

ORIGINAL RESEARCH

Interleukin-8 as a potential cytokine marker in male infertility

Bolotbek Rysbaev^{1,*}, Dilshod Mirzakulov², Nursultan Abdubaitov¹, Akylbek Usupbaev¹, Marlen Kylychbekov³, Kanyshai Stambekova¹

¹Department of Urology and Andrology of Pre- and Postgraduate Education, Named After I.K. Akhunbaev of the Kyrgyz State Medical Academy, 720020 Bishkek, Kyrgyzstan

²Department of Obstetrics, Gynecology and Surgical Disciplines of Osh State University, 714000 Osh, Kyrgyzstan

³Department of Andrology at the National Hospital, Republican Urological Center, 720017 Bishkek, Kyrgyzstan

***Correspondence**

t.petrushevskaya@kgma.kg
(Bolotbek Rysbaev)

Abstract

Background: Infertility is defined by the World Health Organization (WHO) as the absence of pregnancy after 12 months or more of regular unprotected sexual activity. Male factors contribute to nearly half of infertility cases, with inflammatory conditions of the male reproductive tract playing a significant role. This study aimed to evaluate interleukin-8 (IL-8) levels in seminal plasma and their association with semen parameters in men with chronic abacterial prostatitis/chronic pelvic pain syndrome (CAP/CPPS). **Methods:** A total of 124 infertile men with CAP/CPPS and 20 healthy fertile controls were included in the study. IL-8 levels in serum and seminal plasma were measured using enzyme-linked immunosorbent assay (ELISA). Semen analysis was performed according to WHO guidelines (1999, 2010). Correlation analysis was conducted to assess the relationships between IL-8 levels and semen parameters. **Results:** IL-8 levels were significantly higher in infertile patients compared with controls, both in serum (9.4 ± 5.6 vs. 0.75 ± 0.11 pg/mL; $p < 0.01$) and seminal plasma (283.6 ± 13.1 vs. 82.6 ± 35.0 pg/mL; $p < 0.01$). Seminal IL-8 showed significant negative correlations with sperm concentration, motility, and fertility indices ($p < 0.05$ to $p < 0.001$). No significant differences in IL-8 levels were observed between CAP/CPPS categories IIIA and IIIB. **Conclusions:** Elevated IL-8 levels are associated with impaired semen quality in men with CAP/CPPS. Seminal IL-8, in particular, may serve as a sensitive biomarker of local immune activation in the male reproductive tract. Further studies are required to determine its diagnostic accuracy and clinical applicability.

Keywords

Male infertility; Cytokines; Interleukin-8; Chronic abacterial prostatitis

La interleucina-8 como posible marcador citocínico en la infertilidad masculina

Resumen

Antecedentes: La infertilidad se define por la Organización Mundial de la Salud (OMS) como la ausencia de embarazo tras 12 meses o más de relaciones sexuales regulares sin protección. Los factores masculinos contribuyen aproximadamente a la mitad de los casos de infertilidad, y las afecciones inflamatorias del tracto reproductor masculino desempeñan un papel importante. El presente estudio tuvo como objetivo evaluar el nivel de interleucina-8 (IL-8) en el plasma seminal y su asociación con los parámetros seminales en hombres con prostatitis crónica abacteriana/síndrome de dolor pélvico crónico (CAP/CPPS). **Métodos:** Se incluyeron un total de 124 hombres infértiles con CAP/CPPS y 20 controles fértiles sanos. Los niveles de IL-8 en suero y plasma seminal se determinaron mediante ensayo inmunoenzimático (ELISA). El análisis seminal se realizó de acuerdo con los criterios de la OMS (1999, 2010). **Resultados:** Los niveles de IL-8 fueron significativamente más altos en los pacientes infértiles en comparación con los controles, tanto en suero (9.4 ± 5.6 frente a 0.75 ± 0.11 pg/mL; $p < 0.01$) como en plasma seminal (283.6 ± 13.1 frente a 82.6 ± 35.0 pg/mL; $p < 0.01$). La IL-8 seminal mostró correlaciones negativas significativas con la concentración espermática, la motilidad y los índices de fertilidad ($p < 0.05$ to $p < 0.001$). No se observaron diferencias significativas en los niveles de IL-8 entre las categorías IIIA y IIIB de CAP/CPPS. **Conclusiones:** Estos hallazgos indican que niveles elevados de IL-8 se asocian con una peor calidad seminal en hombres con CAP/CPPS. La IL-8 puede considerarse un posible biomarcador que refleja la activación inmune local en el tracto reproductor masculino. Sin embargo, se requieren estudios adicionales para evaluar su rendimiento diagnóstico y su aplicabilidad clínica.

Palabras Clave

Infertilidad masculina; Citocinas; Interleucina-8; Prostatitis crónica abacteriana

1. Introduction

Infertility is estimated to affect approximately 8–12% of couples worldwide, with male factors contributing to nearly half of cases [1]. The contribution of the male factor to an infertile marriage is at least 45–50%, of which in 30–45% of cases the cause remains unidentified (idiopathic male infertility) [2]. In addition to genetic and systemic conditions, male infertility may be associated with comorbid diseases, including metabolic disorders, malignancies, and inflammatory conditions of the reproductive tract [3–10].

Urogenital infections and inflammatory diseases play a significant role in male infertility, accounting for up to 15% of cases [11–14]. Increasing evidence suggests that immune-mediated mechanisms, including cytokine dysregulation, are involved in the pathophysiology of impaired spermatogenesis. Cytokines are naturally present in seminal plasma and are produced by both immune and testicular somatic cells, including Sertoli and Leydig cells, where they participate in the regulation of reproductive function [15–18].

Varicocele is one of the most common findings in men with infertility, being reported in approximately 35–40% of infertile patients, whereas immune-related infertility associated with varicocele has been described in about 15% of cases [19–24].

Interleukin-8 (IL-8) is a pro-inflammatory chemokine involved in neutrophil recruitment and activation and represents a key component of innate immune responses. Elevated IL-8 levels have been reported in various inflammatory conditions of the male reproductive tract and may reflect an inflammatory microenvironment associated with oxidative stress and impaired sperm function. In this context, IL-8 can be considered an integrative marker of local immune activation rather than a direct causal factor.

The relationship between cytokine levels and leukocyte counts in semen remains controversial. While some studies report significant associations, others suggest that cytokines may better reflect subclinical or “latent” inflammation, even in the absence of overt leukocytospermia [25–31].

Chronic abacterial prostatitis/chronic pelvic pain syndrome (CAP/CPPS) is a common condition characterized by persistent pelvic symptoms and immune dysregulation without detectable infection. It has been increasingly recognized that CAP/CPPS may be associated with inflammatory alterations in seminal plasma that negatively affect sperm quality [32–38]. However, the relationship between seminal IL-8 levels and semen parameters in men with CAP/CPPS-related infertility remains insufficiently studied.

The aim of the present study was to determine the level of the proinflammatory cytokine IL-8 in the seminal plasma of infertile men with CAP/CPPS and to evaluate its association with semen quality parameters, considering IL-8 as a marker of local immune activation within the male reproductive tract.

2. Materials and methods

2.1 Study population and general characteristics

The study was conducted between January 2023 and June 2025, during which clinical and laboratory data were collected and analyzed.

This study was based on the analysis of existing clinical, laboratory, and biological material data collected within an institutional research platform at the Republican Scientific Center of Urology. No participants were newly recruited specifically for the present study after ethics approval. The investigation represents a retrospective analysis of previously collected data and biological samples obtained during routine diagnostic evaluation and management of patients, in accordance with institutional research procedures and written informed consent.

The study is based on the results of clinical and laboratory examination of 215 men from infertile married couples and 20 healthy fertile men of reproductive age. Based on the results of assessment of infectious and hormonal status, 91 patients from infertile couples were excluded from further analysis. The final analysis included 124 patients with chronic abacterial prostatitis/chronic pelvic pain syndrome (CAP/CPPS) aged 22–45 years (mean age 30.4 ± 3.9 years). The diagnosis of CAP/CPPS was established according to the criteria proposed by the US National Institutes of Health (NIH, 1995).

All patients with CAP/CPPS (categories IIIA and IIIB according to the NIH, 1995) underwent examination and treatment at the Republican Scientific Center of Urology of the National Hospital of the Ministry of Health of the Kyrgyz Republic. Enzyme-linked immunosorbent assay (ELISA) for the determination of interleukin-8 was performed at the Research Institute of Molecular Biology and Medicine of the National Center of Cardiology and Internal Medicine named after academician M. Mirrakhimov, Ministry of Health of the Kyrgyz Republic.

Inclusion criteria for the main group were:

- Presence of CAP/CPPS (categories IIIA or IIIB according to the NIH, 1995);
- Absence of pregnancy in the marriage for more than 12 months in individuals of reproductive age with regular sexual intercourse and without the use of contraceptives.

Exclusion criteria were: female factor infertility; hormonal disorders (based on blood levels of testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, thyroid-stimulating hormone (TSH) and thyroxine (T4)); confirmed viral–bacterial infections in either partner; pathological processes of the scrotal organs (varicocele, cysts, orchitis, epididymitis, *etc.*); exacerbation of chronic somatic diseases at the time of examination; pronounced impairment of liver and/or kidney function with evidence of vital organs decompensation.

A comprehensive examination of patients with chronic abacterial prostatitis/chronic pelvic pain syndrome (CAP/CPPS) and fertile men included an analysis of anamnestic and clinical data, findings from digital rectal examination of the prostate, laboratory investigations (bacterioscopic and bacteriological analysis of urethral secretions), macroscopic and microscopic examination of

ejaculate, and polymerase chain reaction (PCR)-based testing for sexually transmitted infections. To assess the hormonal profile, the levels of major hormones (testosterone, LH, FSH, prolactin, and estradiol) were determined. Ultrasound examination of the prostate with Doppler imaging was performed, and the concentration of interleukin-8 in blood and seminal fluid was measured using the enzyme-linked immunosorbent assay (ELISA). The present study represents a retrospective analysis of existing clinical and laboratory data, as well as previously collected biological samples, obtained within an approved institutional research platform. No patients were newly recruited specifically for this study. Written informed consent had been obtained from all participants at the time of sample and data collection. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of the Kyrgyz State Medical Academy on 10 June 2025 (Approval No. 26).

2.2 Methods

2.2.1 Pre-analytical procedures

Before the study, patients were advised to avoid exposure to toxic factors (alcohol and smoking), as well as heavy physical exertion and hyperthermic conditions.

Ejaculate was obtained by masturbation after 4–5 days of sexual abstinence directly in the laboratory under conditions minimizing contamination.

To obtain seminal plasma, part of the ejaculate was centrifuged for 20 minutes at 1550 rpm, after which the supernatant was re-centrifuged to remove residual cellular elements. The resulting seminal plasma was stored at -80°C until subsequent measurement of IL-8 levels.

Blood sampling was performed in the morning after an overnight fast by venipuncture into a dry tube (5 mL). Serum was obtained by centrifugation at 1500 rpm for 20 minutes. Serum samples were stored at -80°C until analysis.

2.2.2 Hormonal assays

Serum levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and testosterone were determined by enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions using commercially available test systems.

2.2.3 Semen analysis

Macro- and microscopic semen analysis was performed using the standard protocol recommended by WHO (1999, 2010). The semen analysis included: ejaculate volume; total sperm count in the ejaculate; sperm concentration per 1 mL; motility of spermatozoa categories A + B; sperm viability; sperm morphology with assessment of head, neck and tail defects; liquefaction time and ejaculate pH; presence of leukocytes in the ejaculate; and the Farris fertility index:

$$I = V \times N \times M/100.$$

Where V is the ejaculate volume (mL), N is the number of spermatozoa in 1 mL, and M is the percentage of motile spermatozoa.

Sperm motility was classified into categories A, B, C, and D

according to the following criteria:

- A—rapid progressive motility (*i.e.*, $>25\ \mu\text{m/s}$ at 37°C);
- B—slow or sluggish progressive motility;
- C—non-progressive motility (vibratory or pendulum-like) with a speed $<5\ \mu\text{m/s}$;
- D—immotile spermatozoa.

Given that the key condition of semen fertility is a sufficient number of structurally normal spermatozoa exhibiting progressive motility, we used the following formula to calculate and evaluate ejaculate parameters:

$$\text{CFS} = \text{CS} \times \text{VS} \times \text{PPM} \times \text{NM}.$$

Where:

CFS—concentration of fertile sperm;

CS—sperm concentration per 1 mL;

VS—percentage of viable spermatozoa;

PPM—percentage of spermatozoa with straight-line progressive motility;

NM—percentage of spermatozoa with normal morphology.

We then determined the proportion of functional spermatozoa, termed the sperm fertility index (SFI):

$$\text{SFI} = (\text{CFS} \times 100)/\text{CS}.$$

2.2.4 Enzyme-linked determination of human interleukin-8 concentration in blood and seminal plasma

Semen samples were collected after 3–5 days of sexual abstinence. Following liquefaction, samples were centrifuged at 1500–2000g for 10–15 minutes, and seminal plasma was stored at -80°C until analysis. IL-8 concentrations were measured using a commercially available ELISA kit according to the manufacturer's protocol. All samples were analyzed in duplicate.

The method is based on a solid-phase “sandwich” variant of enzyme-linked immunosorbent assay. The specific reagents of the kit include monoclonal antibodies to IL-8 adsorbed on the surface of the wells of a detachable polystyrene microplate, a conjugate of polyclonal antibodies to IL-8 with biotin, and calibration samples containing IL-8.

At the first stage of analysis, test and control samples are incubated in wells with immobilized antibodies. IL-8 present in the samples binds to the immobilized antibodies; unbound material is removed by washing. The bound IL-8 then interacts during incubation with conjugate No. 1 (biotin-labeled antibodies to human IL-8). Unbound conjugate No. 1 is removed by washing. At the third stage, the bound conjugate No. 1 interacts during incubation with conjugate No. 2 (streptavidin–horseradish peroxidase). After a third washing step, the amount of bound conjugate No. 2 is determined by a color reaction using horseradish peroxidase substrate—hydrogen peroxide—and the chromogen tetramethylbenzidine. The reaction is stopped by addition of stop solution, and optical density in the wells is measured at 450 nm. The intensity of the yellow color is proportional to the amount of IL-8 present in the sample.

2.2.5 Statistical analysis

Statistical processing of the data was performed using STATISTICA 6.0 software (StatSoft Inc., Tulsa, OK, USA) and

a standard statistical software package. Normality of distribution of the variables within groups was assessed using the Levene and Shapiro-Wilk tests. Between-group differences were evaluated by non-parametric χ^2 and Z tests (for qualitative variables), by the Mann-Whitney U-test (for asymmetrically distributed quantitative variables), and by the parametric Student's *t*-test (for normally distributed variables).

Significance of intra-group changes during treatment was assessed, in the case of normally distributed variables, using the paired Student's *t*-test; in the case of asymmetrically distributed variables, using the non-parametric Wilcoxon test (W).

Relationships between variables were analyzed using correlation analysis with calculation of Pearson's or Spearman's correlation coefficient *r*, depending on the distribution of the data. When analyzing the relationship between an ordinal qualitative variable and a quantitative variable, gamma correlation was used. Differences were considered statistically significant at $p < 0.05$.

3. Results

3.1 Baseline characteristics of the study population

A total of 124 patients with CAP/CPPS and 20 healthy fertile men were included in the study. Patients were divided into two groups: Group IIIA ($n = 96$) and Group IIIB ($n = 28$). The control group consisted of age-matched healthy fertile men.

Baseline characteristics of the study population are presented in Table 1.

No significant differences in age were observed between the groups ($p > 0.05$). The mean age was 30.4 ± 4.3 years in Group IIIA, 30.1 ± 2.4 years in Group IIIB, and 30 ± 4.5 years in the control group.

The duration of infertile marriage was similar between Groups IIIA and IIIB (23.4 ± 3.8 vs. 25.1 ± 4.3 months, $p = 0.058$), as was the duration of CAP/CPPS (6.7 ± 2.5 vs. 7.1 ± 2.8 years, $p = 0.474$).

The prevalence of chronic somatic diseases, alcohol consumption, and smoking did not differ significantly between groups (Table 1).

3.2 Clinical and reproductive characteristics

Healthy men in the control group had proven fertility: 65% had children, and 35% had partners in late pregnancy, whereas patients from infertile couples had no history of successful conception.

No clinically significant bacterial or viral infections were detected in semen samples. Microbial flora was present at levels below diagnostic thresholds ($<1 \times 10^3$ CFU/mL) and was dominated by coccal microorganisms. PCR testing for sexually transmitted infections was negative in all groups.

3.3 Hormonal status

Hormonal parameters are presented in Table 2.

No statistically significant differences were observed between infertile patients and controls in serum levels of LH, FSH, prolactin, or testosterone.

Thus, endocrine function in patients with CAP/CPPS was comparable to that of healthy fertile men.

3.4 Semen parameters in patients with CAP/CPPS complicated by infertility

In male fertility disorders, one of the most informative methods of primary diagnosis is semen analysis; its key parameters include sperm concentration, motility characteristics, and the proportion of morphologically normal spermatozoa (WHO, 2010).

In the present study, semen analysis was performed in 20 healthy fertile men (comparison group) and in 124 men from infertile couples. Of the latter, 96 patients were diagnosed with CAP/CPPS category IIIA (presence of signs of inflammatory process in the prostate), and 28 patients with CAP/CPPS category IIIB (no signs of inflammatory involvement of the prostate).

Evaluation of semen parameters in healthy men showed that the main ejaculate characteristics (volume, sperm concentration, proportion of progressively motile spermatozoa, percentage of morphologically normal spermatozoa) conformed to the reference values recommended by WHO. Mean ejaculate volume in this group was 3.9 ± 1.8 mL; total sperm count, 276 ± 145 million; sperm concentration, 74.3 ± 27.1 million/mL; proportion of motile spermatozoa, $79.1 \pm 8.4\%$; proportion of morphologically normal spermatozoa, $85.2 \pm 3.9\%$.

TABLE 1. General characteristics of patients in the main and control groups.

Indicator	Control group ($n = 20$)	Men from infertile couples ($n = 124$)		<i>p</i>
		Group IIIA ($n = 96$)	Group IIIB ($n = 28$)	
Mean age, yr	30.0 ± 4.5	30.4 ± 4.3	30.1 ± 2.4	0.641
Duration of infertile marriage, mon	–	23.4 ± 3.8	25.1 ± 4.3	0.058
Duration of CAP/CPPS, yr	–	6.7 ± 2.5	7.1 ± 2.8	0.474
Men with chronic somatic diseases, %	4 (20%)	15 (15.5%)	4 (14.8%)	1.000
Men regularly consuming alcohol, %	1 (5%)	3 (3.1%)	2 (7.4%)	0.395
Men smoking ≥ 10 cigarettes per day, %	9 (45%)	36 (37.1%)	12 (44.4%)	0.659

p: significance of differences between Groups IIIA and IIIB; all differences were non-significant ($p > 0.05$).

TABLE 2. Evaluation of hormonal status in fertile men and men from infertile couples.

Indicator	Control group (n = 20)	Men from infertile couples (n = 124)		<i>p</i>
		Group IIIA (n = 96)	Group IIIB (n = 28)	
LH, mIU/L	3.51 ± 0.37	3.20 ± 0.19	3.83 ± 0.39	<0.001
FSH, mIU/L	3.76 ± 0.32	3.82 ± 0.35	3.45 ± 0.32	<0.001
Prolactin, mIU/L	223.5 ± 20.3	285.0 ± 18.3	284.6 ± 15.8	0.910
Testosterone, nmol/L	19.07 ± 0.79	17.60 ± 0.80	17.10 ± 0.83	0.005

p: significance of differences between Groups IIIA and IIIB; no differences compared with the control group.

LH: luteinizing hormone; FSH: follicle-stimulating hormone.

It is well established that the fertilizing capacity of semen increases not in parallel with the absolute sperm count, but depends on the proportion of motile and morphologically normal spermatozoa. The indices we used—CFS (concentration of fertile sperm) and SFI (sperm fertility index)—are simple, suitable for outpatient setting and do not require expensive equipment, which is particularly important at present. As shown in Table 3, the mean CFS in the group of fertile men was 41.0 ± 19.0 million/mL, and SFI was $54.4 \pm 11.9\%$.

In the overall group of infertile patients with CAP/CPPS, pronounced abnormalities of semen parameters were found. These patients had significantly lower total sperm count and concentration compared with controls (85.9 ± 65.1 million and 30.0 ± 20.8 million/mL, respectively; $p < 0.001$) (Table 3). The proportion of motile spermatozoa averaged $44.8 \pm 21.1\%$, which was significantly lower than in the control group. The proportion of morphologically normal spermatozoa in CAP/CPPS patients was slightly lower than in controls ($83.3 \pm 8.3\%$ vs. $85.2 \pm 3.9\%$; $p = 0.008$); however, the most frequent morphological defects were neck ($8.7 \pm 5.1\%$) and head abnormalities ($5.9 \pm 4.7\%$). CFS was 7.38 ± 6.89 million/mL, almost five times lower than in fertile men ($p < 0.001$). SFI was also markedly reduced compared with controls. The distribution of semen abnormalities in infertile men with CAP/CPPS is presented in Table 3.1.

In the infertile group, the following semen abnormalities were recorded:

- Oligozoospermia—34.7% of cases;
- Asthenozoospermia—59.7% of cases;
- Teratozoospermia—35.5% of cases.

Both isolated abnormalities and combinations thereof were observed:

- Isolated asthenozoospermia—15.3%;
- Isolated teratozoospermia—20.2%;
- Asthenoteratozoospermia—7.3%;
- Oligoteratozoospermia—2.4%;
- Oligoasthenozoospermia—21.8%;
- Oligoasthenoteratozoospermia—10.5%.

Normal semen parameters (normozoospermia) were found in 25 infertile men with CAP/CPPS (22.6% of cases).

When the semen abnormalities were analyzed separately in Groups IIIA and IIIB, the lowest values of total sperm count and concentration were recorded in Group IIIB— 49.8 ± 27.0 million and 18.7 ± 9.7 million/mL, respectively. These values were lower not only compared with the control group

($p < 0.001$) but also compared with Group IIIA ($p < 0.001$) (Table 3). At the same time, the proportion of morphologically normal spermatozoa in Group IIIB was higher than in Group IIIA ($86.1 \pm 5.3\%$ vs. $82.4 \pm 8.6\%$; $p = 0.008$) and comparable to that of the control group.

Furthermore, CFS in Group IIIB was significantly lower than in Group IIIA (3.93 ± 3.91 million/mL vs. 8.38 ± 7.26 million/mL; $p < 0.001$). The groups did not differ significantly in terms of the proportion of motile spermatozoa ($p = 0.355$) or SFI ($p = 0.703$) (Table 3); however, both indices were markedly reduced in infertile men compared with controls ($p < 0.01$).

Analysis of the frequency of qualitative semen abnormalities in CAP/CPPS patients showed that asthenozoospermia (75% vs. 55.2%; $p = 0.048$) and oligoasthenozoospermia (42.9% vs. 15.6%; $p = 0.006$) were significantly more frequent in Group IIIB than in Group IIIA. Conversely, morphological disorders (teratozoospermia) were less frequent in Group IIIB (14.3% vs. 41.7% in Group IIIA; $p = 0.008$). The groups did not differ significantly in the frequency of other semen abnormalities. The prevalence of normozoospermia was somewhat lower in Group IIIB than in Group IIIA (10.7% vs. 26.0%), although the difference was not statistically significant ($p = 0.123$).

Thus, signs of pathospermia were observed in 77.4% of infertile men. The most frequent disorder was impaired sperm motility (59.7%), whereas the proportions of oligozoospermia and teratozoospermia were 34.7% and 35.5%, respectively. In the majority of cases (64.5%), combinations of two or three semen abnormalities were recorded. Infertile men were characterized by a pronounced decrease in CFS and SFI. Distinct qualitative differences in semen parameters were identified between CAP/CPPS patients of Groups IIIA and IIIB: the former were characterized by a higher frequency of morphologically abnormal spermatozoa (41.7%), whereas the latter exhibited lower sperm concentration and CFS together with a higher frequency of asthenozoospermia (75%) and oligoasthenozoospermia (42.9%).

3.5 IL-8 levels in serum and seminal plasma

Normal gametogenesis and fertilization require the interaction of a large number of cells, which is realized not only via direct cell–cell contacts but also through a complex system of cytokine signaling; hormonal and growth factors are also involved in the regulation of spermatogenesis.

TABLE 3. Main semen parameters in fertile and infertile men.

Parameter	Control	Infertile men (overall)	Group IIIA	Group IIIB	<i>p</i>
Number of subjects, n	20	124	96	28	-
Ejaculate volume, mL	3.9 ± 1.8	3.1 ± 1.4	3.1 ± 1.5	3.0 ± 1.2	0.761
Total sperm count, million	276.0 ± 145	85.9 ± 65.1**	96.4 ± 69.2**	49.8 ± 27.0**	<0.001
Sperm concentration, million/mL	74.3 ± 27.1	30.0 ± 20.8**	33.3 ± 22.1**	18.7 ± 9.7**	<0.001
Progressively motile sperm (A + B), %	79.1 ± 8.4	44.8 ± 21.1**	45.8 ± 20.6**	41.3 ± 22.9**	0.355
Morphologically normal spermatozoa, %	85.2 ± 3.9	83.3 ± 8.3	82.4 ± 8.6	86.1 ± 5.3	0.008
CFS, million/mL	41.0 ± 19.0	7.38 ± 6.89**	8.38 ± 7.26**	3.93 ± 3.91**	<0.001
SFI, %	54.4 ± 11.9	21.7 ± 17.1**	22.0 ± 16.6**	20.5 ± 18.6**	0.703

p: significance of differences between Groups IIIA and IIIB. **: significance of differences compared to control; *p* < 0.01. CFS: concentration of fertile sperm; SFI: sperm fertility index.

TABLE 3.1. Frequency of spermatogenesis disorders in fertile and infertile men.

Parameter	Control	Infertile men (overall)	Group IIIA	Group IIIB	<i>p</i>
Oligozoospermia, %	–	34.7	32.3	42.9	0.368
Asthenozoospermia, %	–	59.7	55.2	75.0	0.048
Teratozoospermia, %	–	35.5	41.7	14.3	0.008
AT, % (asthenoteratozoospermia)	–	7.3	9.4	–	0.207
OT, % (oligoteratozoospermia)	–	2.4	3.1	–	1.000
OAT, % (oligoasthenoteratozoospermia)	–	10.5	13.5	–	0.117
A, % (isolated asthenozoospermia)	–	15.3	15.6	14.3	1.000
T, % (isolated teratozoospermia)	–	20.2	16.7	32.1	0.106
OA, % (oligoasthenozoospermia)	–	21.8	15.6	42.9	0.006
Normozoospermia, %	20 (100%)	22.6	26.0	10.7	0.123

p: significance of differences between Groups IIIA and IIIB.

It has been shown that human seminal fluid contains various cytokines and their soluble receptors. The level of certain cytokines, including IL-8, in seminal fluid is higher than the corresponding serum concentrations, which suggests a potential role for cytokines in the regulation of male fertility.

We therefore studied IL-8 levels in blood and seminal fluid of healthy men and infertile men with CAP/CPSPS. The results are presented in Table 3.2.

As shown in Table 3.2, we found a statistically significant increase in IL-8 levels in subfertile CAP/CPSPS patients, serum IL-8 exceeded that of healthy fertile men by 12.5-fold (9.4 ± 5.6 pg/mL vs. 0.75 ± 0.11 pg/mL; *p* < 0.01). At the same time, the subgroups of CAP/CPSPS patients did not differ significantly in serum IL-8 (9.2 ± 5.4 pg/mL in Group IIIA vs. 10.0 ± 6.0 pg/mL in Group IIIB; *p* = 0.531), which suggests the presence of latent inflammation in both groups.

When IL-8 in seminal plasma was analyzed, increased local production of the pro-inflammatory mediator IL-8 appears to be a distinctive feature of patients with impaired reproductive function (Table 3.2). Mean IL-8 concentration in seminal plasma of infertile men was 283.6 ± 13.1 pg/mL, significantly higher than in controls (82.6 ± 35.0 pg/mL; *p* < 0.01). Again, there were no significant differences in seminal IL-8 levels between CAP/CPSPS patients with or without signs of inflammation (282.9 ± 13.3 pg/mL vs. 286.0 ± 12.2 pg/mL; *p* =

0.272).

Analysis of IL-8 levels according to semen abnormality type (Table 3.3) showed that serum IL-8 concentrations were comparable in normozoospermia and in various forms of pathospermia: 8.4 ± 5.6 pg/mL in oligozoospermia, 8.7 ± 5.5 pg/mL in asthenozoospermia, 8.5 ± 6.3 pg/mL in teratozoospermia, and 9.8 ± 4.7 pg/mL in normozoospermia (all *p* > 0.05).

Similar findings were obtained for seminal IL-8. Its content was 287.0 ± 12.3 pg/mL in oligozoospermia, 284.6 ± 12.5 pg/mL in asthenozoospermia, 285.6 ± 12.3 pg/mL in teratozoospermia, and 280.0 ± 13.4 pg/mL in normozoospermia (Table 3.3). No significant differences were observed between most groups (all *p* > 0.05), although seminal IL-8 levels were significantly higher in oligozoospermia than in normozoospermia (*p* = 0.038).

Correlation analysis of serum and seminal IL-8 levels with semen parameters yielded the following results. Serum IL-8 was significantly associated with semen characteristics. In Group IIIA, there was a significant negative correlation between serum IL-8 and fertility indices (CFS: *r* = -0.28, *p* = 0.006; SFI: *r* = -0.21, *p* = 0.039) and sperm motility (A + B, %: *r* = -0.21, *p* = 0.039). In Group IIIB, IL-8 correlated with fertility indices (CFS: *r* = -0.74, *p* < 0.001; SFI: *r* = -0.39, *p* = 0.040), sperm motility (A + B, %: *r* = -0.41, *p* = 0.029), total sperm count (*r* = -0.69, *p* < 0.001), and sperm concentration

TABLE 3.2. Interleukin-8 levels in serum and seminal plasma of healthy men and infertile patients.

Indicator	Control	Overall infertile group	Group IIIA	Group IIIB	<i>p</i>
IL-8 in serum, pg/mL	0.75 ± 0.11	9.4 ± 5.6**	9.2 ± 5.4**	10.0 ± 6.0**	0.531
IL-8 in seminal plasma, pg/mL	82.60 ± 35.00	283.6 ± 13.1**	282.9 ± 13.3**	286.0 ± 12.2**	0.272

p: significance of differences between Groups IIIA and IIIB; **: $p < 0.01$ vs. control. IL: Interleukin.

TABLE 3.3. IL-8 levels according to semen abnormalities.

Type of semen abnormality	IL-8 in serum, pg/mL	IL-8 in semen, pg/mL
Oligozoospermia (1)	8.4 ± 5.6	287.0 ± 12.3
Asthenozoospermia (2)	8.7 ± 5.5	284.6 ± 12.5
Teratozoospermia (3)	8.5 ± 6.3	285.6 ± 12.3
Normozoospermia (4)	9.8 ± 4.7	280.0 ± 13.4
<i>p</i> 1–2	0.779	0.315
<i>p</i> 1–3	0.938	0.597
<i>p</i> 1–4	0.275	0.038
<i>p</i> 2–3	0.862	0.672
<i>p</i> 2–4	0.338	0.139
<i>p</i> 3–4	0.334	0.092

p: reliability of differences between different variants of semen abnormality. IL: Interleukin.

($r = -0.75$, $p < 0.001$) (Table 3.4).

Seminal IL-8 appeared to be a more sensitive marker of spermatogenesis efficiency than serum IL-8 and showed significant correlations with sperm concentration, motility, presence of degenerative forms and fertility indices (Table 3.5). Certain differences were observed between Groups IIIA and IIIB. In Group IIIA, seminal IL-8 levels were strongly associated with total sperm count ($r = -0.42$, $p < 0.001$), concentration ($r = -0.46$, $p < 0.001$), motility ($r = -0.37$, $p < 0.001$) and fertility indices (CFS: $r = -0.41$, $p < 0.001$; SFI: $r = -0.30$, $p < 0.001$). In Group IIIB, IL-8 levels were correlated mainly with total sperm count ($r = -0.72$, $p < 0.001$) and the presence of degenerative forms ($r = -0.84$, $p < 0.001$).

Of particular note is the absence of significant correlations between serum or seminal IL-8 levels and leukocyte counts in seminal fluid ($p > 0.05$) (Tables 3.4 and 3.5). This observation suggests that IL-8 may reflect local immune activation independently of leukocytospermia. The lack of association may also be related to the relatively homogeneous study population, in which all patients were diagnosed with CAP/CPPS.

4. Discussion

The present study demonstrates that men with infertility associated with CAP/CPPS exhibit significantly elevated IL-8 levels in both serum and seminal plasma, accompanied by deterioration of key semen parameters. These findings support the concept that chronic immune dysregulation contributes to impaired male reproductive function.

The present findings, demonstrating lower sperm concentration and CFS in patients with CAP/CPPS category IIIB compared with category IIIA, are consistent with previous reports indicating that semen quality may be impaired even in the absence of overt inflammatory signs [39].

Several studies have shown that inflammatory mediators, including IL-8, negatively affect sperm concentration and motility, supporting the concept of cytokine-mediated reproductive dysfunction. Importantly, it has been demonstrated that patients with CAP/CPPS category IIIB may exhibit subclinical inflammation, which is not reflected by leukocyte counts but may still contribute to impaired spermatogenesis [40, 41].

This may explain why, in our study, patients in Group IIIB exhibited more pronounced quantitative abnormalities despite the absence of classical inflammatory features. Furthermore, cytokines such as IL-8 have been shown to represent more sensitive indicators of local immune activation than leukocytospermia, which is consistent with the absence of correlation between leukocyte levels and IL-8 observed in our study [42].

Importantly, IL-8 should not be interpreted as an isolated causal factor in spermatogenic impairment. Rather, it reflects an integrated marker of local inflammatory and immune activation within the male reproductive tract. The observed negative correlations between IL-8 levels and sperm concentration, motility, and fertility indices suggest that the severity of immune activation is closely associated with the degree of reproductive dysfunction.

A notable finding is the absence of significant differences in IL-8 levels between CAP/CPPS categories IIIA and IIIB. This suggests that clinically apparent inflammation (leukocyte-associated) does not fully capture the underlying immune activity. These results are consistent with the concept of subclinical or neuroimmune inflammation, in which cytokine-mediated immune dysregulation persists even in the absence of classical inflammatory markers.

Furthermore, the lack of correlation between IL-8 levels and leukocyte counts in seminal fluid supports the hypothesis that cytokine profiling may provide additional and more sensitive information compared to conventional markers of inflamma-

TABLE 3.4. Correlations between serum IL-8 levels and semen parameters.

Parameter	All patients		Group IIIA		Group IIIB	
	<i>R</i>	<i>p</i>	<i>R</i>	<i>p</i>	<i>R</i>	<i>p</i>
Ejaculate volume, mL	−0.23	0.018	−0.24	0.018	−0.28	0.149
Total sperm count, million	−0.07	0.440	−0.19	0.064	−0.69	<0.001
Sperm concentration, million/mL	0.01	0.912	−0.12	0.244	−0.75	<0.001
Motility A, %	−0.05	0.581	−0.05	0.629	−0.20	0.308
Motility B, %	−0.13	0.150	−0.33	<0.001	−0.44	0.019
Motility C, %	0.20	0.026	0.17	0.098	0.34	0.084
Motility D, %	0.07	0.440	0.20	0.049	0.35	0.068
A + B, %	−0.06	0.508	−0.21	0.039	−0.41	0.029
Abnormal forms, %	−0.07	0.440	−0.14	0.174	0.21	0.283
CFS, million/mL	−0.09	0.320	−0.28	0.006	−0.74	<0.001
SFI, %	−0.07	0.440	−0.21	0.039	−0.39	0.040
Leukocytes	0.14	0.121	0.05	0.629	0.17	0.387

CFS: concentration of fertile sperm; SFI: sperm fertility index; R: Spearman correlation coefficient.

TABLE 3.5. Correlations between seminal IL-8 levels and semen parameters.

Parameter	All patients		Group IIIA		Group IIIB	
	<i>R</i>	<i>p</i>	<i>R</i>	<i>p</i>	<i>R</i>	<i>p</i>
Ejaculate volume, mL	0.04	0.661	−0.02	0.846	0.12	0.542
Total sperm count, million	−0.24	0.010	−0.42	<0.001	−0.72	<0.001
Sperm concentration, million/mL	−0.34	<0.001	−0.46	<0.001	−0.21	0.284
Motility A, %	−0.20	0.050	−0.31	<0.001	0.17	0.387
Motility B, %	−0.23	0.010	−0.31	<0.001	0.02	0.920
Motility C, %	0.11	0.224	0.13	0.207	0.03	0.880
Motility D, %	0.19	0.050	0.27	0.010	0.04	0.841
A + B, %	−0.22	0.020	−0.37	<0.001	0.05	0.801
Abnormal forms, %	0.21	0.020	0.09	0.382	−0.84	<0.001
CFS, million/mL	−0.28	<0.001	−0.41	<0.001	0.23	0.239
SFI, %	−0.23	0.010	−0.30	<0.001	−0.07	0.724
Leukocytes	−0.03	0.739	−0.01	0.922	−0.07	0.724

CFS: concentration of fertile sperm; SFI: sperm fertility index; R: Spearman correlation coefficient.

tion. This finding aligns with previous studies reporting that seminal cytokines may better reflect latent inflammatory processes in the male reproductive tract.

The more pronounced associations observed between seminal IL-8 and semen parameters, compared with serum IL-8, indicate that local cytokine production plays a more direct role in spermatogenic dysfunction. This highlights the importance of assessing seminal plasma rather than relying solely on systemic inflammatory markers.

From a clinical perspective, IL-8 may be considered a marker of inflammatory stress within the reproductive tract and could potentially be useful for patient stratification and monitoring of anti-inflammatory therapy. However, its use as a diagnostic tool remains limited due to the absence of defined thresholds, as well as a lack of sensitivity and specificity data.

The study has several limitations, including its cross-

sectional design, lack of longitudinal follow-up, and assessment of a single cytokine. The complexity of the cytokine network involved in male infertility warrants further investigation. Future prospective studies should evaluate panels of inflammatory markers and explore their predictive and diagnostic value.

Overall, the findings support a broader pathogenetic model in which chronic immune imbalance and cytokine-mediated mechanisms contribute to male infertility, even in the absence of overt infection or leukocytospermia.

5. Conclusions

IL-8 levels in serum and, particularly, seminal plasma are significantly elevated in men with CAP/CPPS-associated infertility and are associated with impaired semen parameters.

Seminal IL-8 shows stronger correlations with sperm concentration, motility and fertility indices than serum IL-8, suggesting a key role of local immune activation in reproductive dysfunction.

IL-8 may be considered a potential biomarker reflecting inflammatory processes in the male reproductive tract; however, further studies are required to establish its diagnostic value and clinical applicability.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

BR and DM—designed the research study. AU—provided technical and material support; critical revision of the manuscript; supervision. BR, DM and NA—performed the research and wrote the manuscript. BR, MK and KS—analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of the Kyrgyz State Medical Academy on 10 June 2025 (Approval no. 26).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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