



## Relationship between interleukin 6 and 8 with Semen characteristics in fertile patients

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### ABSTRACT

Infertile males were tested for the presence of interleukin-6 and interleukin-8, as well as lipid peroxidation in their sperm. A total of 75 infertile men, including 15 fertile men, were used as controls, with semen samples collected by masturbation. Malondialdehyde (MDA) production in the sperm membrane was used to assess the degree of lipid peroxidation in the membrane. Statistics were used to examine the relationship between interleukin-6 (IL-6) and interleukin-8 (IL-8) in seminal plasma and the lipid peroxidation levels in sperm membranes. There was a statistically significant difference in the concentration of IL-6 in the seminal plasma of infertile and fertile men ( $p < 0.05$ ) between the two groups. On the other hand, the concentration of interleukin-8 (IL-8) in the seminal plasma of infertile men was significantly higher than that of fertile men ( $p < 0.05$ ), and the degree of lipid peroxidation in the seminal plasma of infertile men was significantly higher than that of fertile men ( $p < 0.05$ ). In the seminal plasma, the levels of IL-6 and the process of sperm membrane lipid peroxidation were found to be positively correlated with each other ( $p < 0.05$ ), while the levels of IL-8 in the seminal plasma and sperm membrane lipid peroxidation were found to be positively correlated with each other ( $p < 0.05$ ). There seems to be a possible association between plasma IL-8, IL-6, sperm ranks, and sperm membrane lipid peroxidation based on these results.

**Keywords:** interleukin 6; 8, infertility, semen.

### Introduction

Infertility is a condition that leads to a person having a social impact and we see this with the increasing incidence of infertility [1,2]. Sperm is maintained by maintaining a constant temperature in the scrotum, where the countercurrent phenomenon occurs, through which heat is lost and maintained through blood flow in the microcirculatory network [3,4]. Varicocele is a cause and may be social and leads to infertility in some cases in males and is often caused by surgical

intervention (5,6). More than 9-15% of males worldwide suffer from varicocele [7-9]. Several studies have shown that 9-10% of males suffer from infertility for every 50 infertile men who suffer from varicocele [10]. Varicocele affects the cells of the sperm. Sperm damage can be direct or indirect [11,12] and immunological infertility is one of the main problems in male infertility and is often associated with varicocele and this condition is responsible for 10-15% of all infertility cases [13]. During many studies, factors related to fertility

immunity have been considered since 2010 [14,15]. By studying cells in terms of secretion or production of cytokines, cytokines are considered small peptides that can participate in various immune activities of the body [16,17]. The signal transmitted by cytokines may regulate the growth or proliferation of cells and their differentiation and other functions of the testes [18]. Cytokines are new regulators produced by immune cells and have an important role in the testes and interstitial cells and have a prominent role in Sertoli cells and sperm cells in terms of germ cell growth and also affect their differentiation and also affects the reproductive endocrine glands and finally in the formation of sperm [19,20]. The weakness of cytokine secretion may have a significant impact on the function of the male reproductive system and may lead to infertility [21,22].

### Methods

75 patients (20-44 years old) are suffering from infertility, and their main complaint is infertility. Samples were taken from the Infertility Center in Al-Sadr Teaching City, Najaf, Iraq. Analyses were performed and the levels of IL-6 and 8 in the plasma of seminal were checked, A paired Student's t-test was present to use for locating the statistically significance differences in values.

### Ethical Approval:

Ethical approval was granted by the Ethical Committee for Human and Animal Research at the University of Kufa in 2024. The committee confirmed that the guidelines of the Ethical Committee for Human Research were followed and

that this was done following the conditions that must be followed and stated in the Health Guide for Human Samples and the Use of Laboratory Animals.

### Results

The result indicated a significant reduction ( $p < 0.05$ ) in the sperm concentration in infertile patients unexplained, Asthenozoospermia and Oligozoospermia comparison with the control group. In addition, there was a significant drop ( $p < 0.05$ ) in motility of the sperm, sperm activity, and normal sperm morphology in patients with unexplained, Asthenozoospermia and Oligozoospermia compared with the control group in Table (1)

The outcomes exhibited a significant increase ( $p < 0.05$ ) of Interleukin 6 level in both patients unexplained, Asthenozoospermia and Oligozoospermia compared with the control group shown in figure (1).

The outcomes explain a significant increase ( $p < 0.05$ ) in Interleukin 8 level in both patients unexplained, Asthenozoospermia and Oligozoospermia compared with the group of control shown in Figure (2).

There was a significant positive relationship between IL-6 levels in the plasma of seminal and the lipid peroxidation found in a membrane in spermatozoa ( $p$ ), and a significant positive relationship between IL-8 levels in the plasma of seminal and the lipid peroxidation membrane in sperm ( $p < 0.05$ ).

**Table 1.** semen and sperm parameters in infertile patients compared with the control group

Parameters	Control	unexplained	Asthenozoospermia	Oligozoospermia	L.S.D. 0.05
Sperm concentration (million/ml)	68.66± 2.17 A	45.32± 3.2 B	32.02± 1.18 C	12.15± 1.07 D	4.521
Sperm Percentage of the progressive motile (%)	71.1.5± 3.15A	58.14± 2.11 B	28.16± 2.13 C	18.19± 1.11 D	5.892
Sperm Percentage of the Normal morphology (%)	70.21± 3.15 A	54.12± 2.45 B	34.1 ± 1.2 C	20.08± 4.16 D	5.195
Sperm Vitality Percentage (%)	85.31± 1.55 A	63.24± 2.85 B	50.42± 5.2 C	30.44± 3.85 D	6.942
Malone Didehyde Concentrate	5.13± 0.44 A	7.32± 0.72 B	9.07± 1.24 C	13.41± 1.45 D	1.147

The results in the table represent mean ± standard error S.E.

Number of fertile mens' = 15

Number of mens with unexplained = 25

Number of mens with Asthenozoospermia = 25

Number of mens with Oligozoospermia = 25

The dissimilar letters show significant differences (P<0.05)

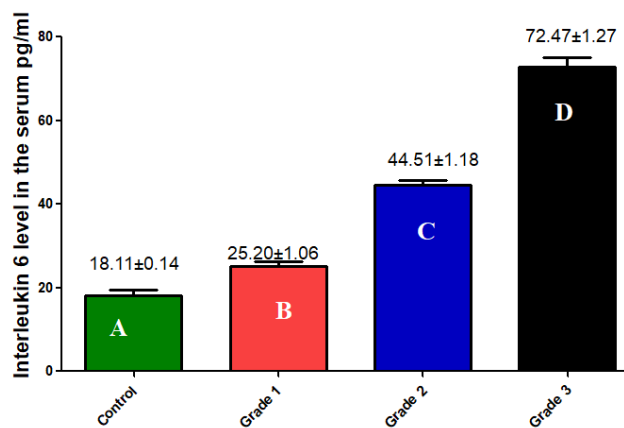


Figure 1. The comparison of Interleukin 6 level in the serum between infertile men compared with the control group

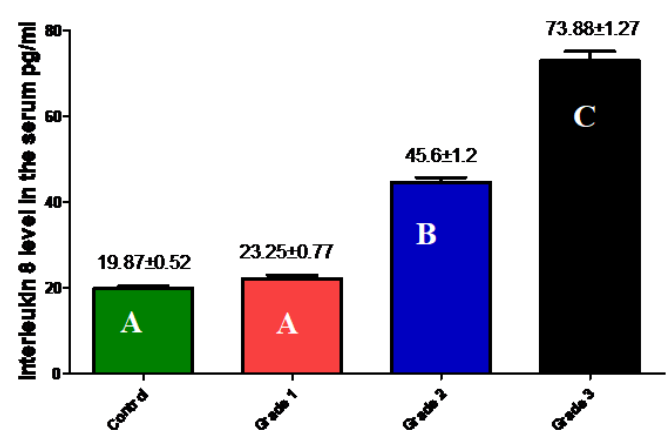


Figure 2. The comparison of Interleukin 8 level in the serum between infertile men compared with the control group

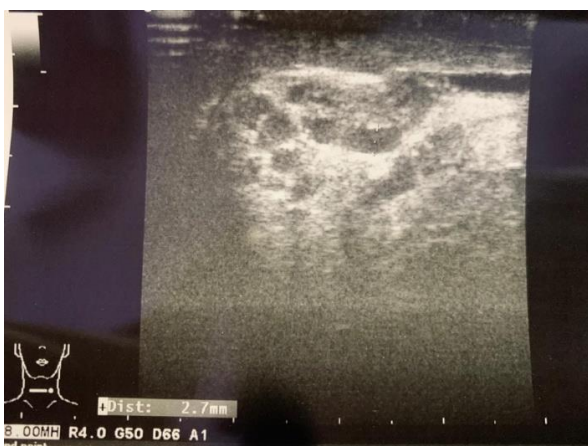


Figure 3. Show the expansion of the vein and show the varicocele grade 2

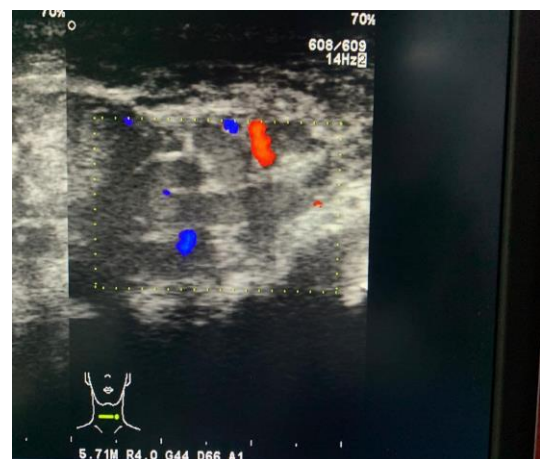


Figure 4. Show the expansion of the vein and show the varicocele grade 1

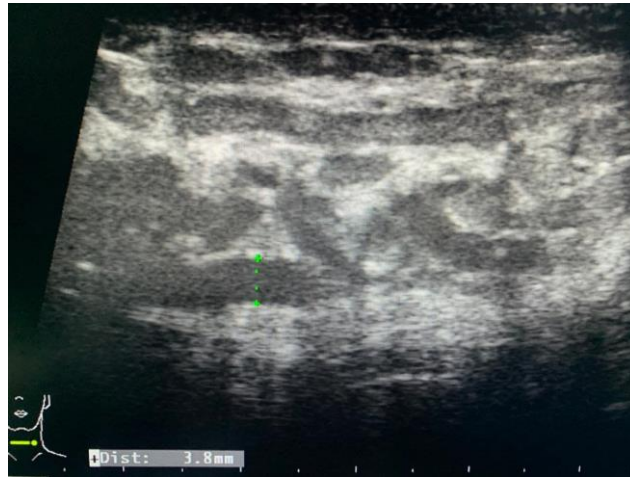


Figure 5. Show the expansion of the vein and show the varicocele grade 3

Table 2. Correlation between Interleukin 8 & 6 and the semen and sperm parameters

Interleukin 8 with Sperm concentration	R= - 0.651
Interleukin 8 with Sperm progressive motile	R = - 0.623
Interleukin 8 with Sperm Normal morphology	R = -0.691
Interleukin 8 with Sperm Vitality	R = - 0.543
Interleukin 8 with Malone Didehyde Concentrate	R = 0.826
Interleukin 6 with Sperm concentration	R= - 0.534
Interleukin 6 with Sperm progressive motile	R = - 0.605
Interleukin 6 with Sperm Normal morphology	R = - 0.634
Interleukin 6 with Sperm Vitality	R = - 0.637
Interleukin 6 with Malone Didehyde Concentrate	R = 0.866

## Discussions:

In this study, the results showed significant differences between groups. It can be speculated that some factors lead to an effect on sperm production and freedom, as well as their normal shape. These results are consistent with the results of two other studies that concluded that varicocele or other causes can have an undesirable effect on semen characteristics [23, 24].

It is likely that varicocele treatment or the use of some medications that lead to the restoration of fertility in men is clearly possible. Thus, it has a confident effect on factors such as the level of sex hormones such as FSH and testosterone levels in serum as well as sperm count and motility. Therefore, we can say that varicocele removal or treatment is a real approach to restoring fertility from male and sexual diseases [25].

A relationship was found between infertility and immune markers in this study, as markers showed a significant increase in the level of cytokines 6 and 8 among infertility groups compared to control groups [26; 27].

Elevated levels of interleukin 6 and 8 in infertile patients lead to stress on androgen production, thus leading to decreased spermatogenesis efficiency, according to a study conducted on Leydig cells. Leydig cells play an important role in evoking male characteristics through the production of testosterone, and any damage to these cells can affect male fertility. *Toxoplasma gondii* is an intracellular parasite capable of attacking any nucleated cell, including cells of the male reproductive system. Therefore, we evaluated the ability of the RH strain of *Toxoplasma* to infect TM3 Leydig cells and the effect of this pathogen on the production of testosterone and sex hormones. First, by performing adhesion, contamination, and intracellular expansion assays, we tracked a dramatic expansion in the amount of infected Leydig cells, which exceeded 48 hours after

infection with *T. gondii*. Time-dependent cultures of TM3-contaminated cells showed increased levels of testosterone as well as monocyte chemoattractant protein-1 (MCP-1) and interferon- $\gamma$  (IFN- $\gamma$ ), consistent with strong *T. gondii* contamination [28]. The study also found a significant increase in cytokines 8 and 6, which is consistent with the findings of other researchers. The results also revealed a link between cytokines 6 and 8 because the test effect caused them to increase together. Increased varicose veins and elevated IL-6 and IL-8 lead to increased oxidative stress and decreased oxygen delivery to the spermatogenic zones, according to a study that states: Oxidative stress is the result of an imbalance between oxygen species receptors and cancer-protective factors in the body that can cause tissue damage. Oxidative stress has a critical role in the pathogenesis of persistent prostatitis/persistent pelvic pain and male infertility. Chronic pelvic pain and prostatitis are major risk factors for male infertility due to the age of unreasonable radical species that damage sperm, proteins, DNA, and lipids and lead to impaired vitality and decreased sperm motility. Here we present a comprehensive survey of the importance of oxidative stress in chronic prostatitis/pelvic pain and male infertility, and we demonstrate the defensive effects of cancer-protective agents against radical species [29,30].

It may explain the interactive promoter species formed by male sperm and leukocytes, which are stimulated by large ranks of IL-6. Furthermore, IL-8 is classified by its chemotactic effect on both T cells and basophils, as well as by exerting a proangiogenic effect on vascular smooth muscle cells. IL-8 is one of the cytokines that shows a major feature in a variety of inflammatory disorders.

## Conclusion

The effect of infertility can have a depressing effect on sperm quality, and therefore its presence



in sperm researchers has an inverse relationship between semen quality and sperm and the level of cytokines 6 and 8 with each other because the effect of the testicles led to their elevation including on the two types of sperm.

#### Conflict of interest:

All authors declare that there is no conflict of interest

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