



Determination lipid peroxidation (MDA) and catalase levels with prostate specific antigen (PSA) level in Iraqi patients suffering from prostate cancer.

Noora Wael Rasheed*

Department of Medical Laboratory Techniques, Al Rafidain University College, Baghdad



Abstract

Background: Prostate cancer (PCa) is a disease that usually happens with old men which is associated with the level of PSA in blood. Objective: the current study is carried out to investigate the level of PSA in prostate cancer patients and compare it with control, also inspect the level of MDA. Materials and Methods: The study was conducted on 75 controls and 155 patients that were previously diagnosed with PCa. Blood samples were collected from each individual of the participant (patients and control) to examine PSA, MDA and assays, as well as BMI, Catalase, testosterone, blood group and prolactin were measured in both groups and correlated with age, level of both PSA and MDA. Results: the factors were tested according to the protocols to each one for each individual (patients and control) and were compared to reach one of these factors has correlation with prostate cancer and which one has not. The collected data were represented in 7 tables and 3 figures. Conclusions: ten important points are the findings of the current study, among them are; no correlation between blood groups in (AB-, O+, O-) with PCa, significant correlation between blood groups (A-, B-, AB+) with Psa, high level of prolactin is a PCa marker, no significant correlation between Biomass Index and PCa and there is a negative correlation between PSA, MDA with PCa.

Keywords: PCa, MDA, PSA, BMI, Iraqi patients

1. Introduction

The prostate is a gland that can be found only in males. It makes some fluids that are part of semen, prostate cancer (PCa) is the most common of non-skin cancer and one of the main reasons for death in men as a specific cancer^[1]. Prostate cancer begins when cells in the prostate gland start to develop and enlarged in an uncontrolled growth^[2]. Mainly, prostate cancer is a major public health problem in western countries, particularly in the elderly men, and with the life development, life expectancy and the prevalence PCa have been increased, there is also an expected increase of the disease due to economic burden.^[3]

Prostate cancer starts when a certain cells (prostate gland cells) in the body begin to grow up and developed without control due to unknown reasons, however, almost all prostate cancers are considered as adenocarcinomas.^[4]

Usually, PCa will lead to urological problems in the aging men and manifest with disturbing obstructive and irritative symptoms. In addition to androgen and age dependence, oxidative stress, infection and

inflammation are the other accepted predisposing factors for PCa^[5]

Oxidative stress can be defined as an increase in oxidative parameters or a decline in antioxidant defense mechanisms Malondialdehyde (MDA) which is considered as the main and the principal end product of the lipid peroxidation pathway and it is used as a marker to reflect oxidative status in normal subjects, and PCa patients, this will eventually lead to an increase in free radicals that causes overproduction of MDA level which is commonly known as a marker of oxidative stress and the antioxidant status in cancerous patients.^[6] Catalase (CAT) is an antioxidant enzyme, it is responsible for eliminating the free radicals, and the antioxidants are said to have been overwhelmed by the free radicals. This happens when the production of free radicals exceeds the level of the body's natural antioxidant defense mechanisms and it can cope with; consequently, creating a cellular oxidative environment which triggers the oxidation of essential biomolecules like DNA, protein and lipids, leading to multiple disease, however,

*Corresponding author e-mail: noora.waal@ruc.edu.iq

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superoxide and hydrogen peroxide, can stand in the antioxidant defense mechanisms.^{[7][8]}

Antioxidants such as polyphenols, ascorbic acid, vitamin A, alpha-lipoic acid, thioredoxin, glutathione, melatonin, coenzyme Q, beta carotenoids, alpha-tocopherols as well as antioxidant enzymes including superoxide dismutase, catalase, glutathione-peroxidases, glutathione reductases and glutathione-s-transferases have been widely investigated for the prevention and treatment of diseases resulting from oxidative damage.^{[9][10]}

In the current study, the MDA was determined via measuring the level of PSA.

2. Material and Methods

The blood samples were collected on a period from February 2021 to June 2021 from oncology teaching hospital /Baghdad/Iraq. The study groups were divided into two major groups, control and patients. The study was conducted on 75 controls (age between 58 and 85 years). And 155 patients (age between 61 and 88 years), that were diagnosed previously with prostate cancer. The study sample were evaluated through an inclusive medical history and according to (IPSS) the International Prostate Symptom Score. To determine the symptom severity, questionnaire forms were distributed to measure the peak urinary flow rate and digital rectal examination (DRE).

PSA (Prostate specific antigen) test was carried out to every contributor; the patients group comprised 155 males there PSA values were higher than the normal levels, contributors were also underwent to TRUS (Transrectal Ultrasound), and for more confirmation biopsy was taken to ensure the PCa, the excluded criteria were determined by the researchers such as; previous medical, hematuria, presence tract infection, renal and liver diseases and diagnosis of any malignancy, the use of anti-inflammatory drugs, antioxidant supplementation and alcohol intake.

2.1. Ethical approvals

The approval was obtained from the contributors, and from ethical committees of the institution and from the Iraqi Ministry of Health and Environment. Blood samples and prior to prostate biopsy, were taken from each individual for MDA, PSA, and assays. These limitations were compared between the control and patients prostate cancer. The correlation between SPA with age, BMI, MDA, Catalase, testosterone,

blood group and prolactin were measured in both groups.

2.2. Detection of (MDA) Malondialdehyde serum level

Malondialdehyde was detected in human serum according to instructions of the manufacturer instructions of kit Abcam, USA, and catalog number: ab238537.^[11]

2.3. Detection of Catalase (CAT) Activity in serum level

Catalase was detected in human serum using Colorimetric method according to the manufacturer instructions of kit Elabscience, USA Catalog No: E-BC-K031-S.^[12]

2.4. Detection of Testosterone and Prolactin

Testosterone and Prolactin hormone were measured using ELISA kits depending on the manufacturer instructions monobind USA Catalog No: 3725-300 and 4425-300 respectively.^{[13][14]}

2.5. Detection of PSA

PSA was identify in human serum upon the the instruction of the manufacturer AFIAS, fluorescence Immunoassay. PSA was determined in plasma, serum and the whole blood.^[15]

3. Statistical analysis

The IBMSPSS Statistics for Windows version 26.0 was used to calculate the mean, SE and the probability by using T-test. The probability value was significant when it was > 0.05 .^[16]

3. Results and discussion

Regarding the demographic parameters presented in table 1, the study indicated that the demographic parameter is similar in the both study groups and there was no significant differences among a certain group type (AB-, O+, O-) while the PCa increases in patients with significantly in (A-, B-, AB+) in the study groups, this result match with the finding of Shahait et al 2018^[17] that indicate the non-correlation of PCa with blood group, and also match with the finding of Wang et al., 2017^[18] showing a significant correlation between blood group and PCa

It is clear from table 2 the correlation between the level of testosterone and the risk of prostate cancer, this because it plays an important and significant role in the health developments in men such as hypogonadism, and androgen deficiency which reflected as many symptoms among them are erectile

dysfunction, diminished libido and decreases in the energy as explained by Michaud et al., 2015^[19], the research also indicate that testosterone can be also used in PCa therapy. The significance correlation between testosterone in this study is also match with the findings of Xu et al., 2017^[20] that found the obvious conflict between PC and the level of testosterone.

Table 1: Blood group of patients and control

Blood groups	Control group No. (%)	Patients group No. (%)	Probability
A+	10 (22.2%)	4 (8.9%)	
A-	1 (2.2%)	4 (8.9%)	
B+	6 (13.3%)	2 (4.4%)	
B-	2 (4.4%)	4 (8.9%)	
AB+	8 (17.8%)	12 (26.7%)	
AB-	3 (6.7%)	4 (8.9%)	
O+	14 (31.1%)	14 (31.1%)	
O-	1 (2.2%)	1 (2.2%)	
Total	45 (100.0%)	45 (100.0%)	
Probability			

Table 2: The level of testosterone in study groups

Groups	Testosterone level mean \pm SE	Probability
Control	955.78 \pm 153.81	3.7 x 10 ⁻²⁵
Patients	3969.20 \pm 138.54	

Groups	Prolactin level mean \pm SE	Probability
Control	10.27 \pm 0.89	7.02 x 10 ⁻²⁰
Patients	23.49 \pm 0.68	

Table 3: level of prolactin in control and patient

The results show that the level of prolactin hormone that secreted from pituitary gland which is located in the brain, also affected with prostate cancer, the level of this hormone is high in the PC patients compared with control group. In 2012 Sethi and his coworkers^[21] shows that prolactin level can indicates the presence of cancer, and controlling its

level can be a good approach in cancer treatment. However Porcaro et al., 2019^[22] found that the low level of PRL clinically indicate of non-prostate cancer disease of the organ which correlate with the finding of the current study

Table 4: Body mass index results of the study groups

Groups	BMI mean \pm SE	Probability
Control	29.22 \pm 0.48	0.011
Patients	30.90 \pm 0.44	

Body Mass Index (BMI) in both control and patients groups, the results shows that there is no significant correlation between BMI and prostate cancer, this result does not match with the finding of Haque et al., 2014^[23] which consider the BMI is strongly correlated with PC, while Giovannucci et al., 2003^[24] and Engeland et al., 2003^[25] shows a non-significant statistical and a minor risk of association between PC and BMI.

Groups	MDA level mean \pm SE	Probability
Control	9.46 \pm 1.09	0.127
Patients	11.85 \pm 1.11	

Table 5: MDA results of the study groups

Arif et al., 2018^[26-28]. In our study shows that elevation of MDA level in patients can be a marker for prostate cancer via the expression of p53, while Lepara et al.,^[29] indicate that the level of MDA may and may not correlated with prostate cancer and can be used as an indication of monitor the progression of prostate cancer, however in the current study the level of MDA in control and patients groups were 9.46 \pm 1.09 and 11.85 \pm 1.11 respectively as appears in figure 2, which doesn't shows a significant relationship between PC and the level of MDA.

Table 6: Level of catalase in the study groups

Groups	Catalase level mean \pm SE	Probability
Control	0.47 \pm 0.04	0.783
Patients	0.48 \pm 0.03	

There weren't any significant differences of catalase between control and patients groups. (0.47 and 0.48 respectively), this results equivalent to a study made by Bostwick et al., 2000^[30] which indicate a very low possibility of correlation between prostate cancer and the level of catalase. This finding was confirmed by Christophe et al., 2017^[31,32], the study encourage to use reactive oxygen species (ROS) as an indication for prostate cancer rather than catalase level.

Groups	PSA level mean \pm SE	Probability
Control	1.85 \pm 0.76	2.66 x 10 ⁻²⁰
Patients	20.04 \pm 1.0	

Table 7: Level of PSA in the study groups

The levels of PSA in control and patients groups 1.85 \pm 0.76 and 20.04 \pm 1.0 respectively, it is clearly from the results that there is a very significant correlation between the level of PSA and prostate cancer which is equivalent with the finding of Ito et al 2000^[33] that consider the level of PSA can be considered as an early indication of PC (one year before), while another study carried out by Vickers et al., 2010^[34] and Ilic et al., 2018^[35] find that PSA-driven algorithms is a good indication to diagnose PC with no needs for biopsy.

The current study also shows that there is no correlation between age of the patient and the

Table 9: studied parameters correlation between control group

		Testosterone	Prolactin	BMI	MDA	Catalase	PSA	Age
Testosterone	r	1	0.751**	0.345*	0.000	0.099	0.841**	0.024
Prolactin	r		1	0.395**	0.028	-0.012	0.480*	0.064
BMI	r			1	-0.076	-0.157	0.428*	-0.080
MDA	r				1	0.054	0.024	-0.170
Catalase	r					1	0.064	-0.043
PSA	r						1	-0.207
Age	r							1
**. Correlation is significant at the 0.001 level (2-tailed).								
*. Correlation is significant at the 0.05 level (2-tailed).								
r. Pearson Correlation								

Table 10 : Studied parameters correlation between patients' group

		Testosterone	Prolactin	BMI	MDA	Catalase	PSA	Age
Testosterone	R	1	0.055	-0.078	0.224	0.242	0.248	-0.078
Prolactin	R		1	-0.025	-0.022	-0.047	-0.054	0.093
BMI	R			1	-0.244	-0.241	0.062	-0.049

prostate cancer as shown in table 8. However Kurian et al., 2018^[36-37] doesn't agree with that, the study recommend that age could is a factor of health problem and can contribute in PC and advice for a periodic check up

Table 8: Age mean of the studied groups

Groups	Age mean \pm SE	Probability
Control	73.51 \pm 0.94	1.0
Patients	73.51 \pm 1.16	

Tables 9, and 10 represent the correlation between the studies factors in control group and patients group respectively, and using Pearson R correlation coefficient, the statistical finding (using 2-tailed) shows that there is a negative correlation between MDA and PSA with prostate cancer^[38], and as it appears in table 7, most of the studied factors shows a negative correlation while only few of them shows a very week association with prostate cancer, however, the level of PSA has a direct connection with PCa, .

MDA	R				1	0.090	-0.350*	-0.066
Catalase	R					1	0.067	-0.100
PSA	R						1	0.219
Age	R							1
*. Correlation is significant at the 0.05 level (2-tailed).								
r. Pearson Correlation								

Conclusions

The finding of the current study are:

No correlation between blood groups in (AB-, O+, O-) with PCa. We found Significant correlation between blood groups (A-, B-, AB+) with Psa. High level of testosterone is a PCa marker. High level of prolactin is a PCa marker. No significant correlation between Body Mass Index and PCa. No significant correlation between MDA and PCa and No significant correlation between catalase and PCa. High level of PSA is significantly considered as a PCa marker.

There isn't correlation between age and PCa. There is a negative correlation between PSA, MDA with PCa

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. Secondary Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012.
2. Gronberg H. Prostate cancer epidemiology. *Lancet* 2003;361:859
3. Epidemiology of prostate cancer. Kumar RJ, Barqawi AB, Crawford ED. *US Oncol Rev.* 2005;1:1-6.
4. Aydin A, Arsova-Sarafinovska Z, Sayal A, Eken A, Erdem O, Erten K, et al. Oxidative stress and antioxidant status in non-metastatic prostate cancer and benign prostatic hyperplasia. *Clin Biochem.* 2006;39(2):176-9.
5. Klein EA, Casey G, Silverman R. Genetic susceptibility and oxidative stress in prostate cancer: integrated model with implications for prevention. *Urology.* 2006;68(6):1145-51.
6. Ahmad M, Suhail N, Mansoor T, Banu N, Ahmad S. Evaluation of oxidative stress and DNA damage in benign prostatic hyperplasia patients and comparison with controls. *Indian J Clin Biochem.* 2012;27(4):385-8.
7. Marklund SL. Extracellular superoxide dismutase and other superoxide dismutase isoenzymes in tissues from nine mammalian species. *Biochem J.* 1984;222:649-655.
8. Chelikani P, Fita I, Loewen PC. Diversity of structures and properties among catalases. *Cell Mol Life Sci.* 2004;61:192-208.
9. S. Hercberg, P. Galan, P. Preziosi, et al. The SU. VI. MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals *Arch Int Med,* 164 (2004), pp. 2335-2342
10. B. Halliwell, J. Rafter, A. Jenner Health promotion by flavonoids, tocopherols, tocotrienols, and other phenols: direct or indirect effects? Antioxidant or not? *Am J Clin Nutr,* 81 (2005), pp. 268S-276S
11. Fujita Y et al. Angiotensin II type 1a receptor loss ameliorates chronic tubulointerstitial damage after renal ischemia reperfusion. *Sci Rep* 11:982 (2021).
12. Kim J et al. Intense Pulsed Light Attenuates UV-Induced Hyperimmune Response and Pigmentation in Human Skin Cells. *Int J Mol Sci* 22:N/A (2021).
13. Chen J et al. Decreased blood vessel density and endothelial cell subset dynamics during ageing of the endocrine system. *EMBO J* 40:e105242 (2021)
14. Van Simaey G et al. [18F]-JK-PSMA-7 and [18F]-FDG tumour PET uptake in treated xenograft human prostate cancer model in mice. *Eur J Nucl Med Mol Imaging* 48:1773-1784 (2021).
15. Brooks DE, Devine DV, Harris PC, et al. RAMP(TM): A rapid, quantitative whole blood immunochromatographic platform for point-of-care testing. *Clin. Chem.* 1999; 45:1676-1678.
16. Frankel S, Smith GD, Donovan J, Neal D. Screening for prostate cancer. *Lancet* 2003; 361:1122-1128.
17. IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.

18. Shahait M1 , Fares S2 , Mukherji D3 , Hout M1 , Bachir BG1 , Khauli R1 and Bulbul MA. The Impact of ABO Blood Group on Biochemical Recurrence after Radical Prostatectomy. *International Archives of Urology and Complications* 2018; 4(20):40 DOI: 10.23937/2469-5742/1510040.
19. Wang F-M, Zhang Y, Zhang G-M, Liu Y-N, Sun L-J, Liu Y. Association of ABO Blood Types and Clinicopathological Features of Prostate Cancer. *Disease Markers*. 2017; 2017: 237481. <https://doi.org/10.1155/2017/9237481>
20. Michaud JE, Billups KL, Partin AW. Testosterone and prostate cancer: an evidence-based review of pathogenesis and oncologic risk. *Therapeutic Advances in Urology*. 2015;7(6):378-387. doi:10.1177/1756287215597633
21. Xu, X., Chen, X., Hu, H. *et al.* Current opinion on the role of testosterone in the development of prostate cancer: a dynamic model. *BMC Cancer* **15**, 806 (2015). <https://doi.org/10.1186/s12885-015-1833-5>
22. Sethi BK, Chanukya GV, Nagesh VS. Prolactin and cancer: Has the orphan finally found a home?. *Indian J Endocrinol Metab*. 2012;16(Suppl 2):S195-S198. doi:10.4103/2230-8210.104038
23. Porcaro AB, Tafuri A, Sebben M, Cacciamani G, Ghimenton C, Brunelli M, Petrozziello A, Monaco C, Migliorini F, Siracusano S, Artibani W. Low Preoperative Prolactin Levels Predict Non-Organ Confined Prostate Cancer in Clinically Localized Disease. *Urol Int*. 2019;103(4):391-399. doi: 10.1159/000496833. Epub 2019 Feb 14. PMID: 30763940.
24. Haque R, Van Den Eeden SK, Wallner LP, Richert-Boe K, Kallakury B, Wang R, Weinmann S. Association of body mass index and prostate cancer mortality. *Obes Res Clin Pract*. 2014 Jul-Aug;8(4):e374-81. doi: 10.1016/j.orcp.2013.06.002. Epub 2013 Aug 6. PMID: 25091359; PMCID: PMC4122983.
25. Giovannucci E, Rimm EB, Liu Y, Leitzmann M, et al. Body Mass Index and Risk of Prostate Cancer in U.S. Health Professionals, *JNCI: Journal of the National Cancer Institute*, Volume 95, Issue 16, 20 August 2003, Pages 1240–1244, <https://doi.org/10.1093/jnci/djg009>
26. Engeland, A., Tretli, S. & Bjørge, T. Height, body mass index, and prostate cancer: a follow-up of 950 000 Norwegian men. *Br J Cancer* **89**, 1237–1242 (2003). <https://doi.org/10.1038/sj.bjc.6601206>
27. Abdullah, L. W., Saied, S. M., & Saleh, M. Y. (2021). Deep eutectic solvents (Reline) and Gold Nanoparticles Supported on Titanium Oxide (Au–TiO₂) as New Catalysts for synthesis some substituted phenyl (substituted-3-phenyloxiran) methanone Enantioselective Peroxidation. *Egyptian Journal of Chemistry*, 64(8), 4381-4389.
28. Hassan, Y. I., & Saeed, N. H. M. (2012). Kinetics and Mechanism of Oxidation of Diethyl Ether by Chloramine-T in Acidic Medium. *E-Journal of Chemistry*, 9(2), 642-649.
29. Arif M, Rashid A, Majeed A, Qaiser F, Razak S. Evaluation of correlation between expression of P53 and Malondialdehyde levels in prostate cancer patients. *J Pak Med Assoc*. 2018 Sep;68(9):1373-1377. PMID: 30317268.
30. Lepara Z, Lepara O, Fjkic A, Rebic D, et al. Serum malondialdehyde (MDA) level as a potential biomarker of cancer progression for patients with bladder cancer. *ROM. J. INTERN. MED.*, 2020, 58, 3, 146–152. DOI: 10.2478/rjim-2020-0008
31. Bostwick, D.G., Alexander, E.E., Singh, R., Shan, A., Qian, J., et al. (2000), Antioxidant enzyme expression and reactive oxygen species damage in prostatic intraepithelial neoplasia and cancer. *Cancer*, 89: 123-134. [https://doi.org/10.1002/1097-0142\(20000701\)89:1<123::AID-CNCR17>3.0.CO;2-9](https://doi.org/10.1002/1097-0142(20000701)89:1<123::AID-CNCR17>3.0.CO;2-9)
32. Ayoob, A., Sadeek, G., Saleh, M. (2022). Synthesis and Biologically Activity of Novel 2-Chloro -3-Formyl -1,5-Naphthyridine Chalcone Derivatives. *Journal of Chemical Health Risks*, 12(1), 73-79. doi: 10.22034/jchr.2022.688560
33. Christophe G, Pedro Buc C. "Catalase, a remarkable enzyme: targeting the oldest antioxidant enzyme to find a new cancer treatment approach" *Biological Chemistry*, vol. 398, no. 10, 2017, pp. 1095-1108. <https://doi.org/10.1515/hsz-2017-0131>
34. Ito K, Kubota Y, Suzuki K, Shimizu N, Fukabori Y, Kurokawa K, Imai K, Yamanaka H. Correlation of prostate-specific antigen before

- prostate cancer detection and clinicopathologic features: evaluation of mass screening populations. *Urology*. 2000 May;55(5):705-9. doi: 10.1016/s0090-4295(99)00568-3. PMID: 10792085.
35. Vickers AJ, Cronin AM, Roobol MJ, Hugosson J, Jones JS, et al. The relationship between prostate-specific antigen and prostate cancer risk: the Prostate Biopsy Collaborative Group. *Clin Cancer Res*. 2010 Sep 1;16(17):4374-81. doi: 10.1158/1078-0432.CCR-10-1328. Epub 2010 Aug 24. Erratum in: *Clin Cancer Res*. 2011 Jun 1;17(11):3852. PMID: 20736330; PMCID: PMC2937360.
36. Al-Thakafy, N., Al-Enizzi, M., Saleh, M. (2022). Synthesis of new Organic reagent by Vilsmeier – Haack reaction and estimation of pharmaceutical compounds (Mesalazine) containing aromatic amine groups. *Egyptian Journal of Chemistry*, 65(6), 1-2. doi: 10.21608/ejchem.2021.101851.4729
37. Ilic D, Djulbegovic M, Jung JH, et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. *BMJ*. 2018;362:k3519. Published 2018 Sep 5. doi:10.1136/bmj.k3519
38. Qusay Falih, I., A.H. Alobeady, M., Banoon, S., Saleh, M. (2021). Role of Oxidized Low-density Lipoprotein in Human Diseases: A Review. *Journal of Chemical Health Risks*, 11(Special Issue: Bioactive Compounds: Their Role in the Prevention and Treatment of Diseases), 71-83. doi: 10.22034/jchr.2021.684227