Serum 17-Hydroxyprogesterone in Correlation With Semen Analysis Results and Hormonal Profile of Infertile Men

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Abstract- Semen analysis and the evaluation of male reproductive hormones remain integral to the assessment of infertile men. Recent studies have demonstrated that serum 17-hydroxyprogesterone (17-OHP) levels serve as a reliable marker of the intratesticular testosterone environment. This study aims to determine the correlation between serum 17-OHP levels, seminal fluid analysis (SFA), and the hormonal profiles in infertile men. In this cross-sectional study, one hundred serum and seminal fluid samples were collected from infertile men attending the Al-Kafeel IVF center, Karbala, from October 2024 to May 2025. Participants were divided into four groups according to their SFA results. All included men underwent seminal fluid analysis according to WHO 2021 guidelines, and serum levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), total testosterone (TT), prolactin, estradiol (E2), and 17-OHP were measured using the ELISA technique. The current study showed no significant correlation between 17-OHP and any of the measured hormones in the normozoospermia group, and a strong, statistically significant negative correlation between serum 17-OHP and FSH across all groups (r= -0.375, *P*=0.000). There was also a negative correlation between sperm concentration and serum 17-OHP across all groups (r= -0.234, *P*=0.019). In the asthenozoospermia group, serum 17-OHP exhibited a highly significant negative correlation with sperm concentration and semen viscosity (r= -0.670, *P*=0.001) and (r= -0.590, *P*=0.005), respectively. A significant positive correlation was found between serum 17-OHP and sperm motility in the asthenozoospermia group (r=0.538, *P*=0.012), and a positive correlation with round cells in the oligoasthenoteratozoospermia (OAT) group (r=0.438, *P*=0.025). The study emphasizes the complex relationship between 17-OHP levels and sperm parameters. Although 17-OHP showed a strong negative association with FSH, statistically significant correlations may still have limited or unclear clinical implications, necessitating further studies.

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Introduction

Traditional seminal fluid analysis (SFA) and serum hormone testing—testosterone (TT), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2)—are used in the evaluation of male infertility (1). Healthy testicular function and spermatogenesis are regulated by hormones through the intratesticular actions of the pituitary gonadotropins LH and FSH. LH stimulates Leydig cells within the testicular interstitium to synthesize and secrete testosterone. FSH also plays a critical role in regulating spermatogenesis through its

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action on Sertoli cells (2). Estradiol in men is important for modulating libido, erectile function, and spermatogenesis (3). The effects of prolactin on male reproductive function and semen quality vary and may be independent of the influence of gonadotropic hormones. Prolactin upregulates spermatogenesis and stimulates testosterone synthesis by modulating LH receptors on Leydig cells; thus, it may have a positive impact on semen quality (4). 17-hydroxyprogesterone (17-OHP) is an intermediate in the steroidogenic pathway (conversion of cholesterol to testosterone) and has recently been demonstrated to be a reliable biomarker of intratesticular testosterone levels. It also mediates binding to androgen receptors found in Leydig, Sertoli, and peritubular cells. In adult men, intratesticular testosterone concentrations are approximately one hundred times higher than serum levels (5). To date, 17-OHP has been most commonly used for the screening and treatment of patients with congenital adrenal hyperplasia (6). With emerging evidence regarding its role in regulating spermatogenesis and semen parameters, it could serve as a valuable marker for predicting sperm quality in the future. Given the apparent consistency in results among various studies comparing 17-OHP levels and semen parameters in infertile men (7), the present study was designed to evaluate the correlation between 17-OHP, semen analysis parameters, and reproductive hormones in infertile men.

The primary objective of this study was to assess the relationship between 17-OHP levels, key semen characteristics (sperm concentration, motility, and morphology), and reproductive hormone profiles (FSH, LH, total testosterone, and prolactin) in infertile men. The main outcome measures were the direction and magnitude of the correlations between these parameters and 17-OHP.

Materials and Methods

A cross-sectional study was conducted between October 2024 and May 2025. One hundred serum and semen samples were collected from men presenting with subfertility. The men were divided into four groups according to their seminal fluid analysis (SFA) results: normozoospermic (n=25), oligozoospermic (n=26), asthenozoospermic (n=21), and oligoasthenoteratozoospermic (OAT) (n=28). Serum levels of LH, FSH, testosterone (T), E2, prolactin, and 17-OHP were assessed in all participants.

The included men attended Al-Kafeel IVF Center, Al-Kafeel Super-Speciality Hospital, Karbala, seeking infertility treatment. A medical history was obtained, including age, duration of infertility, weight, and height. Men diagnosed with endocrinopathies or testicular diseases were identified. Men with azoospermia and those receiving medical treatment for male infertility were excluded.

A commercially available ELISA kit (Company, Country) was used to assess serum 17-OHP levels; the intra-assay coefficient of variation was reported to be less than 8%, while the inter-assay coefficient of variation was less than 10%.

Data were collected and analyzed using SPSS version 26. Statistical analyses were performed using the ANOVA test, t-test, and chi-squared test. The degree of association between continuous variables was measured using Pearson's correlation coefficient (r), and the level of statistical significance was set at $P \leq 0.05$.

Results

The mean age of the men was 30.85±7.03 years, and the mean body mass index (BMI) was 27.6±5.78 kg/m2. The mean duration of infertility was 4.78±3.85 years. Table 1 indicates highly significant differences in serum testosterone and FSH levels (P=0.000) and in testosterone and E2 levels (P=0.003) among the four groups. Regarding serum levels of LH, prolactin, and 17-OHP, no significant differences were observed among the studied groups.

Across all study groups, there was a statistically significant weak negative correlation between 17-OHP levels and sperm concentration (r= -0.234, P=0.019). A significant negative correlation was also observed in the asthenozoospermia group (r= -0.670, P=0.001).

Serum 17-OHP levels in the asthenozoospermia group showed a moderately positive correlation with sperm motility (r=0.538, P=0.012) and a moderately negative correlation with semen viscosity (r= -0.590, P=0.005). In the oligozoospermia group, 17-OHP showed a moderately positive correlation with seminal round cells (r=0.438, P=0.025), as shown in Table 2.

Serum 17-OHP levels and FSH showed a statistically significant weak-to-moderate negative correlation across all study groups (r= -0.357, P<0.001), as shown in Table 3. No significant correlation was found between 17-OHP and the other reproductive hormones tested.

Table 4 shows that there were no significant positive or negative correlations between 17-OHP and any of the hormones in the normozoospermia group.

17-OHP and FSH levels in the oligozoospermia (r= -0.428, P=0.029), asthenozoospermia (r= -0.484, P=0.026), and OAT groups (r= -0.461, P=0.014) show a

moderately negative and statistically significant connection (Tables 5, 6, and 7).

Table 1. Hormone biomarkers in the studied groups

Parameter	Groups	N	Mean Rank	Chi-Square	Df	Asymp. Sig.
	Normozoospermia	25	40.46			
	Oligozoospermia	26	61.41			
17-OHP pg/ml	Asthenozoospermia	21	47.50	6.922	3	0.074 ns
	oligo-astheno-terato-zoospermia	28	49.48			
	Total	100				
	Normozoospermia	25	86.98			
	Oligozoospermia	26	28.69			
TT ng/ml	Asthenozoospermia	21	46.05	57.747	3	0.000 ***
	oligo-astheno-terato-zoospermia	28	41.52			
	Total	100				
	Normozoospermia	25	86.44			
	Oligozoospermia	26	31.63			
FSH mIu/ml	Asthenozoospermia	21	42.52	53.413	3	0.000 ***
	oligo-astheno-terato-zoospermia	28	41.91			
	Total	100				
	Normozoospermia	25	53.96			
	Oligozoospermia	26	63.98			
E2 pg/ml	Asthenozoospermia	21	50.36	13.967	3	0.003 **
	oligo-astheno-terato-zoospermia	28	35.00			
	Total	100				
	Normozoospermia	25	46.10			
	Oligozoospermia	26	45.00			
LH mIu/ml	Asthenozoospermia	21	59.45	3.347	3	0.34 ns 1
	oligo-astheno-terato-zoospermia	28	51.93			
	Total	100				
	Normozoospermia	25	76.56			
	Oligozoospermia	26	72.94			
Prolactin ng/ml	Asthenozoospermia	21	29.38	00	3	0.153 ns
	oligo-astheno-terato-zoospermia	28	22.23			
	Total	100				

Asymp. Sig.= *P*, N = number, df = degree of freedom, * correlation is significant at the 0.05 level

Table 2. The correlation between 17-OHP and sperm parameters in the studied groups

Sperm parameters		17- OHP of Total patient n= 100	17- OHP Normozoospermia n=25	17- OHP Oligozoospermia, n=26	17- OHP Asthenozoospermia n=21	17- OHP OAT n=28
Sperm concentration million\ml	**r**	- 0.234*	0.160	0.005	- 0.670**	0.024
	p	0.019	0.446	0.982	0.001	0.905
Sperm count million\ejac.	**r**	- 0.047	0.147	0.260	0.226	- 0.141
	p	0.630	0.483	0.199	0.325	0.475
Progressive A+B %	**r**	0.048	- 0.161	0.164	0.538*	0.088
	p	0.636	0.453	0.423	0.012	0.658
Morphology %	**r**	- 0.048	0.018	0.352	- 0.130	0.104
	P	0.634	0.932	0.078	0.574	0.598
Semen volume (ml)	**r**	0.147	- 0.003	0.271	0.363	- 0.152
	P	0.144	0.990	0.180	0.106	0.440
Viscosity mm	**r**	- 0.115	0.150	- 0.140	- 0.590**	0.294
	P	0.255	0.476	0.494	0.005	0.129
Round cells million/ml	**r**	0.184	0.023	0.438*	0.248	0.221
	P	0.067	0.913	0.025	0.276	0.259

N = number, r = Pearson's correlation coefficient, ** correlation is significant at the 0.01 level, * correlation is significant at the 0.05 level

Table 3. The correlation between serum level of 17-OHP and reproductive hormones in the studied groups

Serum parameter		LH mIU\ml	FSH mIU\ml	TT ng/ml	Prolactin ng\ml	E2 pg\ml
17-OHP pg\ml	r	- 0.0.097	- 0.357**	-0.022	- 0.144	- 0.114
	p	0.338	0.000	0.826	0.153	0.258

N = number, r = Pearson's correlation coefficient, ** correlation is significant at the 0.01 level.

Table 4. The correlation between 17-OHP and reproductive hormones in the normozoospermia group (N=25)

Serum parameter		LH mIU\ml	FSH mIU\ml	TT ng/ml	Prolactin ng\ml	E2 pg\ml
17-OHP pg\ml	**r**	- 0.080	- 0.304	0.122	- 0.206	- 0.322
	p	0.709	0.149	0.571	0.323	0.125

N = number, r = Pearson's correlation coefficient, * correlation is significant at the 0.05 level

Table 5. The correlation between 17-OHP and hormones in the oligozoospermia group (N=26)

Serum parameter		LH mIU\ml	FSH mIU\ml	TT ng/ml	Prolactin ng\ml	E2 pg\ml
17-OHP pg\ml	r	- 0.236	- 0.428*	0.221	- 0.144	0.099
	p	0.247	0.029	0.278	0.482	0.632

N = number, r = Pearson's correlation coefficient. * Correlation is significant at the 0.05 level

Table 6. The correlation between 17-OHP and hormones in asthenozoospermia group (N=21)

Serum parameter		LH mIU\ml	FSH mIU\ml	TT ng/ml	Prolactin ng\ml	E2 pg\ml
17-OHP pg\ml	**r**	0.109	- 0.484*	0.300	- 0.158	- 0.271
	p	0.638	0.026	0.187	0.495	0.236

N=number, r=Pearson's correlation coefficient, * correlation is significant at the 0.05 level

Table 7. The correlation between 17-OHP and hormones in Oligoasthenoteratozoospermia group (N=28)

Serum parameter		LH mIU\ml	FSH mIU\ml	TT ng/ml	Prolactin ng\ml	E2 pg\ml
17-OHP pg\ml	r	0.313	- 0.461*	0.241	0.141	0.059
	P	0.105	0.014	0.275	0.465	0.765

N= number, r = Pearson's correlation coefficient, * correlation is significant at the 0.05 level

Discussion

As supported by evidence, male factor infertility contributes to approximately 50% of all infertility cases. This highlights the necessity of understanding the mechanisms by which gonadotropic hormones and intratesticular testosterone (TT) affect semen quality and sperm parameters. Serum and intratesticular androgens are recognized as vital elements in sperm production and maturation. 17-OHP is a steroid hormone that acts as an intermediate precursor in the testosterone synthesis pathway and could be associated with impaired semen parameters, reduced sperm quality, and decreased male fertility potential (8).

Adequate androgen concentrations within the phospholipid membrane (serving as a model of the cell membrane) may be advantageous for the testicular microenvironment regarding testosterone metabolism, biochemical communication, and sperm maturation. Testosterone is an androgen that plays a critical role in sperm maturation and is typically released in small amounts to prevent molecular damage (9).

Recent research suggests that serum 17-OHP concentrations may be linked to spermatogenesis. Physiologically, 17-OHP is associated with the steroidogenic acute regulatory (StAR) protein located in the outer mitochondrial membrane of Leydig cells. This protein is responsible for transporting cholesterol to the inner mitochondrial membrane as the initial step in testosterone biosynthesis (10). The results across all studied groups exhibited statistically significant variance in serum levels of testosterone, FSH, and E2; in contrast, serum levels of LH, prolactin, and 17-OHP showed no such variance. Consistent with previous research, the results of the current study illustrate that testosterone, FSH, and E2 play an important role in the regulation of spermatogenesis and male reproductive health in general (11). Despite remaining relatively stable among the studied groups, it is reasonable to assume that LH, prolactin, and 17-OHP have complex roles in male infertility (12).

The most remarkable finding was the inverse relationship between sperm concentration and 17-OHP levels, which was clearly evident in the asthenozoospermic group. This suggests that individuals with impaired sperm motility may be more susceptible to the negative effects of high 17-OHP levels than those with low sperm concentrations. The exact role of 17-OHP is not yet fully understood, although elevated serum levels may serve as an indicator of adrenal or testicular

dysfunction (13).

In men with asthenozoospermia, a statistically significant negative correlation was found between semen viscosity and 17-OHP. This may indicate that 17-OHP impacts the metabolic processes essential for optimal sperm production, progressive motility, and the composition and quality of seminal fluid. These findings further highlight the complex dual role of 17-OHP in male infertility (14).

The significant inverse correlation between serum 17-OHP and FSH levels across the three infertility subgroups—oligozoospermia, asthenozoospermia, and OAT—could be related to the hypothalamic-pituitary-gonadal (HPG) feedback mechanism, whereby elevated 17-OHP may suppress FSH levels and thereby interfere with spermatogenesis, as FSH is an important regulator of sperm production (6,15). Further research on the potential regulatory pathways linking adrenal steroid hormones such as 17-OHP to FSH dynamics and male fertility is needed to fully elucidate this interaction.

In contrast, 17-OHP did not show any significant correlation with the other reproductive hormones—LH, prolactin, or testosterone—in any of the studied groups. This suggests that the influence of 17-OHP on male fertility may be more specifically related to sperm production processes rather than to the broader reproductive hormonal profile (16).

Studies conducted in men after FSH treatment found an inverse relationship between 17-OHP levels and sperm parameters, with no association observed with pre-treatment sperm parameters. This finding suggests that 17-OHP levels may be more closely linked to treatment response (17,18). Thus, the findings of the current study provide insight into the interplay among 17-OHP, other reproductive hormones, and sperm parameters in infertile men.

Since elevated serum 17-OHP showed a negative correlation with serum FSH levels, sperm concentration, and semen viscosity, it could be used as a biomarker to identify specific infertility-related abnormalities, particularly in men with asthenozoospermia and oligozoospermia. In cases where the cause of infertility is not readily apparent through SFA or hormonal evaluation, assessment of 17-OHP levels may provide additional diagnostic insight. Furthermore, given the noteworthy relationship between 17-OHP and FSH, reproductive specialists should also consider adrenal function and its possible effects, as men with decreased fertility and elevated serum 17-OHP levels may benefit from treatments targeting adrenal hyperactivity or abnormalities in steroidogenesis.

In the steroidogenic pathway, 17-OHP is a crucial intermediate that links androgen production and progesterone metabolism. It is a precursor in testosterone biosynthesis and is derived from cholesterol through a series of enzymatic processes. Clinically, 17-OHP is most frequently used to screen for and monitor congenital adrenal hyperplasia.

Importantly, 17-OHP is produced in both testicular Leydig cells and the adrenal cortex. Intratesticular testosterone (ITT) concentrations, which reflect active local steroidogenesis, are reported to be 50–100 times higher than circulating serum testosterone levels. In gonadotropin-suppressed males receiving human chorionic gonadotropin, prior interventional studies showed a substantial association between 17-OHP and intratesticular testosterone. However, this association may vary depending on the therapeutic setting and hormonal milieu (6).

Thus, circulating 17-OHP may reflect both intratesticular androgen synthesis and systemic steroidogenic activity. Its correlation with semen parameters in this study is biologically plausible, possibly due to its role in the regulation of spermatogenesis and testosterone synthesis.

Serum 17-OHP levels and semen parameters may have been influenced by unmeasured confounders such as body mass index, metabolic variables, psychological stress, and mild adrenal dysfunction, despite the use of stringent exclusion criteria.

This study emphasizes the complex relationship between 17-OHP and sperm parameters. The strong negative association between 17-OHP and FSH suggests that 17-OHP may inhibit spermatogenesis. However, statistically significant correlations may still have limited or unclear clinical implications, necessitating further studies.

Advanced research is recommended to determine whether 17-OHP is a suitable therapeutic target for male infertility and to better understand the underlying physiological mechanisms.

Limitations

As this is a cross-sectional study, a definitive cause-and-effect relationship between serum 17-OHP levels and sperm parameters cannot be established. Therefore, longitudinal studies tracking the relationship between sperm parameters and hormonal changes over time are recommended to provide more conclusive insight into these associations. Additional research is also needed on the adrenal-pituitary-gonadal interactions and other

possible mechanisms underlying the correlation between serum 17-OHP and FSH levels.

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