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Evaluate the Serum of Irisin, Omentin-1, and Oxidative Status in Males with Prostatic Cancer

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Abstract

Background: Prostate cancer is a classic public health problem in males and has broadly different levels of mortality and morbidity. As an endocrine gland, adipose tissue synthesizes and secretes a variety of bioactive peptides, such as irisin and omentin-1. Adipokines and oxidative stress potentially contribute to the proliferation of prostatic carcinoma cells. The relationship between irisin, omentin-1, and oxidative stress has not been widely investigated in prostate cancer. Therefore, the present research assessed whether there is a significant correlation between irisin and omentin-1 levels and oxidative status in prostate cancer individuals.

Methods: The present research recruited 40 individuals diagnosed with prostate cancer and 40 healthy individuals for comparative purposes. All individuals underwent demographics, biochemicals, and serum adipokines (irisin and omentin-1) data analysis.

Results: The means of total prostate-specific antigen (43.3±20.5 vs. 2.5±1.2) and free prostate-specific antigen (2.1±1.4 vs. 0.08±0.02) were highly significant increases in the prostate cancer patients than in the healthy individuals. Furthermore, the means of omentin-1 (31.6±12.8 vs. 23.5±14.1) and total oxidant stress (22.4±10.6 vs. 9.1±3.6) were highly significant increases in patients with prostate cancer than in healthy individuals. In contrast, the means of irisin (343.5±240.2 vs. 716.4±142.3) and total antioxidant capacity (2.2±1.2 vs. 3.3±1.3) were highly significant decreases in patients with prostate cancer than in healthy individuals. No significant relationship was demonstrated between all parameters in the two groups under study.

Conclusion: The study findings indicate that irisin and omentin-1 could serve as biomarkers for predicting prostate cancer.

Keywords: FNDC5 protein, ITLN1 protein, Oxidative Stress, Prostatic Neoplasms.

Introduction

Prostate cancer is a prevalent kind of no-cutaneous malignancy affecting men worldwide (1). Prostate cancer is a heterogeneous complex malignant growth that shows broadly different levels of mortality and morbidity. In recent years, prostate cancer has progressively been perceived as a severe and overall general well-being concern (2). A significant cause of this kind of cancer is still unclear, but recent epidemiologic reports have shown some exciting clues like obesity, family history, smoking, age, and sedentary lifestyle (3).

Obesity has been the subject of a significant number of research. This research has shown the critical risk of obesity in prostatic cancer and other types of cancers like breast, pancreas, colon, and ovary (4).

Adipose tissues secrete a different bioactive peptide known as adipokines, which precipitate in numerous processes inside human bodies (5). Over the past two decades, various researchers have sought to determine the role of adipose tissue in the progression of several types of cancer by participating in the onset of inflammation and carcinogen

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formation (6). Recent evidence suggests a close association between changes in the levels of adipokines and prostatic cancer (7). Irisin (FNDC5) is a 22-24 KD peptide synthesized by fat cells and skeletal muscle (8). Irisin plays an essential role in the regulation of homeostasis of body energy (9). Vivo and vitro studies have clearly shown a correlation between irisin and cancer. In a study that set out to determine irisin in breast cancer, which is a cancer correlated with obesity like prostatic cancer, the level of irisin was found to be significantly decreasing compared with healthy individuals (10). A recent study reported the role of irisin in regulating the division and proliferation of prostate cancer cells (11).

Omentin-1 (ITLN1) is a 34 KD peptide with anti-inflammatory and anti-insulin resistance effects (12). Recently, researchers have demonstrated that omentin-1 has a critical role in cell differentiation and speeding up cell death (apoptosis) in cancer cells (13). Many related studies found that individuals with renal cell cancer and colorectal cancer have different circulating concentrations of omentin-1, suggesting that omentin-1 may be involved in the development of cancer (14). However, there has been limited investigation into omentin-1 in prostate cancer.

Oxidative stress refers to the incapacity of a biological system to remove reactive oxygen species in cells and tissues resulting from an imbalance between their production and accumulation (15). A considerable amount of published research illustrates the role of oxidative stress and the resulting oxidative damage as essential variables influencing the formation and progression of cancer (16). Furthermore, several studies have found a linkage between oxidative stress with irisin and omentin-1 in metabolic diseases (17,18). However, few observations have demonstrated the relationship between oxidative stress and adipokines in prostate carcinogenesis patients.

The current research was designed to evaluate the serum level of irisin and omentin-1 in males with prostatic cancer and reported any correlation between irisin and omentin-1 with oxidative stress variables.

Materials and Methods

Study design and participants

A random sample of 40 males with prostate cancer and 40 healthy males were recruited over five months (2023-2024) ranging from 50-65 years of matched age. The Oncology Teaching Hospital in Medical City, Baghdad, diagnosed all participants in the current study based on the American Urological Association (AUA), where a biopsy was taken from the prostate to look for cancer cells and define via Gleason grading system (19) from 6 to 10 score. The cells look similar to normal prostate cells when the Gleason score is ≤ 6, while the cells look abnormal when the Gleason score is ≥ 8. In the current study, males with prostate cancer participated when the Gleason score was ≥ 8.

Exclusion Criteria

Individuals with metabolic diseases, cardiovascular diseases, acute and chronic infective diseases, kidney diseases, muscle diseases, other malignancies or benign tumors, and those who performed routine heavy exercise and took supplements or vitamins were excluded from our study based on these factors may potentially influence the level of irisin and omentin-1 or even oxidative stress variables.

Blood Sample Collections

In the present study, five milliliters of venous blood were taken from all participants after overnight fasting for 8-12 hrs. Five milliliters of whole blood were placed into a gel tube and left to clot for 10 minutes. Three milliliters of blood serum were separated at room temperature after centrifugation at 1814 x g and kept at -70 °C until analyzed.

Calculation of Body Mass Index

Body mass index (BMI) is calculated by dividing an individual's weight (measured in

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kilograms, Kg) by the square of their height (measured in meters, m^2).

Measurement of Biochemical Parameters

Total prostate-specific antigen (TPSA) and free prostate-specific antigen (FPSA) were determined using the ECLIA (electrochemiluminescence-immunoassay) through the Roche Cobas e411 autoanalyzer system (Roche-Hitachi Diagnostics, Japan). The colorimetric methods developed by Erel (20,21) were used to measure the levels of total oxidant stress (TOS) and total oxidant capacity (TAC). Determination of TOS is conducted by oxidizing iron from a ferrous state to a ferric state using serum oxidants in the presence of an acidic medium. Iron in a ferric state enhances the formation of a pigmented compound with xylene orange; the overall concentration of oxidant molecules in serum can be measured using a spectrophotometer. The compound H_2O_2 was utilized as a calibrator for the TOS test. Determination of TAC depends upon the Fenton reaction, where the presence of antioxidants in serums inhibits oxidative processes, resulting in no change in color. In addition, the TAC of the serums can be evaluated. Irisin (pg/mL) and omentin-1 (ng/mL) have been measured using sandwich-ELISA kits according to the protocol manufacturer (Elabscience, Texas, USA).

Statistical Analysis

The statistical significance of the demographic and biochemical data among prostate cancer and healthy individual groups was analyzed through GraphPad Prism software (San Diego, California, USA). A student's t-test was conducted to evaluate mean ± standard deviation and statistical significance (p-value) to compare the means of the two groups under study. P-value < 0.05 has been considered statistically significant. The current study employed Spearman's correlation coefficient to examine the correlations between variables.

Results

Table 1 displays the demographic data of the studied groups (prostate cancer and healthy individuals). The findings revealed no significant differences in terms of BMI and age between the group diagnosed with prostate cancer and the healthy control group.

Table 2 compares the experimental data of TPSA, FPSA, TOS, and TAC serums in prostate cancer and healthy individual groups. These data show the highest TPSA, FPSA, and TOS values in prostate cancer patients compared with healthy control individuals, with higher significant differences. In contrast, the lower total antioxidant capacity values in prostate cancer patients compared with healthy control individuals also show substantial differences.

Figure 1 compares the means of serum irisin and omentin-1 in prostate cancer and control groups. The most important clinically relevant finding was that the serum level of irisin strongly decreased in prostate cancer patients compared with healthy individuals, with highly significant differences. Conversely, the prostate cancer group had a higher mean of serum omentin-1 than the control group, with highly significant differences.

Table 3 displays Spearman's correlation coefficient between different parameters among the two studied groups (prostate cancer and control). The present study's multiple regression analysis did not demonstrate any significant correlation among variables in the two groups.

Table 1. Statistical analysis of descriptive characteristics among prostate cancer and healthy groups.

Variable	Prostate Cancer Group (N=40)	Control Group (N=40)	P-value	Significant
Age (years)	54.1±14.5	52.3±11.1	0.682	**NS**
BMI (Kg/m^2)	27.1±5.1	26.8±3.3	0.136	**NS**

BMI: Body Mass Index, **NS:** Non-Significant.

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Table 2. Compares serum TPSA, FPSA, and oxidative stress status in prostate cancer and control groups.

Variable	Prostate Cancer Group (N=40)	Control Group (N=40)	P-value	Significant
TPSA (ng/mL)	43.3±20.5	2.5±1.2	<0.0001	**HS**
FPSA (ng/mL)	2.1±1.4	0.08±0.02	<0.0001	**HS**
TOS (µmol /mL)	22.4±10.6	9.1±3.6	<0.0001	**HS**
TAC (mmol /mL)	2.2±1.2	3.3±1.3	0.031	**S**

TPSA: Total Prostate-Specific Antigen, **FPSA:** Free Prostate-Specific Antigen, **TOS:** Total Oxidative Stress, **TAC:** Total Antioxidant Capacity, **HS:** Highly Significant, **S:** Significant.

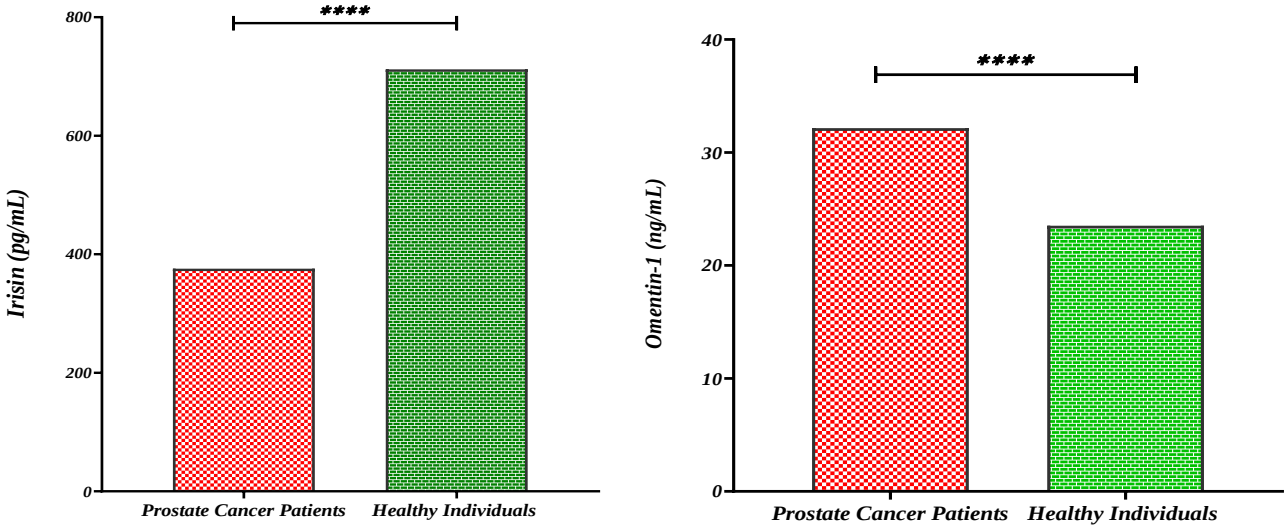

Fig. 1. Compares serum of irisin and omentin-1 in prostate cancer and control groups. The results are shown as mean, and **** indicates statistically significant differences with P-value = <0.0001.

Table 3. Spearman's correlation coefficient of irisin and omentin-1 with other variables in the two studied groups.

Variable / Groups	Irisin		Omentin-1	
	r	P	r	P
BMI (Kg/m^2)				
Control	0.171	0.323	0.284	0.144
PC	0.312	0.116	0.301	0.109
TPSA (ng/mL)				
Control	0.211	0.325	0.387	0.425
PC	-0.183	0.222	0.333	0.460
FPSA (ng /mL)				
Control	0.215	0.240	0.220	0.265
PC	-0.254	0.201	0.103	0.495
TOS (µmol /mL)				
Control	-0.244	0.171	0.411	0.241
PC	0.211	0.422	-0.238	0.206
TAC (mmol /mL)				
Control	0.170	0.370	0.247	0.376
PC	0.161	0.396	0.188	0.396

*r: linear Correlation Coefficient, P: P-value.

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Discussion

Several works have demonstrated that adipokines and oxidative stress could be significant factors in prostate malignant tumor growth (22, 23). However, no research has examined the correlation between irisin and omentin-1 with oxidative stress in prostate carcinogenesis. Therefore, the present study assessed whether there is a significant correlation between irisin and omentin-1 levels and oxidative status in prostate cancer individuals.

The most important clinically relevant finding in the current research was that the mean of serum irisin strongly decreased in prostate cancer patients compared to healthy individuals, with a highly significant difference. This finding agrees with the recent research (24) finding, which showed significantly decreasing irisin levels in a group with prostatic carcinoma than in the control group. The decreasing value of serum irisin in prostatic carcinoma supports the evidence for a correlation between irisin and cancer. The findings of studies on the levels of irisin in cancer have been contentious. The results of previous research showed a decreasing level of serum irisin in colorectal cancer (25) and breast cancer (26). On the other hand, recent previous reports observed the increasing level of serum irisin in gastrointestinal (GIS) cancers (27), ovarian, endometrial cancers, cervical (28), and hepatocellular carcinoma (29). Irisin hormone positively or negatively affects cancer tissue proliferation, invasion, and migration in different types of benign and malignant tumors (30,31). A primary reason for decreasing the level of irisin in individuals with prostatic cancer is still unclear. Some critical interpretations need to be considered in this subject. According to prostatic cancer cell line studies, irisin can prevent the development of prostatic malignant tumors and trigger apoptosis by blocking the epithelial-to-mesenchymal transition (EMT), crucial in advancing prostate cancer by affecting different signaling pathways (32). On the other hand, prostate cancer is a type of tumor that relies on hormones for its development. Approximately 90% of prostatic cancer cases are associated with the stimulation of the male sex hormones called androgens (33), the axis of insulin/ IGF-1 (Insulin-Like Growth Factor-1) (34), and other adipokines (35), which are related to prostate cancer.

In recent years, omentin-1 has been identified as one of the adipokines prominent in human adipose tissue. Multiple studies have investigated changes in the levels of omentin-1 in different types of cancer patients and suggested that omentin-1 has a possible contribution to the development of carcinogenesis (36). However, the investigation of omentin-1 levels in prostate cancer has been rarely explored, particularly among the Iraqi population. In the current investigation, we investigated that the mean of serum omentin-1 showed a highly significant increase in prostate cancer patients compared to healthy individuals. Our results agree with those of another study, which indicates a highly significant increase in omentin-1 in males with prostatic carcinoma compared to healthy males (37). The specific clarification of the pathophysiology of omentin-1 in cancer remains unclear. Prior research has clarified a potential mechanism that pertains to the relationship between cancer and omentin-1 (38), which finds omentin-1 enhanced apoptosis in hepatocellular carcinoma by increasing the ratio of bax-to-bacl-2 and inhibiting the activation of caspases-3. In addition, a recent investigation has shown that omentin-1 can enhance phosphorylation and activation of the Akt signaling pathway (39). Concurrently, the PI3K/Akt-eNos Ras pathway contributed an essential part in the development of tumors (40).

In recent decades, evidence from epidemiological, experimental, and clinical investigations has consistently shown a significant association between oxidative stress markers and the initiation and advancement of prostate cancer (23). The findings in the current study indicate that Individuals with prostatic cancer have a significantly elevated level of total oxidative

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stress compared to healthy individuals. In contrast, total antioxidant capacity is significantly decreased in males with prostatic carcinoma than healthy males. Our results agree with the findings of previous research (41), in which levels of total oxidative stress are markedly increasing, while total antioxidant capacity is decreased in males with prostatic cancer. Eventually, the decrease in total antioxidant capacity level could be explained by the fact that the activities of antioxidant compounds decrease when the balance of reactive oxygen species-antioxidant compounds in prostatic tissue is destroyed (42). Furthermore, the lifestyle of males with prostatic carcinogenesis in the current study might have contributed to a decrease in antioxidant species and may have contributed to the development of prostatic carcinogenesis (43).

Maintaining glucose homeostasis and reducing inflammation rely heavily on irisin and omentin-1 (44), accompanied by a reduction in reactive oxygen species. This suggests that cancer patients have a relationship between irisin and omentin-1 with reactive oxygen species (45). However, the correlation between irisin, omentin-1, total oxidative stress, and total antioxidant capacity was not assessed. Thus, the current research is the first to investigate the correlation between irisin, omentin-1, total oxidative stress, and total antioxidant capacity in prostatic cancer. No significant relationship was observed between irisin and omentin-1 with total oxidative stress and total antioxidant capacity in the two studied groups investigated. Unknown variables mediated by the body's irisin and omentin-1 with the oxidative stress system might account for the absence of correlations. Further investigations are required to establish the relationship between irisin and omentin-1 with oxidative stress in prostatic carcinoma. A limitation of the current study is that the number of patients was relatively small. Notwithstanding this limitation, further experimental parameters are needed to more closely examine the correlation between irisin and omentin-1 with oxidative status.

Two of the more significant findings to emerge from this study are that the level of irisin significantly decreases and the level of omentin-1 substantially increases in patients with prostatic cancer compared with healthy individuals. From our results in the current study, irisin and omentin-1 levels could be used as a marker for prostatic cancer diagnosis.

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Ethical Consideration

The study is carried out by the guidelines outlined in the Declaration of Helsinki and approved by the scientific and ethical committee at the College of Science/Mustansiriyah University (PG/270 on 23/10/2023). Moreover, all subjects provided ethical consent.

Conflicts of interest

Researchers do not have any conflicts of interest.

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