Cell. Mol. Biol. (ISSN: 1165-158X)

Journal Homepage: www.cellmolbiol.org

Cellular and Molecular Biology

Original Article

Evaluation of serum levels of irisin, tumor necrosis factor and some biochemical variables in males with prostate cancer in Baghdad City

Hanan Shihab Ahmad[1*], Araf Sabah Abdulwahed[2], Marwan Abdulrazzaq Kamil[3]

[1] *Al Door Technical Institute, Northern Technical University, Mosul, Iraq*
[2] *Tikrit University, College of Girls' Education, Tikrit, Iraq*
[3] *Al Door Technical Institute, Northern Technical University, Mosul, Iraq*

Article Info

Article history:

Received: August 17, 2024
Accepted: December 08, 2024
Published: December 31, 2024

Use your device to scan and read the article online

Abstract

Prostate cancer is the most common type after the age of fifty. It affects males and affects the prostate gland, which protects the function of sperm by producing semen. The current study was designed to evaluate prostate cancer infection effects on some biomarkers such as irisin, Tumor necrosis factor-TNF-α, prostate acid phosphates -PAP, Glutathione-GSH, malondialdehyde-MDA, urea, and creatinine. The study was conducted on 50 males infected with prostate cancer and 30 healthy males (control group) who attended the Baghdad Teaching Hospital –Medical City Center/Baghdad, Iraq, from 20/6/2024 to 1/8/2024. The results of the current research showed a significant elevation in (Irisin, TNF-α, PAP, MDA, urea, and creatinine) concentration and a significant decrease in (GSH) concentration in the serum of patients compared to the healthy subjects in the probability of P≤0.05. Irisin and some variables are important physiological biomarkers that can support the diagnosis of prostate cancer.

Keywords: Antioxidant, Irisin, Prostate cancer, TNF-α

1. Introduction

Prostate cancer is the second leading cause of death among men in most developed countries in the world [1]. Age is the most important factor for prostate cancer, as men under the age of 40 are unlikely to develop prostate cancer [2], as found by about 96 % of most prostate cancers are adenocarcinomas and 4% of the transitional epithelium of the urethra or ducts. Symptoms do not usually appear in the early stage and are often diagnosed during routine rectal examinations, as most patients die in the initial stages of the disease for reasons unrelated to the malignancy of prostate cancer. In most patients, the average age of those infected is 72 years [3].

Irisin is a polypeptide hormone that was discovered in 2012 by Bostrom. It is produced as a result of the cleavage of a protein called FNDC5. It is present in human serum and is widely expressed in the skeletal muscle and heart [4].

Tumor necrosis factor-alpha (TNF-α) is a potent, multifunctional cytokine that exerts a wide range of effects on various cell types. It has been shown to influence hormone synthesis, placental formation, fetal development, and steroidogenesis [5]. Additionally, TNF-α plays a significant role in placental differentiation and the process of childbirth. Structurally, TNF-α is a homotrimeric protein composed of 157 amino acids and is primarily produced by activated macrophages, T lymphocytes, and dendritic cells. This cytokine is crucial for initiating the acute inflammatory response and has the capacity to activate the adaptive immune response [6]. It has also been found that tumor necrosis factor works to stimulate inflammatory responses not only directly by stimulating. Inflammatory gene expression but indirectly by causing cell death, stimulating inflammatory immune reactions and disease progression [7].

Research into antioxidants has recently become increasingly active in various fields [8], looking into the two types of natural and synthetic antioxidants, and due to their use as supplements and nutritional and functional components [9]. Therefore, antioxidants are defined as a molecule or compounds that hinders or delays the oxidation of biomolecules and works at low concentrations compared to other concentrations. Protected molecules by inhibiting the formation of free radicals and their ability to interact with

* Corresponding author.
E-mail address: hanan.sha@ntu.edu.iq (H. S. Ahmad).
Doi: http://dx.doi.org/10.14715/cmb/2024.70.12.21

their biological targets by giving them electrons, and this is what primary antioxidants do and thus produce stable, non-reactive radical and non-radical species that can be decomposed later through enzymes and other processes [10, 11]. Glutathione is one of the antioxidants, as it is the most abundant low molecular weight thiol inside cells and body tissues, which plays an essential role in many cellular processes, including its work as an antioxidant and its role in regulating protein function and stability, gene expression, cell proliferation, and regulating signals between cells [12]. It is an important non-enzymatic antioxidant that is manufactured within the body [13].

2. Materials and Methods

2.1. Study subjects

A case-control study was conducted on 50 male patients enrolled at Baghdad Teaching Hospital –Medical City Center /Baghdad, Iraq. Fifty of them were diagnosed with prostate cancer and thirty with healthy males (control group) with ages ranging from 35 to 70 years. The study was done during the period from 20/6/2024 to 1/8/2024 in Baghdad, Iraq. The current study was designed to evaluate the effects of prostate cancer on various physiological parameters, including irisin, tumor necrosis factor (TNF), prostate acid phosphatase (PAP), glutathione, malondialdehyde, urea, and creatinine in blood serum. These parameters were measured using a kit developed by Cloud-Clone Corp, an American company. For the assessment of antioxidants, glutathione (GSH) levels were determined according to the researchers' method [14, 15]. While the MDA was measured according to the researcher's method [16], as for kidney function the urea, was calculated according to the law of the researcher's method [17]. Creatinin was estimated according to Tietz et al. [18] method. Also, the activity of prostate acid phosphates-PAP was measured using the researcher's method [19].

2.2. Statistical analysis

The data were analyzed using SPSS version 27. The differences of significant M ± SD were estimated by the Independent-Samples T-test. A probability of (P) value <0.05 is regarded as significant.

3. Results

The physiological and biochemical variables studied were analyzed in two test groups. The results of the current research showed a significant (P≤0.05) elevation in (Irisin, TNF-α, PAP, MDA, Urea, and Creatinine) concentration and a significant (P≤0.05) decrease in (GSH) concentration in the serum of male patients compared to healthy males (Table 1; Fig. 1-7).

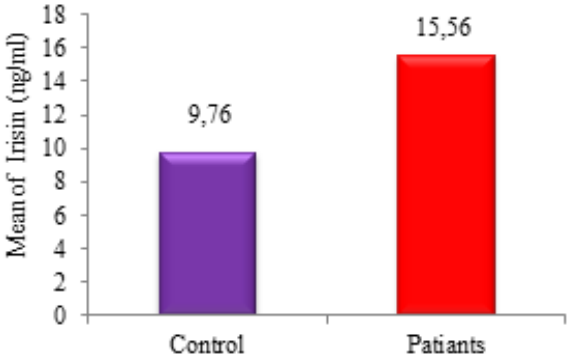

Fig. 1. Irisin concentration in the blood serum of both groups.

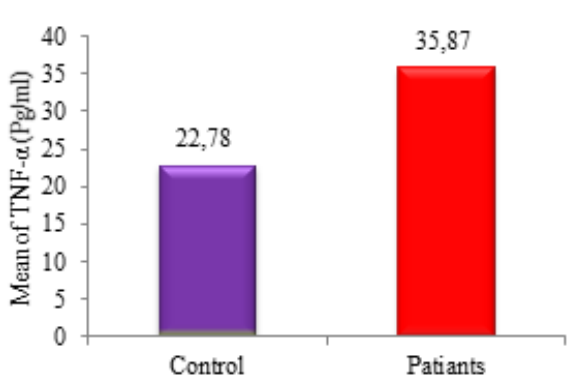

Fig. 2. TNF-α concentration in the blood serum of both groups.

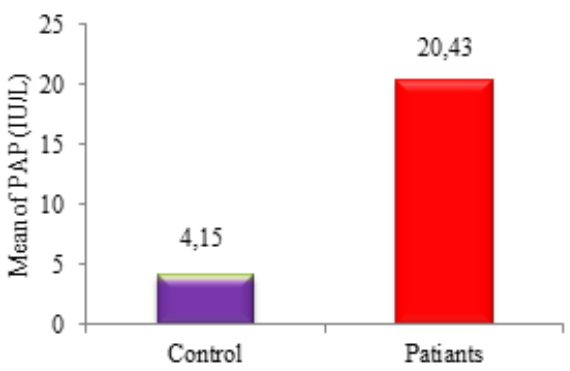

Fig. 3. PAP activity in the blood serum of both groups.

Table 1. The mean ± S.D of all parameters in the two study groups.

Groups / Parameters	Mean ± SD	
	Control (n = 30)	Patients (n = 50)
Irisin (ng/ml)	9.76±2.13	15.56±3.23
TNF-α (pg/ml)	22.78±5.76	35.87±6.34
PAP (IU/L)	4.15±1.01	20.43±4.31
GSH (mmol/L)	3.12±0.67	1.45±0.12
MDA (mmol/L)	4.32±1.54	15.56±3.21
Urea (mg/dl)	25.34±5.78	40.87±7.56
Creatinine (mg/dl)	0.31±0.021	0.61±0.031

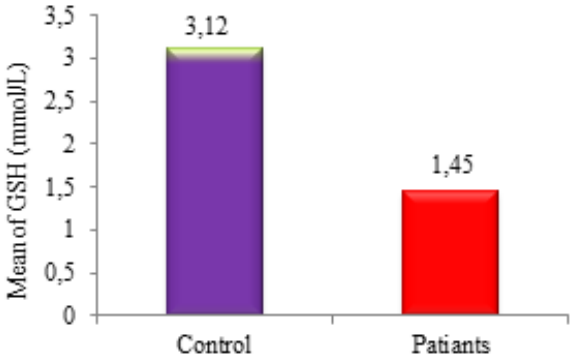

Fig. 4. GSH concentration in the blood serum of both groups.

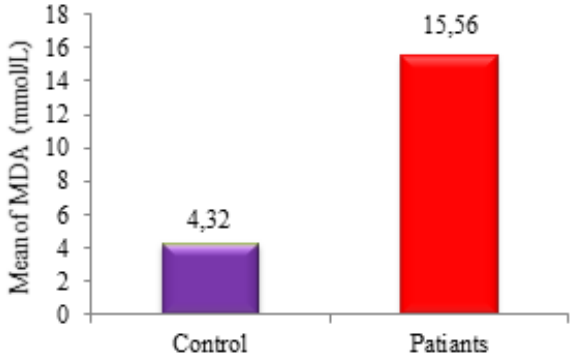

Fig. 5. MDA concentration in the blood serum of both groups.

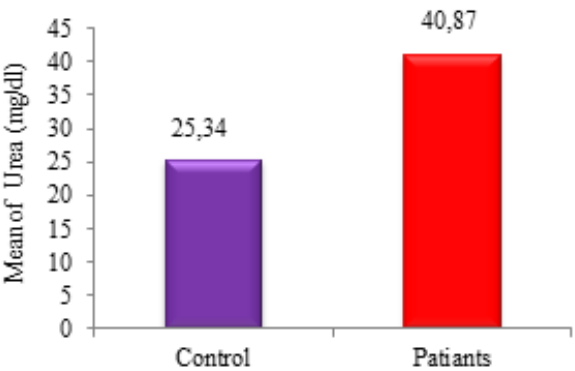

Fig. 6. Urea concentration in the blood serum of both groups.

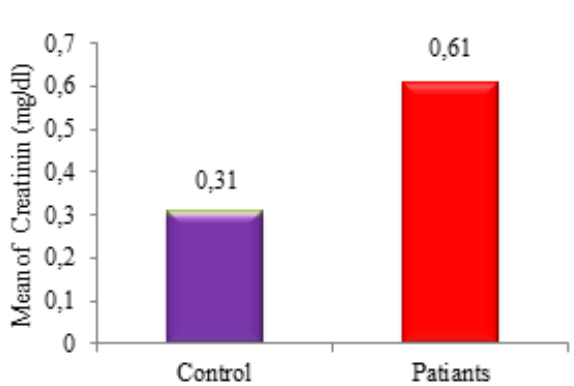

Fig. 7. Creatinin concentration in the blood serum of both groups.

4. Discussion

The results of the current study showed a high concentration of irisin in patients with prostate cancer, as the results of the research agreed with previous research [20, 21], which indicated a high concentration of irisin in patients with prostate cancer. This may explain the reason for the increase in insulin resistance, which leads to an increase in glucose in the blood, and that this rise causes an increase in the cofactor to activate the increase in the number of peroxisomes, which leads to an elevated in FNDCS5 gene expression resulting from that increase in the concentration of irisin in the blood. In addition, many studies have shown that high fat concentration leads to an increase in the concentration of irisin when following a diet containing saturated fatty acids [22, 23]. A study revealed that irisin expression increases in patients with metabolic disorders, prostatic hyperplasia, and cervical cancer [24]. Although previous studies have shown that irisin is a promising biomarker for early diagnosis of various types of cancer, it has been shown that in some types of cancer, its levels increase and in other types, it decreases. In addition, its levels may vary based on factors including muscle mass and participation in physical activities [25].

The results of the current research indicated high levels of tumor necrosis factor in prostate cancer patients, as the results of the study agreed with Nakashima et al. [26], which indicated high levels in patients with cancerous tumors. TNF-α is one of the inflammatory cytokines that is linked to the development of tumors. Tumor necrosis factor is linked to the development of prostate cancer, as its levels were found to be high in patients who suffer from severe relapses that lead to death [26].

Also, the results of the current study showed a high concentration of APA in patients with prostate cancer. There are numerous studies have recorded the risk of prostate cancer and serum prostate acid phosphates (PAP) levels in patients diagnosed with prostate carcinoma and compared with those without prostate cancer [27]. The results agree with Sarwar et al. [28], who showed an increase in PAP in prostate cancer patients compared to healthy males. The enzyme acid phosphatase has been studied as a guide to diagnosing prostate cancer in blood serum, as its levels are useful in the event of recurrence of prostatic tumor even after radical prostatectomy.

Also, the result showed a significant reduction in GSH and elevated MDA in patients compared to the control group. The results agree with Saroja et al. [29], who showed a significant reduction in GSH in males with prostate cancer. The oxidant/antioxidant balance has been implicated in the pathophysiology of prostate cancer. We investigated oxidative damage and antioxidant status in high-risk prostate cancer subjects [30, 31]. Also, oxidative stress and accumulated DNA damage increase the risk of prostate cancer [32]. The present data outline that chronic inflammation-mediated ROS production might play an important role in causing DNA damage, leading to neoplastic transformation in prostate epithelial cells. Our previous prospective 5-year study looking at needle biopsy specimens established a correlation between intraprostatic inflammation and neoplastic changes in prostatic tissue [33, 34].

As well as the research results indicated an increase in urea levels in patients with prostate cancer compared to the group of unaffected patients. The research results agreed with Franko et al. [35], which indicated an increase in urea levels in patients with the disease. High levels of

urea indicate the presence of inflammatory conditions, including acute or chronic nephritis or kidney dysfunction caused by tumors in patients, as blood urea has been linked to kidney disease and cases of hyperuric acid, as well as excessive consumption of foods that contain protein, which contributes to a slight increase in levels of urea [36].

Li et al. [37] showed a significant difference in blood urea nitrogen in the prostate cancer and benign prostatic hyperplasia group, as it can be predicted whether urea nitrogen plays a role in prostate enlargement and cancer. On the other hand, the results of the research indicated an increase in creatinine levels in patients suffering from prostate cancer, as the research results agreed with the results of Gu et al. [38], who found high levels of creatinine in patients with prostate enlargement compared to the control group. In recent years, it has been found that the level of creatine is related to the levels of prostate-specific antigen, and changes in kidney function can affect PSA levels, and changes in kidney function can affect its levels. In addition, Ahmad and Noman [39] determined that creatine in serum has clinical value in diagnosing various tumor diseases, including cancer—ovarian and prostate enlargement [40]. High levels of serum creatine may be involved in the conversion of nutrients and ATP in the growth of prostate tumor cells and the role of lipids in the development of prostate cancer hyperplasia, which leads to an increased prevalence of prostate tumors and poor prognosis of cancer patients [41].

5. Conclusion

This study reinforces the multifactorial nature of prostate cancer, with inflammation, oxidative stress, and metabolic changes playing significant roles. Chronic inflammation and oxidative stress are pivotal in prostate cancer pathogenesis, contributing to DNA damage and tumor progression. Irisin, TNF-α, PAP, urea, and creatinine are promising biomarkers for early detection, disease progression, and treatment efficacy in prostate cancer. The interplay between metabolic factors, such as glucose metabolism, lipid involvement, and kidney function, highlights the complexity of prostate cancer's systemic effects. The identified biomarkers provide insights into disease mechanisms and hold the potential for improving early diagnosis and personalized treatment strategies.

References

1. Archibald WJ, Ziemer RE, Newman JS (2019) Ask Mayo Expert: Anemia Workup in 1919. Mayo Clin Proc 94: 1904. doi: 10.1016/j.mayocp.2019.05.014
2. Obradovic AZ, Dallos MC, Zahurak ML, Partin AW, Schaeffer EM, Ross AE, et al (2020) T-cell infiltration and adaptive treg resistance in response to androgen deprivation with or without vaccination in localized prostate cancer. Clin Cancer Res 26: 3182-3192. doi: 10.1158/1078-0432.CCR-19-3372
3. Mazhar D, Gillmore R, Waxman J (2005) COX and cancer. QJM 98: 711-718. doi: 10.1093/qjmed/hci119
4. Campanella C, Pace A, Caruso Bavisotto C, Marzullo P, Marino Gammazza A, Buscemi S, et al (2018) Heat shock proteins in alzheimer's disease: Role and targeting. Int J Mol Sci 19: 2603. doi: 10.3390/ijms19092603
5. Carpentier PA, Dingman AL, Palmer TD (2011) Placental TNF-α signaling in illness-induced complications of pregnancy. Am J Pathol 178: 2802-2810. doi: 10.1016/j.ajpath.2011.02.042
6. Sana M, Rashid M, Rashid I, Akbar H, Gomez-Marin JE, Dimier-Poisson I (2022) Immune response against toxoplasmosis-some recent updates RH: *Toxoplasma gondii* immune response. Int J Immunopathol Pharmacol 36: 3946320221078436. doi: 10.1177/03946320221078436
7. van Loo G, Bertrand MJM (2023) Death by TNF: a road to inflammation. Nat Rev Immunol 23: 289-303. doi: 10.1038/s41577-022-00792-3
8. Xiao F, Xu T, Lu B, Liu R (2020) Guidelines for antioxidant assays for food components. Food Front 1: 60-69. doi: 10.1002/fft2.10
9. Parcheta M, Świsłocka R, Orzechowska S, Akimowicz M, Choińska R, Lewandowski W (2021) Recent developments in effective antioxidants: The structure and antioxidant properties. Materials (Basel) 14: 1984. doi: 10.3390/ma14081984
10. Pisoschi AM, Pop A, Iordache F, Stanca L, Bilteanu L, Serban AI (2021) Antioxidant determination with the use of carbon-based electrodes. Chemosensors 9: 72. doi: 10.3390/chemosensors9040072
11. Roy Z, Bansal R, Siddiqui L, Chaudhary N (2023) Understanding the role of free radicals and antioxidant enzymes in human diseases. Curr Pharm Biotechnol 24: 1265-1276. doi: 10.2174/1389201024666221121160822
12. Wang L, Ahn YJ, Asmis R (2020) Sexual dimorphism in glutathione metabolism and glutathione-dependent responses. Redox Biol 31: 101410. doi: 10.1016/j.redox.2019.101410
13. Ham YH, Pan G, Chan HW, Chan W (2022) LC-MS/MS quantitation of formaldehyde-glutathione conjugates as biomarkers of formaldehyde exposure and exposure-induced antioxidants: A new look on an old Topic. Chem Res Toxicol 35: 858-866. doi: 10.1021/acs.chemrestox.2c00027
14. Tietz NW (1999) Textbook of clinical chemistry. 3rd ed. Burtis CA, Ashwood ER, Saunders WB. 819-861, 1245-1250.
15. Sedlak J, Lindsay RH (1986) Estimation of total, protein-bound, and nonprotein sulfhydryl groups in tissue with Ellman's reagent. Anal Biochem 25: 192-205. doi: 10.1016/0003-2697(68)90092-4
16. Guidet B, Shah S (1989) The level of malondialdehyde after activation with H_2O_2 and $CuSO_4$ and inhibition by deferoxamine and molsidomine in the serum of patient with acute Myocardial infarction. National J Chem 5: 139-148.
17. Searle PL (1984) The Berthelot or indophenol reaction and its use in the analytical chemistry of nitrogen. A review. Analyst 109: 549-568. doi: 10.1039/AN9840900549
18. Tietz NW, Burtis CA, Ashwood ER (1986) Clinical guide to laboratory tests. 3rd ed.
19. Fishman WH, Lerner F (1953) A method for estimating serum acid phosphatase of prostatic origin. J Biol Chem 200: 89-97.
20. Alshanqiti KH, Alomar SF, Alzoman N, Almomen A (2023) Irisin induces apoptosis in metastatic prostate cancer cells and inhibits tumor growth in vivo. Cancers (Basel) 15: 4000. doi: 10.3390/cancers15154000
21. Sumsuzzman DM, Jin Y, Choi J, Yu JH, Lee TH, Hong Y (2019) Pathophysiological role of endogenous irisin against tumorigenesis and metastasis: Is it a potential biomarker and therapeutic? Tumour Biol 41: 1010428319892790. doi: 10.1177/1010428319892790
22. Natalicchio A, Marrano N, Biondi G, Spagnuolo R, Labarbuta R, Porreca I, et al (2017) The myokine irisin is released in response to saturated fatty acids and promotes pancreatic β-cell survival and insulin secretion. Diabetes 66: 2849-2856. doi: 10.2337/db17-0002
23. Osella AR, Colaianni G, Correale M, Pesole PL, Bruno I, Buongiorno C, et al (2018) Irisin serum levels in metabolic syndrome patients treated with three different diets: A post-hoc analysis from a randomized controlled clinical trial. Nutrients 10: 844. doi:

10.3390/nu10070844

24. Kuloglu T, Celik O, Aydin S, Hanifi Ozercan I, Acet M, Aydin Y, et al (2016) Irisin immunostaining characteristics of breast and ovarian cancer cells. Cell Mol Biol (Noisy-le-grand) 62: 40-44.
25. Zhu H, Liu M, Zhang N, Pan H, Lin G, Li N, et al (2018) Serum and adipose tissue mRNA levels of ATF3 and FNDC5/irisin in colorectal cancer patients with or without obesity. Front Physiol 9: 1125. doi: 10.3389/fphys.2018.01125
26. Nakashima J, Tachibana M, Ueno M, Miyajima A, Baba S, Murai M (1998) Association between tumor necrosis factor in serum and cachexia in patients with prostate cancer. Clin Cancer Res 4: 1743-1748.
27. Muniyan S, Chaturvedi NK, Dwyer JG, Lagrange CA, Chaney WG, Lin MF (2013) Human prostatic acid phosphatase: structure, function and regulation. Int J Mol Sci 14: 10438-10464. doi: 10.3390/ijms140510438
28. Sarwar S, Adil MA, Nyamath P, Ishaq M (2017) Biomarkers of prostatic cancer: An attempt to categorize patients into prostatic carcinoma, benign prostatic hyperplasia, or prostatitis based on serum prostate specific antigen, prostatic acid phosphatase, calcium, and phosphorus. Prostate Cancer 2017: 5687212. doi: 10.1155/2017/5687212
29. Saroja M, Balasenthil S, Nagini S (1999) Tissue lipid peroxidation and glutathione-dependent enzyme status in patients with oral squamous cell carcinoma. Cell Biochem Funct 17: 213-216. doi: 10.1002/(SICI)1099-0844(199909)17:3<213::AID-CBF831>3.0.CO;2-B
30. Shukla S, Srivastava JK, Shankar E, Kanwal R, Nawab A, Sharma H (2020) Oxidative stress and antioxidant status in high-risk prostate cancer subjects. Diagnostics (Basel) 10: 126. doi: 10.3390/diagnostics10030126
31. Abd Alhaqmuhamad A, Abdulrahman MA, Ahmad HS (2019) Effect of nanoparticles on liver functions and antioxidant in female rabbits treated with Domperidone. Indian J Forensic Med Toxicol 13: 554. doi: 10.5958/0973-9130.2019.00348.7
32. Wu JD, Lin DW, Page ST, Lundgren AD, True LD, Plymate SR (2009) Oxidative DNA damage in the prostate may predispose men to a higher risk of prostate cancer. Transl Oncol 2: 39-45. doi: 10.1593/tlo.08217
33. MacLennan GT, Eisenberg R, Fleshman RL, Taylor JM, Fu P, Resnick MI, et al (2006) The influence of chronic inflammation in prostatic carcinogenesis: a 5-year followup study. J Urol 176: 1012-1016. doi: 10.1016/j.juro.2006.04.033
34. Chen W, Jia L, Gupta S, MacLennan G (2019) The role of chronic inflammation in prostate carcinogenesis: A follow-up study. Ann Urol Oncol 2: 1-8. doi: 10.32948/auo.2019.01.14
35. Franko A, Shao Y, Heni M, Hennenlotter J, Hoene M, Hu C, et al (2020) Human prostate cancer is characterized by an increase in urea cycle metabolites. Cancers (Basel) 12: 1814. doi: 10.3390/cancers12071814
36. Lerner LB, McVary KT, Barry MJ, Bixler BR, Dahm P, Das AK, et al (2021) Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia: AUA GUIDELINE PART I-initial work-up and medical management. J Urol 206: 806-817. doi: 10.1097/JU.0000000000002183
37. Li SN, Cui YF, Luo ZY, Lou YM, Liao MQ, Chen HE, et al (2021) Association between blood urea nitrogen and incidence of type 2 diabetes mellitus in a Chinese population: a cohort study. Endocr J 68: 1057-1065. doi: 10.1507/endocrj.EJ20-0794
38. Gu X, Wu J, Liu X, Hong Y, Wu Y, Tian Y (2022) Role of serum creatinine levels in prognostic risk stratification of prostate cancer patients. Med Sci Monit 28: e937100. doi: 10.12659/MSM.937100
39. Ahmad HS, Noman SJ (2024) Investigating the impact of C. krusei and chitosan treatment on liver and kidney function: A comprehensive study. Int J Des Nat Ecodynamics 19: 3. 997-1006. doi: 10.18280/ijdne.190329
40. Schwameis R, Postl M, Bekos C, Hefler L, Reinthaller A, Seebacher V, et al (2019) Prognostic value of serum creatine level in patients with vulvar cancer. Sci Rep 9: 11129. doi: 10.1038/s41598-019-47560-3
41. Allott EH, Howard LE, Cooperberg MR, Kane CJ, Aronson WJ, Terris MK, et al (2014) Serum lipid profile and risk of prostate cancer recurrence: Results from the SEARCH database. Cancer Epidemiol Biomarkers Prev 23: 2349-2356. doi: 10.1158/1055-9965.EPI-14-0458