes were excluded.

Statistical evaluation

SPSS 26 was employed for statistical evaluation. A general descriptive statistic was employed to characterize the major findings, and a one-way analysis of variance test was employed to compare the groups. A separate T-test was also employed. To determine the Pearson correlation between variables, Microsoft Excel 2021 was used. The cutoff value for the markers was also determined using the receiver operating characteristic curve (ROC) analysis.[24]

Table 1. Testing the normality of the parameters using Shapiro-Wilk test.

	Shapiro-Wilk		
Parameters	Statistic	df	Sig.
PSA	3.623	120	0.092*
DPP4	3.910	120	0.094*
PON1	2.881	120	0.081*
Vit.D	3.884	120	0.099*

*Significant at 0.05 level (i.e. the data follows normal distribution).

Table 2. Concentration study of PSA, PON-1, DPP-4, and Vitamin D in chemotherapy, hormonal therapy prostatic cancer patients and healthy control.

parameters	G1 Control [Mean ± SD] n = 30	G2 PCa. With Chemotherapy [Mean ± SD] n = 30 *p*-value	G3 PCa. With Hormonal therapy [Mean ± SD] n = 30 *p*-value	*p*-value between G2 & G3
PSA ng/ml	0.804 ± 0.042	71.65 ± 4.065 <0.0001*	5.98 ± 0.681 <0.0001*	<0.0001*
PON-1 ng/ml	61.99 ± 9.82	115.33 ± 15.92 <0.0001*	65.85 ± 6 0.075	<0.0001*
DPP4 ng/ml	8.51 ± 1.09	22.79 ± 2.12 <0.0001*	10.93 ± 1.96 <0.0001*	<0.0001*
VitaminD ng/ml	18.92 ± 2.36	4.39 ± 0.69 <0.0001*	11.85 ± 1.61 <0.0001*	<0.0001*

NS: non-significant (p-value > 0.05), S: significant (0.01 < p-value ≤ 0.05), *HS: high significant(p-value ≤ 0.01).

Results and discussion

Before applying some statistical tests such as t-tests and ANOVA tests to the real data, we tested the normality assumption for all the parameters using the Shapiro-Wilk test. Table 1 shows the results for normality test of parameters (PSA, DPP4, PON1 and Vitamin D). Shapiro-Wilk test results, as all *p*-values are greater than 0.05, verifies that the data followed normal distribution, which is a fundamental assumption for these parametric tests.

Table 2 shows the biochemical features of the sample population sera of Iraqi male PCa patients treated with chemotherapy (G2), hormonotherapy (G3), and healthy controls (G1).

PSA level in serum

The results showed a highly significant increase in PSA levels in sera from G2 and G3 patients compared to G1. PSA levels were shown to increase significantly in G2 compared to G3, this agrees with similar studies done by Pathirana *et al.*[25] The PSA is one of the crucial diagnostic markers for the diagnosis of prostate cancer,[26] and despite the recent availability of numerous diagnostic markers, the PSA is still an accurate marker for diagnosis. This accounts for the wide range of the marker in patients. The significance of PSA is influenced by the disease's stage and rate of development, and its use extends beyond simple diagnosis to include post-treatment monitoring. Considering that the majority of men with a PSA score under 4 ng/ml do not have prostate cancer, most prostate adenocarcinoma patients with elevated blood PSA levels have advanced malignancies. The PSA values fall as a result of some of these instances responding to hormone therapy in first cases, this result agrees with similar studies done by Nakanishi *et al.*[27] Advanced instances do not improve with therapy; thus, their concentrations are still high. The purpose of therapy is to extend the patient's life.[28,29] Patients with prostate cancer may have an increase in PSA values following hormone and chemotherapies for a variety of causes, including:

After receiving treatment and even in the absence of high amounts of testosterone, certain prostate cancer cells can adapt and discover different ways to activate androgen receptor signaling. This may result in ongoing expansion and PSA production. It is possible that chemotherapy won't entirely eradicate all cancer cells from the prostate or nearby tissues. Continuing production of PSA by residual cancer cells may result in increased levels. Chemotherapy causes cell death, which destroys cancer cells. Inflammation brought on by this cell death may lead to the release of PSA into circulation.[30] Chemotherapy-resistant cancer cells may eventually proliferate and accelerate the growth of tumors. PSA production might increase as the tumor develops.[31] The body's hormone balance especially that of testosterone, which promotes the formation of prostate cancer, might be upset by chemotherapy. Increased PSA levels can result from

hormonal changes that alter the behavior of cancer cells that are still present. Because various cancer cells within the same tumor may respond differently to treatment, prostate cancer is recognized for its heterogeneity. Even after therapy, certain cells could be more resistant and keep producing PSA. [32]

Efficacy of PON-1 enzyme in serum

Studying the effect of PON-1 is of great importance because it provides indications of Iraqi prostate cancer along with its developmental cases and compares patients after Chemotherapy as well as Hormonal treatment with the control group. The data showed an effective significant increase in the concentration of the PON-1 parameter for G2 compared to the control group, however, there is a non- significant increase between G3 compared with G1 these results are identical with similar studies undertaken by Eroglu *et al.* [12] When comparing the two groups of patients (G2 and G3), a significant increase was recorded between patients with chemotherapy compared to the other group of hormonal treatment. PON1 is an enzyme connected to high-density lipoproteins (HDL) that functions as a lipid peroxidation and oxidative stress defense mechanism. According to the findings of this investigation, PON1 levels may impact the risk of PCa. According to Sekine *et al.,* HDL-cholesterol increases PCa cell proliferation and migration. [33] PON1 activity may impact carcinogenesis not just by limiting exposure to harmful organophosphate metabolites, but also by altering pesticides' potential effects on immune function and oxidative stress. PON1 Arg192Gln and Met55Leu variations have been linked to substrate-dependent activity. The recently found -108T and -162A promoter variations have been linked to enhanced activity. [34] This is the gene that encodes the human serum PON-1 enzyme, which has been linked to lipid metabolism and the removal of carcinogenic lipid-soluble radicals. Furthermore, PON1 genotypes influence the susceptibility of LDL- and HDL-cholesterol to lipid peroxidation. As a result, it was demonstrated that PON1 is a complex enzyme having specialized functional regions for diverse actions. [35] Using multivariable Cox proportional hazard regression models, Kok et al. identified serum TC, HDL-cholesterol, LDL-cholesterol, and TG as possible risk factors for PCa. Higher TC and LDL-cholesterol levels were shown to be strongly related with an increased risk of PCa. [36] Moreover, Abdelhamid *et al.* revealed that polymorphisms in the PON1 gene are linked to prostate cancer and its development. [37] Abudayyak *et al.* also discovered that Turkish males with PON1 genetic alterations are more susceptible to prostate cancer. [38] Therefore, the results showed, in general, an increase in the concentration of PON1 compared to the standard group. [12]

Efficacy of DPP-4 enzyme in serum

As for the enzyme dipeptidyl peptidase IV DPP-4, a significant increase among all patient groups compared to the standard group was recorded. Comparison between patients after chemo and hormonal therapy also showed a significant increase in DPP-4 activity. Therefore, the results of the study were similar with Enz *et al.* [22] The enzyme (DPP-4), also known as cluster of differentiation (CD26), is involved in the control of a number of physiological processes. It is best recognized for its role in the breakdown of incretin hormones and the metabolism of glucose. DPP-4 is involved in the control of the immune system and is present on the surface of numerous cell types, including immune cells. [39] It has been investigated if CD26/DPP-4 expression can serve as a diagnostic and prognostic marker for a variety of illnesses, including different malignancies and inflammatory ailments. DPP-4 is believed to function as a pro-tumor factor in a range of malignancies due to the fact that it affects several tumor-related pathways, so it could be a vital indicator for a number of cancers, including prostate cancer, therefore, this study was concerned with estimating DPP-4 levels. The results of higher levels of CD26 in patients with prostate cancer have been associated with previous studies, so it is necessary to use CD26 inhibitors to extend the life of the patient. [40] Despite receiving chemotherapy, a significant increase in PSA was seen in the second group of prostate cancer patients, and many of them experienced recurrence or malignancy. [22] The primary factor for chemotherapy failure and disease progression is drug resistance in cancer cells. In this situation, angiogenesis plays a crucial role in the interaction between cancer cells and the milieu, and exogenous DPP-4 played a crucial role in promoting angiogenesis. Increased tumor burden and poor tumor differentiation were also predicted by elevated DPP-4 expression. [41]

Vitamin D level in serum

A significant decrease in Vitamin D values for all patient samples in contrast to the standard group, these results were similar with Kumawat *et al.* [42] On the other hand, a vitamin D deficiency occurs compared to the second and the third group. D2 (ergocalciferol) and D3 (cholecalciferol) are the two kinds of vitamin D. [43] Human skin generates vitamin D3 in response to UVB radiation, while vitamin D2 is obtained in our meals from plant sources such as edible (UV-exposed)

Table 3. Correlation between PSA with PON-1, DPP-4 & Vitamin D.

	Factors	PON_1	DPP-4	Vitamin D
PSA				
G2	R (person)	0.095	0.153	0.05
	P	0.616	0.421	0.788
G3	R (person)	–0.491	–0.262	0.193
	P	0.006**	0.162	0.307

NS: non-significant (p-value > 0.05), *S: significant (0.01 < p-value ≤ 0.05), **HS: high significant (p-value ≤ 0.01).

mushrooms, albeit in varying amounts and with reduced efficiency.[44] Each of the forms of vitamin D are physiologically inert and must be transformed to 25(OH)D in the liver by vitamin D-25-hydroxylase. The most common form of vitamin D in circulation is 25(OH)D, and measuring it in the clinical setting provides information about one's vitamin D status.[45] Vitamin D is known as the "sunshine vitamin" because our bodies can manufacture it when subjected to the sun. Individuals with prostate cancer who spend less time outside or reside in places with little sunshine may have lower vitamin D production owing to insufficient solar exposure.[46] Prostate cancer is prevalent in older men, and their skin remains less effective in producing vitamin D when exposed to sunlight as they age.[47] Because of their cancer therapies, some patients may have diminished appetites or dietary limitations, which can lead to lower vitamin D consumption from food sources.[48] Corticosteroids and anticonvulsants, which are routinely provided to prostate cancer patients, can interfere with vitamin D metabolism and absorption.[49] Hormonal medications used to treat prostate cancer may have an effect on vitamin D levels as well. Androgen reduction treatment (ADT), for instance, can cause bone loss, which impairs vitamin D metabolism.[50]

This study is firstly limited to the cross-sectional design. Secondly, the samples under scrutiny were limited to Iraqi prostate cancer patients. Third, participants were treated with (Carbazitaxel or Taxotere Chemotherapy), (Zoladex hormonal drugs) and evaluated their activities and concentrations of the mentioned parameters. Fourth, the parameters referred to may provide indicators about the development of the disease and its stage, and the fact that Vitamin D is anti-cancer. Fifth, this study was conducted on a small sample size precludes generalizability of the findings to a large diverse population.

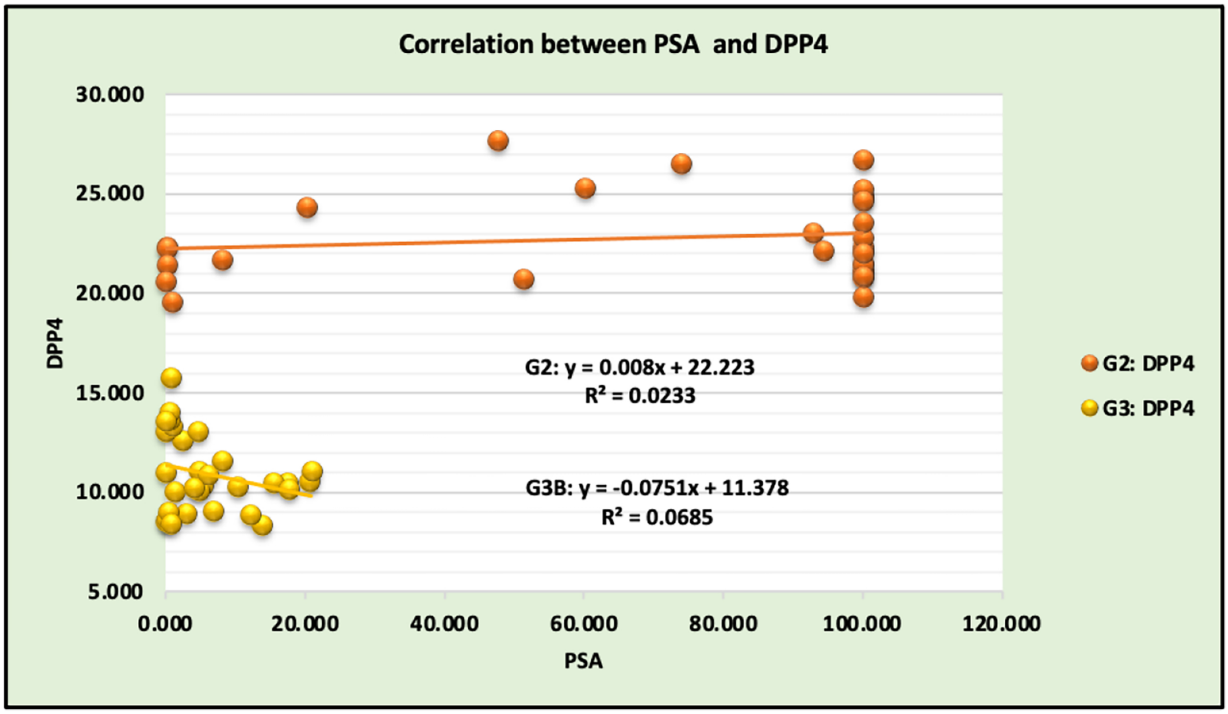

Fig. 1. Correlation between PSA and DPP4.

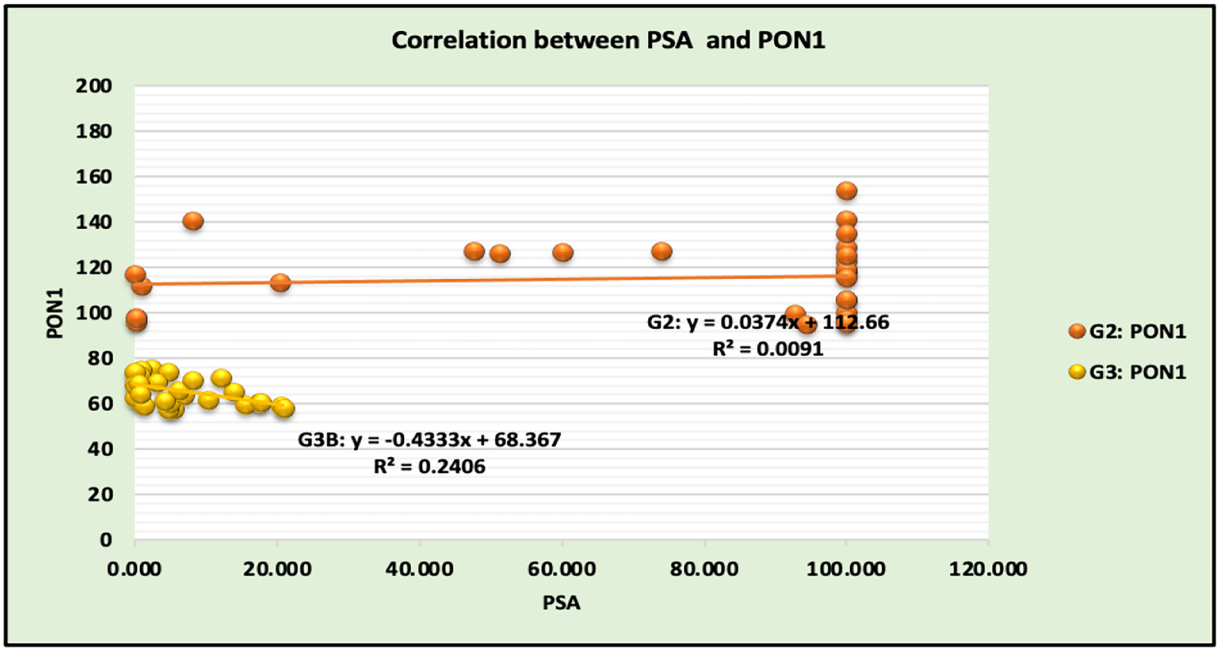

Fig. 2. Correlation between PSA and PON1.

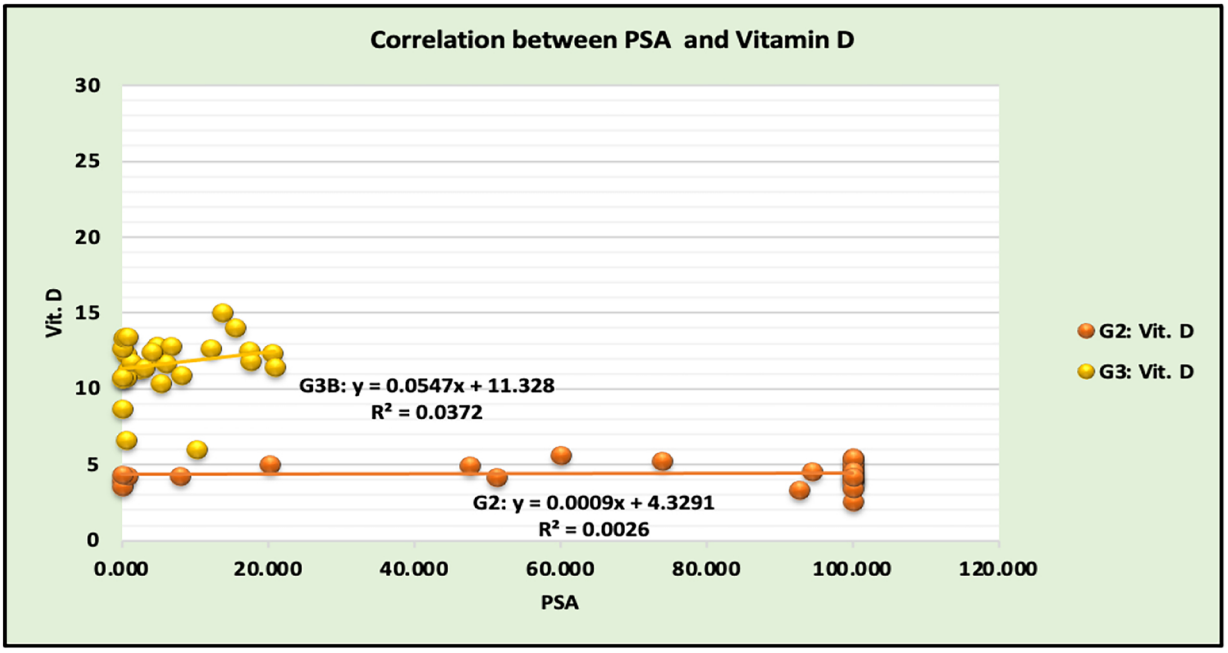

Fig. 3. Correlation between PSA and Vitamin D.

Table 4. Correlation between DPP-4 with PON-1 & Vitamin D.

	Factor	PON-1	Vit.D
DPP-4			
G2	R (person)	0.157	0.454
	P	0.407	0.012*
G3	R (person)	0.365	–0.535
	P	0.047*	0.0002**

NS: non-significant (p-value > 0.05), *S: significant (0.01 < p-value ≤ 0.05), **HS: high significant (p-value ≤ 0.01).

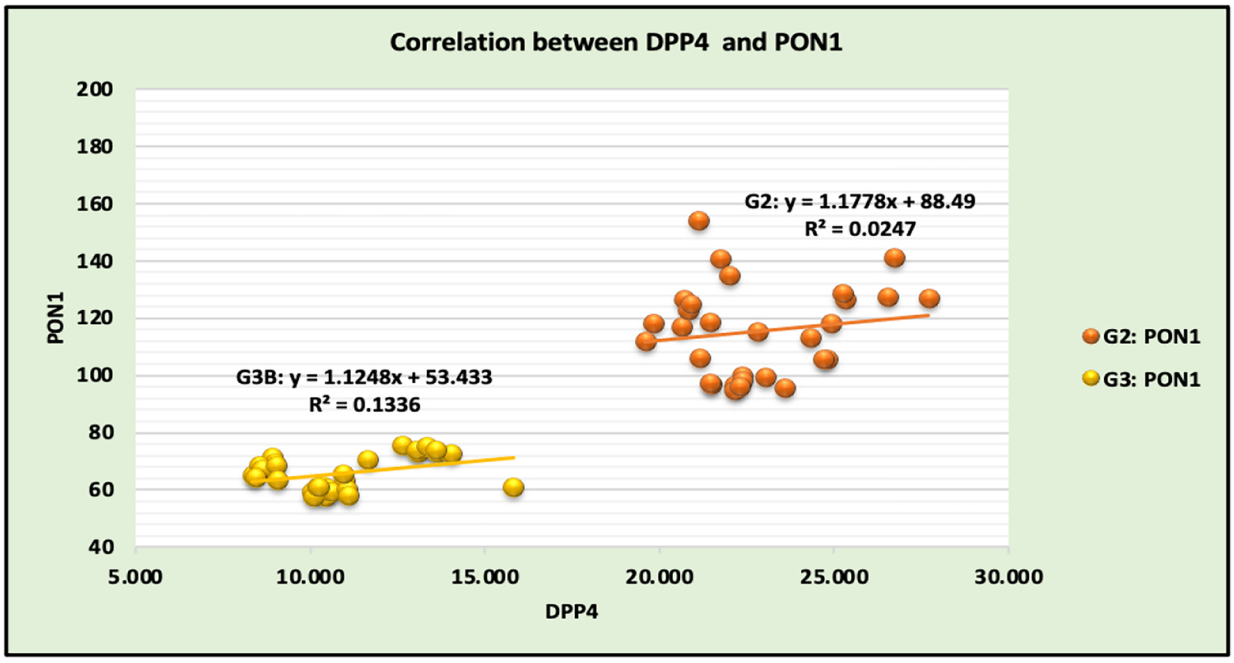

Fig. 4. Correlation between DPP4 and PON1.

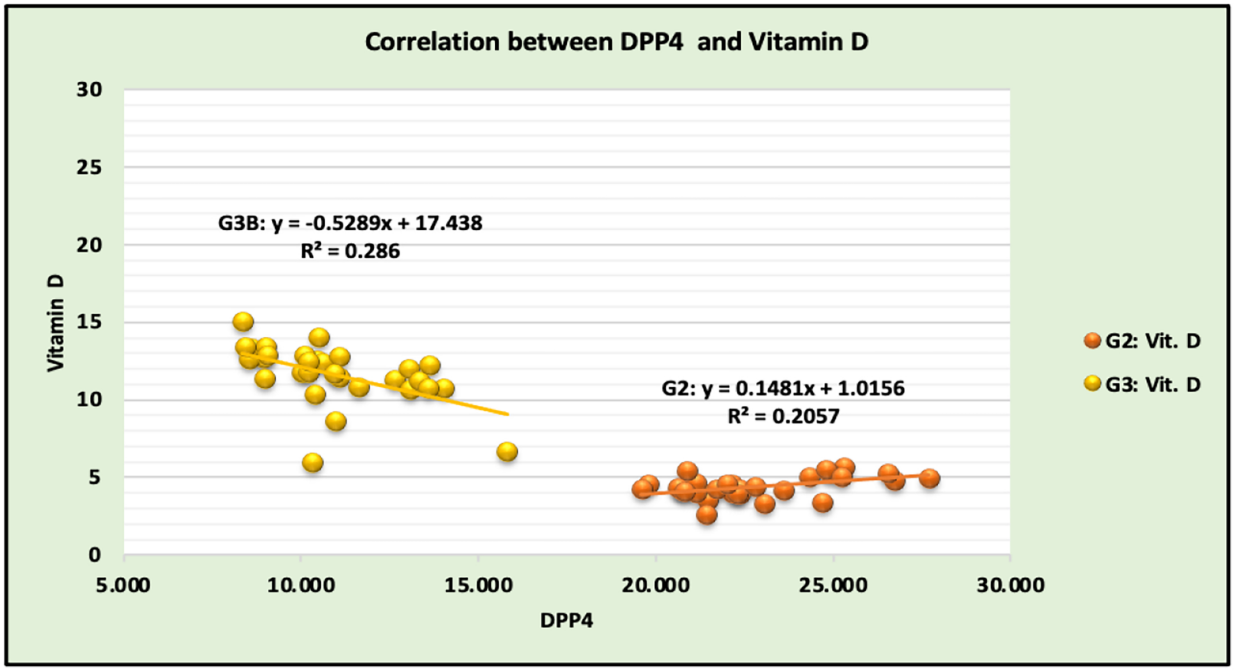

Fig. 5. Correlation between DPP4 and Vitamin D.

Evaluating correlations

Tables 3 and 4 represents the correlation for PSA and DPP-4 with other parameters by use person correlation for G2 and G3 (prostate cancer patients with chemotherapy and hormonal therapy), respectively.

For patients after chemotherapy, all parameters were positively non-significant with PSA; while after hormonal therapy positive associations between PSA with Vitamin D were recorded. However, a negative higher significant correlation with PON-1 and negative non-significant associations with DPP-4 was recorded. Figs. 1 to 3 show the

Table 5. The receiver operating characteristic (ROC), sensitivity, and specificity for PSA.

Variables	Area under the curve	Sensitivity	Specificity	95% C.I.		Cut off value
				L.B.	U.B.	
PSA	0.847	0.935	0.832	0.732	0.963	0.830

associations of PSA with DPP-4, PON-1, and Vitamin D, respectively.

For group 2, non-significant positive correlations were recorded with PON-1, while significant correlations with Vitamin D were scored. Despite this, a highly negative relationship with Vitamin D and a positive, non-significant relationship with PON-1 for group 3 resulted with the DPP-4 enzyme were recorded. These correlations of the enzyme with DPP-4 and Vitamin D can be observed in Figs. 4 and 5, respectively.

Receiver operating characteristic (ROC)

The Receiver Operating Characteristic curve is an equation used to determine the sensitivity and specificity of a test for diagnosis using a graphic that depicts the relationship between sensitivity and 1-specificity. In order to determine it, when the test results are positive, the cut-off points are computed, which corresponds to several places on the displayed curve.[51]

Table 5 shows the (ROC) curve analysis for PSA across all the groups reveals an impressive area under the curve (AUC) value of 0.847. This AUC value is statistically significant at a confidence level of 95%, as indicated by the p-value of 0.001, which is less than the threshold of 0.01.

The optimal cut-off value for PSA is determined to be 0.830, with a sensitivity of 93.5% and a specificity of 83.2%. This suggests a high level of accuracy in distinguishing between the groups. The results are graphically represented in Fig. 6, which visually illustrates the robustness and efficacy of the PSA test across all the groups.

Table 6 shows the (ROC) curve analysis for DPP4 across all the groups revealing an impressive area under the curve (AUC) value of 0.999. This AUC value is statistically significant at a confidence level of 95%, as indicated by the p-value of 0.001, which is less than the threshold of 0.01.

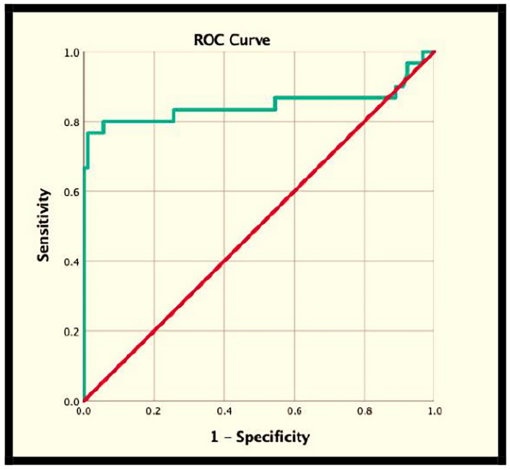

Fig. 6. The receiver operating diagnosis for PSA.

The optimal cut-off value for DPP4 is determined to be 18.845, with a sensitivity of 98.3% and a specificity of 99.2%. This suggests a high level of accuracy in distinguishing between the groups. The results are graphically represented in Fig. 7, which visually illustrates the robustness and efficacy of the DPP4 test across all the groups.

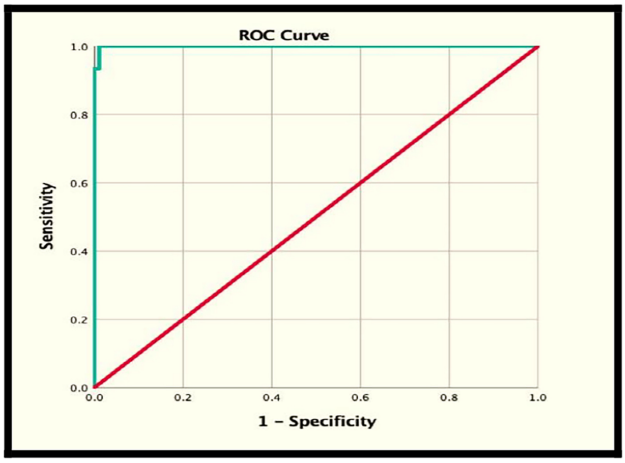

Fig. 7. The receiver operating diagnosis for DPP4.

Table 6. The receiver operating characteristic (ROC), sensitivity, and specificity for DPP4.

Variables	Area under the curve	Sensitivity	Specificity	95% C.I.		Cut off value
				L.B.	U.B.	
DPP4	0.999	0.983	0.992	0.997	1	18.845

Table 7. The receiver operating characteristic (ROC), sensitivity, and specificity for PON1.

Variables	Area under the curve	Sensitivity	Specificity	95% C.I.		Cut off value
				L.B.	U.B.	
PON1	0.854	0.913	0.818	0.787	0.920	96.769

Table 8. The receiver operating characteristic (ROC), sensitivity, and specificity for Vitamin D.

Variables	Area under the curve	Sensitivity	Specificity	95% C.I.		Cut off value
				L.B.	U.B.	
Vitamin D	0.937	0.927	0.952	0.902	0.963	15.5

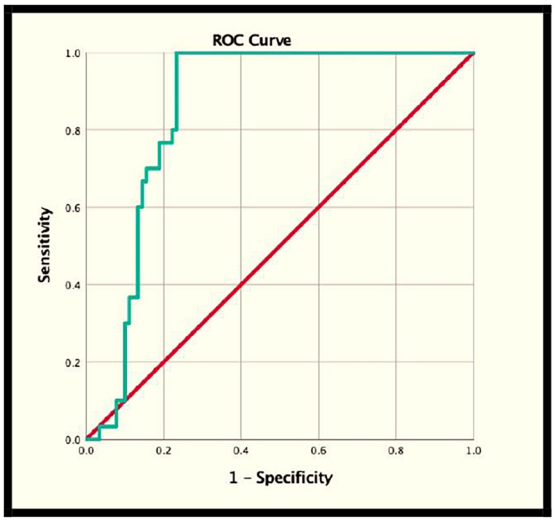

Fig. 8. The receiver operating diagnosis for PON1.

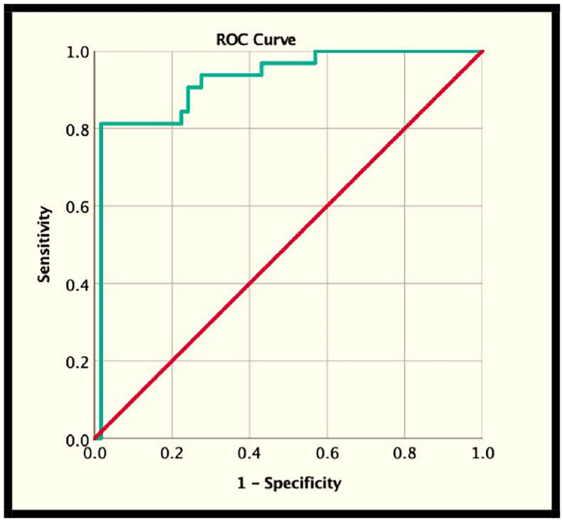

Fig. 9. The receiver operating diagnosis for Vitamin D.

Table 7 shows the (ROC) curve analysis for PON1 across all the groups revealing an impressive area under the curve (AUC) value of 0.854. This AUC value is statistically significant at a confidence level of 95%, as indicated by the p-value of 0.006, which is less than the threshold of 0.01.

The optimal cut-off value for PON1 is determined to be 96.769, with a sensitivity of 91.3% and a specificity of 81.8%. This suggests a high level of accuracy in distinguishing between the groups. The results are graphically represented in Fig. 8, which visually illustrates the robustness and efficacy of the PON1 test across all the groups.

Table 8 shows the (ROC) curve analysis for Vitamin D across all the groups revealing an impressive area under the curve (AUC) value of 0.937 This AUC value is statistically significant at a confidence level of 95%, as indicated by the p-value of 0.007, which is less than the threshold of 0.01.

The optimal cut-off value for Vitamin D is determined to be 15.5, with a sensitivity of 90.2% and a specificity of 96.3%. This suggests a high level of accuracy in distinguishing between the groups. The results are graphically represented in Fig. 9, which visually illustrates the robustness and efficacy of the Vitamin D test across all the groups.

Conclusion

In addition to PSA and Vitamin D, the two primary indices (PON-1 and DPP-4) are strongly related with prostatic cancer patients. Vitamin D, on the other hand, is dramatically altered with prostate cancer and may be regarded a risk factor as long as they are organized in one cluster with primary biomarkers. According to ROC analysis, the optimum cutoff value for PON-1 is 96.769 ng/ml, while the best cutoff value for the other one (DPP-4) is 18.845 ng/ml. The mentioned parameters demonstrate high level of accuracy.

Acknowledgment

After accomplishing the study, we extend our thanks, appreciation and gratitude first to the patients without whom this study would not have been completed, and thanks to Dr. Karar Al-Moussawi,

Dr. Hosna, Dr. Ahmed Kanaan, and Dr. Ahmed Fawzi at the Al-Amal Center for Oncology, as well as Dr. Furat at the Oncology Teaching Hospital, for their great contributions and assistances to have this research done. All appreciation goes to the mother university, the University of Baghdad for providing the necessary supplies for the research.

Authors' declaration

- Conflicts of Interest: None.
- We hereby confirm that all the figures and tables in the manuscript are ours. Furthermore, any figures and images, that are not ours, have been included with the necessary permission for republication, which is attached to the manuscript.
- No animal studies are present in the manuscript.
- Authors sign on ethical consideration's approval.
- Ethical Clearance: Ethical approval was obtained from the research committee at University of Baghdad.

Authors' contribution statement

Both of the authors A H. A. and A F. A. contributed to the design and implementation of the results and to the writing of the manuscript.

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تقدير باراوكسوناز-1 وثنائي الببتيديل ببتيداز في سرطان البروستاتا العراقي مع الهرمونات وأدوية العلاج الكيميائي; دراسة مقطعية

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المستخلص

سرطان البروستاتا هو مرض شائع عند الذكور، وخاصة عند التقدم في السن. باروكسوناز-1 (PON-1) هو إنزيم موجود في جسم الإنسان ويلعب وظيفة مهمة في منع الإجهاد التأكسدي والالتهابات. ويرتبط في الغالب بالبروتين الدهني عالي الكثافة(.HDL Dipeptidyl peptidase-4 DPP-4) هو إنزيم ينظم مستويات السكر في الدم. يوجد على العديد من أسطح الخلايا: الخلايا المناعية، والخلايا الظهارية، وخلايا البنكرياس. كان الهدف من هذه الدراسة المقطعية هو تحديد الدور الكيميائي الحيوي لتأثير PON-1 وإنزيمات DPP-4 مع القدرة المضادة للسرطان لفيتامين د. تم جمع عينات البحث من مرضى سرطان البروستاتا العراقيين (الذكور الذين تتراوح أعمارهم بين 45-80 سنة)) تم تشخيصها بعد تلقي العلاج الكيميائي (30 عينة G2)، والعلاج الهرموني (30 عينة G3)، مقارنة بمجموعة السيطرة (G1). تم استخدام تقنية ELISA لتقدير مستويات مصل الإنزيمات مع فيتامين د. وسجلت النتائج زيادة في مستويات PON-1 لـ G2 ((115.33±15.92 (قيمة $p<0.0001$)، وزيادة طفيفة لـ((65.85±6)G3 (قيمة $p > 0.05$)، مقارنة بـ ± 61.99))G1 9.82. هناك زيادة في فعالية إنزيم DPP-4 للمرضى بعد العلاج الكيميائي والعلاج الهرموني (22.79±2.12) (قيمة p <0.0001) و (10.93±1.96) (قيمة $p<0.0001$) على التوالي، مقارنة بـ1.09 ± 8.51))G1. كان هناك فقدان شديد لفيتامين D في 0.69 ± 4.39))G2(قيمة $p<0.0001$) و(1.61 ± 11.85) G3(قيمة $p<0.0001$) مقارنة بـ2.36 ± 18.92))G1. وتشير النتائج إلى دور هذه الإنزيمات كمؤشر حيوي لمرضى سرطان البروستاتا وتطوره، ويعتبر نقص فيتامين د أحد عوامل الخطر لدى هؤلاء المرضى.

الكلمات المفتاحية: ثنائي ببتيديل ببتيداز-4، باروكسوناز-1، سرطان البروستات، مستضد البروستات النوعي، فيتامين د.