

Association Between Prostatitis and Some Biochemical Markers in Patients of the AL-Najaf Province, Iraq

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ABSTRACT: One of the most common clinical conditions in men is prostate disease, especially prostatitis, which causes various symptoms, that negatively affect patient life. Our current study investigated the relationship between prostatitis and IL-6, zinc, and ESR levels for patients who visited AL-Sader Medical City in the province of AL-Najaf, between March and November 2023. our study included 90 samples of people infected with prostatitis and 30 samples of healthy people between the ages of (20-40) years. The level of IL-6 was calculated using the ELISA technique, The level of zinc as an antioxidant asses by using the spectrophotometer and ESR was measured by using the Westergren technique to determine the inflammation case in patients and compared with the healthy group. The results showed an increase in the level of IL-6 in patients with prostatitis compared with a healthy group (908.72 ± 140.19 , 214.16 ± 85.56) pg/ml respectively. but showed a decrease in the level of Zinc in prostatitis patients compared with the healthy group (38.93 ± 10.92 U/ml, 89.36 ± 9.61 U/ml) respectively. Also showed an elevated level of ESR, where according to (48.41 ± 13.49) mm/hour in patients group compared with a healthy group (14.60 ± 4.14) mm/hour. The data was analyzed by SPSS program version 23, where the factor effect was considered significant when $p < 0.05$. we conclude from our current study the significant relationship between IL-6, Zinc levels, and prostatitis, as well as the role of the ESR test as an indicator of prostatitis

KEYWORDS: prostatitis, Zinc, IL-6, and ESR.

INTRODUCTION

The prostate is a gland in men located directly under the bladder, and it surrounds the urethra. The gland, in addition to the nearby seminal vesicles, produces a lot of semen fluid. The prostate is the size of a walnut in young men, but it enlarges with age. this gland is exposed to inflammation known as Prostatitis is pain, swelling, inflammation, or both in the prostate gland. it is a common syndrome characterized by various symptoms, including irritative urinary symptoms, sexual dysfunction, and pelvic pain. Previous studies have also proven that the percentage of men's visits to urology units is due to prostatitis (**Graziani et al, 2023**).

Many men, especially those between the ages of 30 and 50 years old suffer from prostatitis, an inflammation of the prostate gland that causes a variety of symptoms and indications, Worldwide, prostatitis is a serious health issue for males, with an estimated 8-16% of cases being bacterial. Uropathogenic infections in the semen, define both acute and chronic bacterial prostatitis (**Al-hadrawi et al, 2023**).

IL-6 is a natural protein produced by various cells in the body, and it helps regulate the immune reaction, and thus; It is an important indication of the presence of high activity in the immune system, as the protein in the body rises above the normal level in the case of infections, autoimmune diseases, heart disorders, and some types of cancer (**Tylutka, et al, 2024**). Since the beginning of its discovery as a cytokine derived from T lymphocytes, it can stimulate the differentiation of B lymphocytes and transform them into antibody-producing cells, which also stimulates their secretion of immunoglobulins IgA, IgG, and IgM, and is often used as a Marker of Inflammation and it is a pro-inflammatory cytokine (**Ohsugi, 2020**). It regulates physiological processes including the acute response, inflammation, immune response, the body's defense mechanisms, blood formation, and cellular growth (**Chen et al., 2018**). IL-6 can reach major organs through the bloodstream and stimulates systemic responses. This process is referred to as the acute phase response. With other cytokines, IL-6 acts synergistically to induce systemic inflammatory responses (**Topolyanskaya, 2021**).

Zinc is one of the most important trace elements that ensure that the body controls balance throughout life, although its total content in the body is quite low, averaging 1.5-3.0 g, absorption of zinc decreases with old so it can cause an increase in infection with the disease (**Steinbrenner et al 2020**).

Association Between Prostatitis and Some Biochemical Markers in Patients of the AL-Najaf Province, Iraq

Zinc plays a major role in physiological and structural processes, as it acts as a natural regulator of programmed cell death and cell division. It also can stabilize cell membranes and has a role in the functioning of the immune system through its effect on B and T cells (Zarezadeh,2024). Zinc is concentrated in the man's body in the prostate gland, where the prostate fluid is 590 µg/gram compared to its percentage in the plasma, 1µg/gram, which reflects the effective role of zinc in the physiology of the prostate gland (Shahrokhi Nejad,2024). where it acts as an antioxidant (Rosa et al. 2021), experimental studies have proven that bacterial prostatitis Chronic disease is accompanied by a decrease in the concentration of zinc in the prostate fluid, as prostate cells lose their ability to accumulate zinc, but in humans, the relationship between plasma zinc levels and prostate zinc has not been proven. (Bratchikov et al. 2020; Santos et al. 2020; Daragó et al. 2021).

Erythrocyte sedimentation rate (ESR) is a blood test that can show the effect of inflammation in the body. Many health problems can cause sedimentation rate test results to fall outside the normal range. It is often used with other tests to help diagnose inflammatory diseases (Tishkowski et al, 2020).

Our study aimed to investigate the extent of the effect of prostatitis on the level of interleukin 6 as an immune indicator of inflammation, the level of zinc as an effective oxidizing agent in the body, and the Erythrocyte sedimentation rate as a general inflammatory indicator.

PATIENTS AND METHOD

The Period and place of study

The current study was made on patients who visited AL-Sader Medical City in the province of AL-Najaf. through the period from March to November 2023.

Samples collection

our study included 90 patients infected by prostatitis disease and 30 people without any disease as control, whose ages ranged from 20 to 40 years, who visited AL-Sader Medical City in the AL-Najaf province, in the period from March to November 2023. 5ml blood drawn from patients. The samples of blood were divided into two parts the first part was put in the Jel tube, was centrifuged to get the serum at 3000 rpm/ 5 minutes, and stored at -20 C until used to assess the IL-6 level by ELISA technique, and Zinc level in the blood using a spectrophotometer (Al-Hadrawi et al,2023), the second part used for measured the erythrocyte sedimentation rate (ESR) calculated using the Westergren technique (Ramsay and Lerman,2015).

Inclusion Criteria: All samples from people infected by prostatitis

Exclusion Criteria: any sample from people infected by other prostate disease

Result: Our study included 120 samples distributed into two groups. The first group included 90 samples from people with prostatitis, and the second group included 30 samples from healthy people for comparison of the results (Table 1). They ranged between the ages of 20-40 years. (Table 2)

Table (1) Explained the study sample.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid patient	90	75.0	75.0	75.0
control	30	25.0	25.0	100.0
Total	120	100.0	100.0	

Table (2) shows the maximum and minimum ages of the study sample

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age of patients	90	20.00	20.00	40.00	33.5222	5.11931
Valid N	90					

The results of the current study recorded a significant increase in the level of IL-6 in patients with prostatitis compared to healthy individuals 908.72±140.19, 214.16±85.56 pg/ml respectively. (Figure 1)

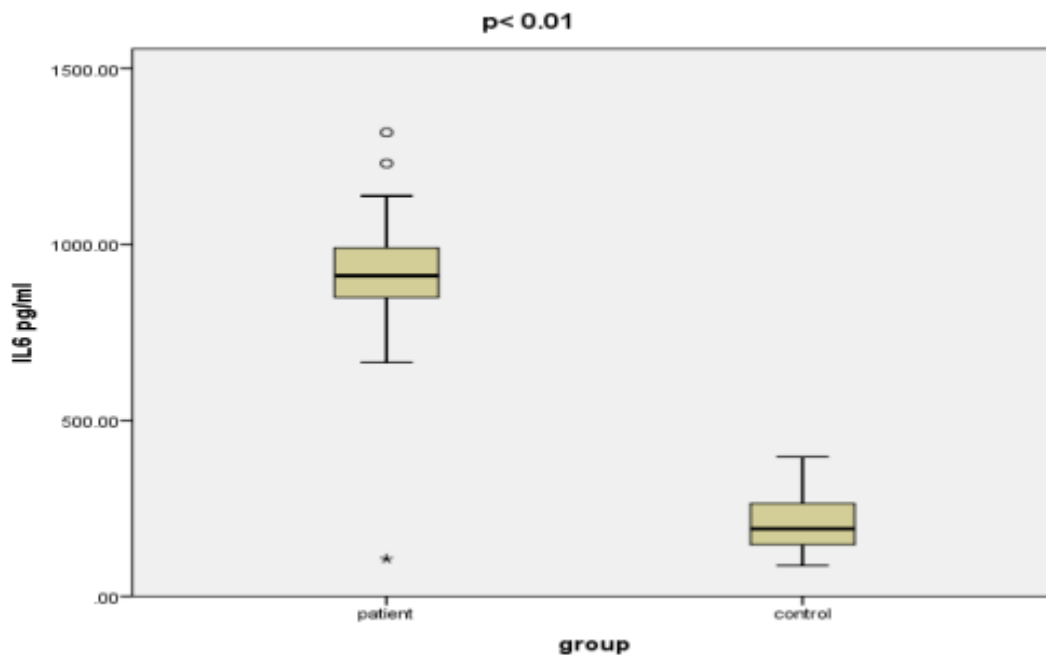


Figure (1): shows levels of IL-6 for the patients group compared with the control group.

The results of the study recorded a significant decrease in the level of Zinc in patients with prostatitis compared to healthy individuals ($38.93 \pm 10.92, 89.36 \pm 9.61$) U/ml respectively (Figure 2).

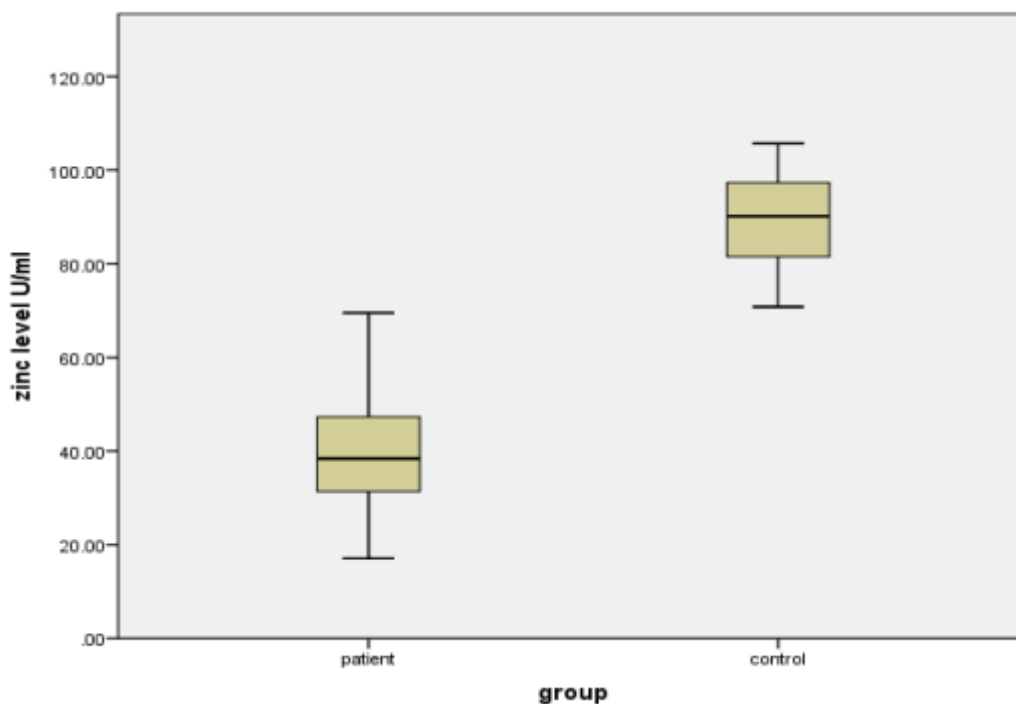


Figure (2): shows levels of Zinc for the patients group compared with the control group.

Also, the results of the study recorded a significant increase in the level of ESR in patients with prostatitis compared to healthy individuals ($48.41 \pm 13.49, 14.60 \pm 4.14$) mm/hour respectively (Figure 3).

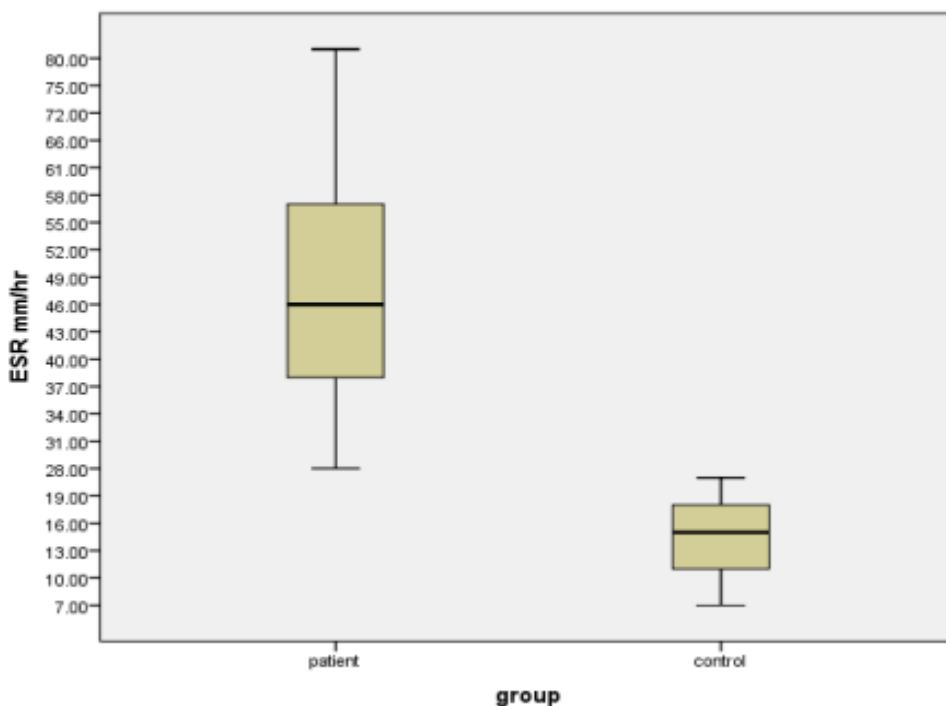


Figure (3): shows levels of ESR for the patients group compared with the control group.

Our study also showed a significant relationship between the studied parameters and the incidence rate of prostatitis (p value < 0.01) (Table 3).

Table (3) shows the significant relationship between the study parameters and prostatitis

		IL6	zinc level U/ml	ESR
IL6	Pearson Correlation	1	-.824**	.745**
	Sig. (2-tailed)		.000	.000
	N	120	120	120
zinc level U/ml	Pearson Correlation	-.824**	1	-.685**
	Sig. (2-tailed)	.000		.000
	N	120	120	120
ESR	Pearson Correlation	.745**	-.685**	1
	Sig. (2-tailed)	.000	.000	
	N	120	120	120

**Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

There are differences in the levels of interleukin 6 between the patient's group compared to the healthy group, as the average reached its level in the serum of patients (908.72 140.19 pg/L), while its average level reached (214.16 85.56pg/L) in the healthy group .Cytokines are glycoproteins that are manufactured and released by a variety of cells in response to different stimuli and affect the interactions and movement of some cells. They are important in sending cellular signals, and their release affects the behavior of the cells around them (Suzuki, 2018). There are two types of cytokines, pro- inflammatory cytokines and anti-inflammatory cytokines(Karsten et al, 2018). Cytokines participate in systemic inflammation and modulate the immune system, so they play important roles in inflammatory diseases, infectious diseases, and the fight against cancer and other diseases (Harvanová et al, 2023).IL-6 is one of the cytokines that has many anti-inflammatory and hormone-like properties and has a significant effect on

Association Between Prostatitis and Some Biochemical Markers in Patients of the AL-Najaf Province, Iraq

immune cells and other cell types (Akindoyeni *et al* 2024). IL-6 plays a vital role in differentiating host defense mechanisms such as hematopoiesis and response the immune system is responsible for the formation of acute phase proteins through its effect on liver cells, as well as affects neutrophil production, and B-cell growth, and has anti-regulatory T-cell activity (Tang *et al*, 2019).

Minerals such as zinc are considered essential factors in the human body due to their effective role in completing physiological and biochemical processes, especially in maintaining the endocrine glands, specifically the prostate glands, and this confirms its role in the functioning of the ideal male reproductive system (Chasapis *et al*, 2020). where zinc plays an important role in maintaining prostate health and preventing prostate cancer. Scientists have found that cancerous prostate tissue contains a lower amount of zinc than healthy organ tissue. Individuals, especially the elderly, who have low levels of zinc are more likely to suffer from an enlarged prostate, known as benign prostatic hyperplasia, prostatitis, and prostate cancer (Shahrokhi *et al*, 2024). Low zinc levels, as indicated by the current study, are associated with prostatitis, which poses a risk to the patient and the possibility of developing prostate cancer, most previous studies indicate a low zinc level when infected with prostate cancer because of its effective role in programmed cell death and completing the important Krebs cycle in releasing citrate into the semen as a main component of it (Shahrokhi *et al*, 2024).

The erythrocyte sedimentation rate increased in the patient's group, reaching (48.41 ± 13.49) mm/hr., while its rate reached (14.60 ± 4.14) mm/hr. in the healthy group. The results of the statistical analysis showed there are highly significant differences between the two groups of patients and healthy people at probability ($P \leq 0.05$). This increase in the rate of erythrocyte sedimentation is due to the inflammation that occurs in the prostate gland and hemoglobin concentration, the ESR analysis is not specific to prostatitis only but It is used to indicate the extent of disease activity and the extent of response to treatment, as it is a quantitative analysis of red blood cells, where it is arranged in the tube at a specific time that depends on the concentration of the protein in the serum, where it interacts with Red blood cells and leads to an increase in their sedimentation rate (Bruera *et al*, 2022). The increased production of acute condition proteins as a result of inflammation in the body leads to an increase in the rate of sedimentation of red blood cells as a result of increased blood viscosity.

CONCLUSIONS

We conclude from our current study the important relationship between IL-6, zinc levels, and prostatitis, in addition to the role of the ESR test as an indicator of prostatitis. However, we still need additional studies to support these studies and confirm the relationship.

RECOMMENDATION

- must be added of zinc to the diet and maintain levels, to help reduce prostate disease rates.
- Measuring the level of IL-6 as an indicator of the presence of prostatitis.
- Conducting the ESR test periodically as an indicator of inflammation in the body.

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Conflicts of Interest

No conflict of interest.

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REFERENCES

- 1) Graziani A, Grande G, Martin M, Ferraioli G, Colonnello E, Iafrate M, Dal Moro F, Ferlin A. (2023). Chronic Prostatitis/Chronic Pain Pelvic Syndrome and Male Infertility. *Life* (Basel). Aug 7;13(8):1700. doi: 10.3390/life13081700. PMID: 37629557; PMCID: PMC10455764.
- 2) Tylutka, A., Walas, Ł., & Zembron-Lacny, A. (2024). Level of IL-6, TNF, and IL-1 β and age-related diseases: a systematic review and meta-analysis. *Frontiers in Immunology*, 15, 1330386.
- 3) Ohsugi, Y. (2020). The immunobiology of humanized Anti-IL6 receptor antibody: From basic research to breakthrough medicine. *Journal of Translational Autoimmunity*, 3, 100030.
- 4) Al-hadrawi, K. K., & ALGarawy, R. T. (2023). Caspase-3 level is associated with bacterial prostatitis in male infertility. *Journal of Survey in Fisheries Sciences*, 10(3S), 4208-4215.
- 5) Topolyanskaya S. (2021). Interleukin 6 in aging and age-related diseases. *The Clinician*, 14(3-4), 10-17.
- 6) Steinbrenner H, Klotz LO (2020) Selenium and zinc: "antioxidants" for healthy aging? *Zeitschrift für Gerontologie und Geriatrie* 53(4): 295–302.
- 7) Zarezadeh, R., Abbasi, K., Aboutalebi Vand Beilankouhi, E., Navali, N., Hakimi, P., Fattahi, A., & Farzadi, L. (2024). Programmed cell death 4: A novel player in the pathogenesis of polycystic ovary syndrome. *Cell Biochemistry and Function*, 42(1), e3905.
- 8) Al-hadrawi, K. K., ALGarawy, R. T., & Darweesh, M. F. (2022). The Impact of IL-35, Bacterial Prostatitis in Development Male Infertility in Najaf Province Patients. *The Egyptian Journal of Hospital Medicine*, 89(1), 4278-

Association Between Prostatitis and Some Biochemical Markers in Patients of the AL-Najaf Province, Iraq

4283.

- 9) Shahrokhi Nejad, S., Golzari, Z., Zangiabadian, M., Salehi Amniyeh Khozani, A. A., Ebrahimi, R., Nejadghaderi, S. A., & Aletaha, A. (2024). The association between zinc and prostate cancer development: A systematic review and meta-analysis. *Plos one*, 19(3), e0299398.
- 10) Rosa AC, Corsi D, Cavi N, Bruni N, Dosio F (2021) Superoxide dis administration: A review of proposed human uses. *Molecules* 26(7): 1844.
- 11) Bratchikov OI, Tyuzikov IA, Dubonos PA (2020) Clinical and experimental rationale for antioxidant therapy of chronic bacterial prostatitis. *Research Results in Pharmacology* 6(1): 11–19. <https://doi.org/10.3897/rpharmacology.6.50940>
- 12) Santos HO, Teixeira FJ, Schoenfeld BJ (2020) Dietary vs. pharmacological doses of zinc: A clinical review. *Clinical Nutrition* 39(5): 1345–1353.
- 13) Chen, L., Deng, H., Cui, H., Fang, J., Zuo, Z., Deng, J., ... & Zhao, L. (2018). Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget*, 9(6), 7204.
- 14) Daragó A, Klimczak M, Stragierowicz J, Jobczyk M, Kilanowicz A (2021) Age- related changes in zinc, copper and selenium levels in the human prostate. *Nutrients* 13(5): 1403.
- 15) Tishkowski, K., & Gupta, V. (2020). Erythrocyte sedimentation rate.
- 16) Ramsay, E. S., & Lerman, M. A. (2015). How to use the erythrocyte sedimentation rate in pediatrics. *Archives of Disease in Childhood-Education and Practice*, 100(1), 30-36.
- 17) Al-Hadrawi, K. K., & ALGarawy, R. T. (2023). The role of some of the level Antioxidant enzymes and Obesity in development infertility women's infertility in Najaf Province Patients, IRAQ. In *BIO Web of Conferences* (Vol. 65, p. 05050). EDP Sciences.
- 18) Karsten E., Breen, E., & Herbert, B. R. (2018). Red blood cells are dynamic reservoirs of cytokines. *Scientific reports*, 8(1), 3101.
- 19) Harvanová, G., Duranková, S., & Bernasovská, J. (2023). The role of cytokines and chemokines in the inflammatory response. *Alergologia Polska-Polish Journal of Allergology*, 10(3), 210-219.
- 20) Akindoyeni, I. A., Ogunsuyi, O. B., Adefegha, S. A., & Oboh, G. (2024). Selenium biofortified jute leaves exhibited increased phenolic content and enhances anti- inflammatory cytokines and immunoglobulin levels in Wistar rats. *South African Journal of Botany*, 166, 603-611.
- 21) Tang Y., Tao, H., Gong, Y., Chen, F., Li, C., & Yang, X. (2019). Changes of serum IL-6, IL-17, and complements in systemic lupus erythematosus patients. *Journal of Interferon & Cytokine Research*, 39(7), 410-415.
- 22) Chasapis, C. T., Ntoupa, P. S. A., Spiliopoulou, C. A., & Stefanidou, M. E. (2020). Recent aspects of the effects of zinc on human health. *Archives of toxicology*, 94, 1443- 1460.
- 23) Bruera S., Ventura, M. J., Agarwal, S. K., Krause, K. J., & Lopez-Olivo, M. A. (2022). The utility of erythrocyte sedimentation rate, C-reactive protein, and procalcitonin in detecting infections in patients with systemic lupus erythematosus: A systematic review. *Lupus*, 31(10), 1163-1174