



Original Article

## Correlation of Biochemical and Endocrinological Profile of Infertile Men with Abnormal Semen Parameters

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### ABSTRACT

**Objectives:** In the investigations of infertile couples, the contribution of male partners has recently caught the attention of researchers, and more and more investigations like DNA fragmentation tests, microfluidics, physiological intracytoplasmic sperm injection, and intracytoplasmic morphological sperm injection are being resorted to for better Assisted Reproductive Technology (ART) results. Male fertility is intrinsically linked to overall health, with a growing body of evidence indicating that medical comorbidities and conditions detrimental to men's health are consistently associated with compromised reproductive function. Considering the fact that 15% of the male human genome is dedicated to reproductive functions, it is plausible that other health disorders may also be associated with impairments in fertility. This study was planned to look into factors which are causing such a rise in male infertility and its association with various semen parameters.

**Material and Methods:** A cross-sectional study was undertaken over an 18-month period at the infertility clinic of a tertiary care centre, enrolling 151 infertile males exhibiting abnormal semen parameters in accordance with the WHO 2010 guidelines. A comprehensive evaluation of their biochemical and endocrinological profiles was performed, and the correlation between these parameters and semen abnormalities was systematically examined.

**Results:** A significant negative correlation was observed between various semen parameters and diastolic blood pressure (DBP), prolactin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), follicle-stimulating hormone (FSH), and oestrogen. DBP (mmHg) correlated negatively with sperm concentration (million/ml) ( $R = -0.161$ ). CRP (mg/l) correlated with sperm concentration and total sperm count ( $\times 10^6$ /ejaculate) ( $R = -0.180$  and  $-0.208$ , respectively). ESR (mm/hour) correlated with sperm concentration and total sperm count ( $R = -0.214$  and  $-0.198$ , respectively). FSH (IU/l) correlated with sperm concentration and total sperm count ( $R = -0.216$  and  $-0.206$ , respectively). Prolactin ( $\mu\text{g/l}$ ) correlated with sperm concentration, total sperm count, and total motile sperm count (TMSC) ( $R = -0.210$ ,  $-0.264$ , and  $-0.191$ , respectively). Oestrogen (pg/ml) showed the strongest negative correlation with sperm concentration, total sperm count, and TMSC ( $R = -0.387$ ,  $-0.357$ , and  $-0.171$ , respectively). Conversely, significant positive correlations were observed between semen parameters and both uric acid and lipid profile. Serum uric acid (mg/dl) correlated positively with sperm morphology (%) ( $R = 0.203$ ). Low-density lipoprotein (mg/dl) correlated with sperm concentration and total sperm count ( $R = 0.231$  and  $0.259$ , respectively), while triglycerides (mg/dl) correlated with sperm concentration and total sperm count ( $R = 0.197$  and  $0.204$ , respectively). However, triglycerides also showed a significant negative correlation with total motility (%) and progressive motility (%) ( $R = -0.186$  and  $-0.180$ , respectively).

**Conclusion:** Our findings demonstrated that DBP, prolactin, ESR, CRP, FSH, and oestrogen exhibited significant negative correlations with various semen parameters, whereas uric acid and lipid profile parameters showed significant positive correlations. These results suggest that systemic health factors exert a considerable influence on male reproductive potential, highlighting the importance of evaluating overall health status in the assessment and management of male infertility.

**Keywords:** Biochemical, Endocrinological, Infertile men, Male infertility, Semen parameters

## INTRODUCTION

Since time immemorial, women all around the world have faced significant societal pressure for childbirth and been blamed for infertility, even though it can affect both male and female partners equally. In the evaluation of infertile couples, the role of male partners has recently gained increased attention from researchers. As a result, advanced diagnostic techniques such as deoxyribonucleic acid (DNA) fragmentation tests, microfluidics, intracytoplasmic morphological sperm injection, physiological intracytoplasmic sperm injection and motile sperm organelle morphology examination are being increasingly utilised to enhance outcomes in assisted reproductive technology (ART).

As per the International Committee for Monitoring Assisted Reproductive Technology and the World Health Organisation (WHO), infertility is a disease of the reproductive system, defined by failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.<sup>[1]</sup> According to the American Society of Reproductive Medicine, it can also be defined as the failure of a couple to conceive after 12 months of regular intercourse without the use of contraception in women <35 years and after 6 months of regular intercourse without the use of contraception in women ≥35 years.

Male factor infertility refers to a man's inability to achieve pregnancy with a fertile female. It is typically identified by abnormal semen parameters in at least one of two sperm analyses conducted 4 weeks apart. In humans, male factor infertility is responsible for 40%–50% of infertility cases among couples and affects approximately 7% of all men.<sup>[2]</sup>

Male infertility can result from a variety of causes, including genetic and congenital abnormalities, hormonal imbalances, infections, vascular issues, immune-related conditions, obstructions, exposure to antispermatoxic substances, or sexual dysfunction.<sup>[3]</sup>

There is a strong connection between male fertility and overall health. Numerous studies have shown that medical conditions and factors negatively affecting men's general health are often associated with reduced reproductive function.<sup>[4]</sup> Given that approximately 15% of the male genome is dedicated to reproductive processes, it is plausible that other health problems may also be linked to fertility issues. Researchers suggest that, beyond shared genetic roots, hormonal, biochemical, and environmental or lifestyle influences may contribute to the relationship between a man's reproductive health and his overall physical well-being.<sup>[5]</sup>

A 13-year study conducted in South India revealed a downward trend in baseline semen quality and sperm

functional parameters among fertile Indian men. Specifically, sperm count declined by 30.31%, while sperm motility and morphology decreased by 22.92% and 51.25%, respectively.<sup>[6]</sup>

Metabolic conditions like diabetes and obesity are marked by persistent high blood sugar levels and excessive fat accumulation in adipose tissue. Elevated glucose and lipid levels in the bloodstream can lead to an oversupply of energy substrates to metabolic pathways in both fat and non-fat cells. This overload may boost the production of reactive oxygen species (ROS), which are believed to contribute to nearly half of male infertility cases, particularly in men with impaired sperm function. While various theories have explored potential mechanisms—including genetic, developmental, and behavioural factors—the precise nature of these associations remains unclear.<sup>[7]</sup>

Over the past several decades, extensive research has focused on the development and management of female infertility, whereas studies addressing male infertility remain comparatively limited. The scientific exploration of male infertility has progressed at a much slower pace, despite its substantial contribution to the global burden of infertility. Male reproductive health is influenced by a complex interplay of biochemical and endocrinological factors. However, the extent of their involvement in determining male fertility potential remains inadequately defined. Addressing this gap is of critical importance, as a clearer understanding of these parameters may not only enable earlier detection of male infertility but also provide opportunities for the development of targeted therapeutic strategies. Such advancements hold the potential to mitigate the rising incidence of male infertility and improve reproductive outcomes for affected couples.

Although numerous studies have explored the correlation between individual biomarkers and semen parameters, such approaches often provide a limited understanding of the multifactorial nature of male infertility. In the present study, we employed a broad panel of biomarkers to identify the determinants most strongly associated with semen parameters and to evaluate the extent of their contribution. By adopting this integrative approach, our work aims to bridge existing knowledge gaps, facilitate early recognition of male infertility, and inform the development of more effective diagnostic and therapeutic strategies.

### Aim

To study the correlation of the biochemical and endocrinological profile of male partners and their abnormal semen parameters in infertile couples.

## MATERIAL AND METHODS

This hospital-based cross-sectional study was conducted over a period of 18 months at the infertility clinic of a tertiary care hospital in North India, following approval from the institutional ethics committee. Semen analysis was performed after 3 days of abstinence as part of the routine evaluation of infertile couples. To minimise interobserver variation, all assessments were conducted by a single examiner. Male partners with one or more abnormalities in semen parameters—including sperm concentration, total sperm count, total and progressive motility, or morphology—based on the WHO 2010 criteria were included in the study. No exclusion criteria were applied [Figure 1].

A sample size of 151 participants was determined based on the estimated prevalence of male factor infertility (40%–50%) among infertile couples. Using this reference, the minimum required sample size was calculated to be 151, with a margin of error of 8% and a 5% level of significance.

For certain semen parameters, including total motility, progressive motility, and sperm morphology, the effective sample size was 131, as complete data were unavailable for 20 infertile men. All other biochemical and semen parameters were analysed using the full cohort. Missing data were handled by case-wise exclusion, and no data imputation methods were applied.

A detailed proforma for male infertility was completed for all participants enrolled in the study. Each participant underwent a comprehensive evaluation, including the following assessments [Table 1]:

1. Lifestyle factors: Blood pressure (BP), body mass index (BMI, kg/m<sup>2</sup>), and waist circumference (WC, cm).
2. Biochemical profile: Hemogram, C-reactive protein (CRP), uric acid, oral glucose tolerance test (OGTT with 75 g glucose), thyroid profile, and lipid profile.
3. Endocrinological profile: Luteinizing hormone (LH, IU/ml), follicle-stimulating hormone (FSH, IU/ml), prolactin (µg/l), oestrogen (pg/ml), and total testosterone (ng/dl).
4. Semen analysis: Performed according to WHO 2010 criteria [Table 2].

The biochemical and endocrinological profiles were systematically compared and correlated with semen parameters [Table 3], and appropriate statistical analyses were performed.

**Table 1:** Reference range of various parameters.

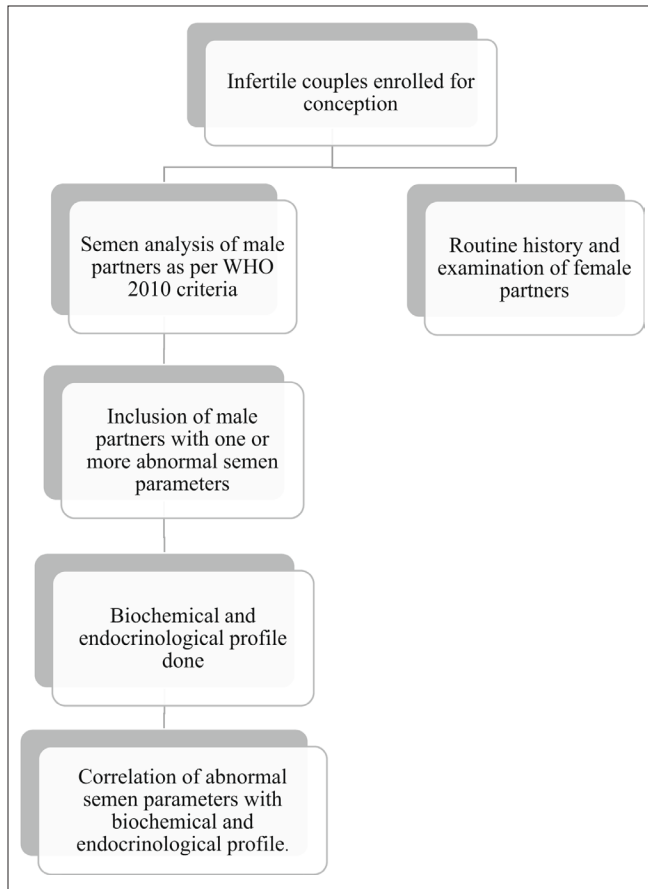
Parameter	*As per hospital lab- specific reference range
<b>BP</b>	
Systolic	<140 mm of Hg
Diastolic	<90 mm of Hg
BMI	<25
WC	<90 cm
<b>Biochemical parameters</b>	
Haemoglobin	11.5–17.0 g/dl
WBC	4000–10,000/cm <sup>2</sup>
Platelets	1.5–5 lakh/cm <sup>2</sup>
ESR	22 mm/hour
CRP	0.3–8 mg/l
<b>Lipid profile</b>	
Total cholesterol	<200 mg/dl
LDL	<100 mg/dl
HDL	40–60 mg/dl
Triglyceride	<150 mg/dl
OGTT	<140 mg/dl
<b>Thyroid profile</b>	
TSH	0.3–5.0 mIU/dl
T3	<200 ng/dl
T4	5–12 µg/dl
Anti-TPO antibody	<60 IU/dl
<b>Endocrinological parameters</b>	
FSH	Upto 11 mIU/ml
LH	0.7–7.4 IU/ml
Total testosterone	0.1–1.0 ng/ml
Oestrogen	15–60 pg/ml
Prolactin	4.0–12 ng/ml

\*Safdarjung hospital lab-specific ranges. BP: Blood pressure, BMI: Body mass index, WC: Waist circumference, WBC: White blood cells, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, OGTT: Oral glucose tolerance test, TSH: Thyroid stimulating hormone, TPO: Thyroid peroxidase, FSH: Follicle stimulating hormone, LH: Luteinising hormone.

**Table 2:** Semen analysis (as per WHO 2010 criteria).

Parameters	Lower reference limit 2010
Sperm concentration (c)	≥15 × 10 <sup>6</sup> /ml
Total sperm count	≥39 × 10 <sup>6</sup> / ejaculate
Progressive motility	≥32% progressive
Total motility (m)	≥40%
Sperm morphology	≥4% normal forms
TMSC-(V × C × M volume × concentration × motility)	≥20 × 10 <sup>6</sup> / ejaculate

TMSC: Total motile sperm count.



**Figure 1:** Flow chart of methodology. WHO: World Health Organisation.

**RESULTS**

**Table 3:** Distribution of semen parameters of study subjects.

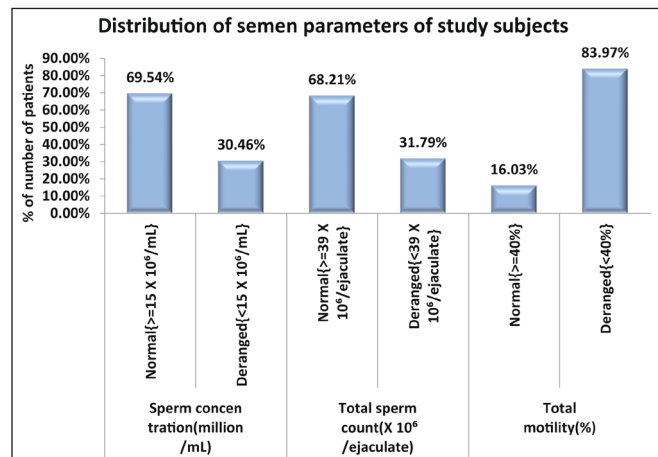
Semen parameters	Frequency	Percentage
<b>Sperm concentration(million/ml)</b>		
Normal ( $\geq 15 \times 10^6/\text{ml}$ )	105	69.54%
Deranged ( $< 15 \times 10^6/\text{ml}$ )	46	30.46%
Mean $\pm$ SD	34.38 $\pm$ 24.08	
Median (25th–75th percentile)	40 (10–52.5)	
Range	0–80	
<b>Total sperm count (<math>\times 10^6/\text{ejaculate}</math>)</b>		
Normal ( $\geq 39 \times 10^6/\text{ejaculate}$ )	103	68.21%
Deranged ( $< 39 \times 10^6/\text{ejaculate}$ )	48	31.79%
Mean $\pm$ SD	102.49 $\pm$ 73.82	
Median (25th–75th percentile)	115 (25–150)	
Range	0–270	

(Continued)

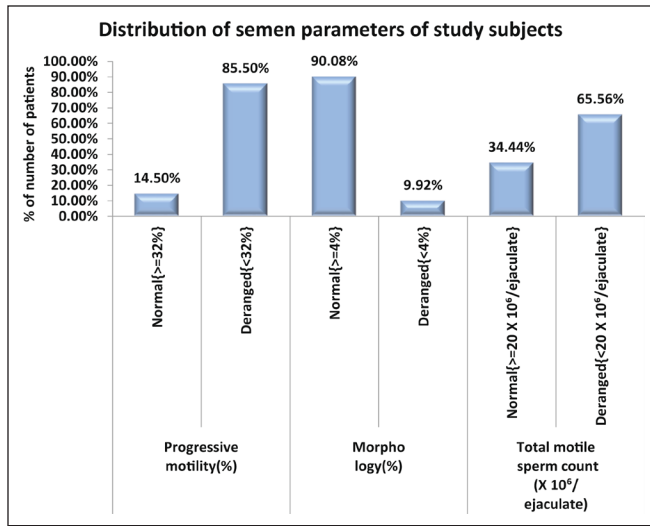
**Table 3:** (Continued)

Semen parameters	Frequency	Percentage
<b>Total motility (%)</b>		
Normal ( $\geq 40\%$ )	21	16.03%
Deranged ( $< 40\%$ )	110	83.97%
Mean $\pm$ SD	22.29 $\pm$ 19.75	
Median (25th–75th percentile)	15 (10–30)	
Range	0–80	
<b>Progressive motility (%)</b>		
Normal ( $\geq 32\%$ )	19	14.50%
Deranged ( $< 32\%$ )	112	85.50%
Mean $\pm$ SD	11.59 $\pm$ 14	
Median (25th–75th percentile)	5 (3–10)	
Range	0–50	
<b>Morphology (%)</b>		
Normal ( $\geq 4\%$ )	118	90.08%
Deranged ( $< 4\%$ )	13	9.92%
Mean $\pm$ SD	32.91 $\pm$ 17.85	
Median (25th–75th percentile)	32 (20–47.5)	
Range	0.2–75	
<b>TMSC (<math>\times 10^6/\text{ejaculate}</math>)</b>		
Normal ( $\geq 20 \times 10^6/\text{ejaculate}$ )	52	34.44%
Deranged ( $< 20 \times 10^6/\text{ejaculate}$ )	99	65.56%
Mean $\pm$ SD	18.1 $\pm$ 19.8	
Median (25th–75th percentile)	14.4 (5.125–22.5)	
Range	0–150	

SD: Standard deviation, TMSC: Total motile sperm count.



**Figure 2:** Distribution of semen parameters of study subjects.



**Figure 3:** Distribution of semen parameters of study subjects.

Among 151 infertile men, normal sperm concentration ( $\geq 15 \times 10^6/\text{ml}$ ) and total sperm count ( $\geq 39 \times 10^6/\text{ejaculate}$ ) were observed in 69.54% and 68.21% of patients, respectively. Abnormalities in motility were most prevalent: total motility ( $<40\%$ ) and progressive motility ( $<32\%$ ) were impaired in 83.97% and 85.50% of cases, respectively ( $n = 131$ ). Normal morphology ( $\geq 4\%$ ) was seen in 90.08% of patients, while

total motile sperm count (TMSC) was reduced ( $<20 \times 10^6/\text{ejaculate}$ ) in 65.56% of cases [Figure 2 and 3].

A significant negative correlation was observed between CRP and both sperm concentration and total sperm count, with correlation coefficients of  $-0.18$  and  $-0.208$ , respectively. Additionally, DBP showed a significant negative correlation with sperm concentration, with a correlation coefficient of  $-0.161$  [Table 4].

No significant correlations were found between BMI, WC (cm), and any semen parameters [Table 4].

A significant negative correlation was observed between ESR and both sperm concentration ( $r = -0.214$ ) and total sperm count ( $r = -0.198$ ) [Table 5].

No significant associations were found between semen parameters and haemoglobin (g/dl), white blood cell count (cells/mm<sup>3</sup>), platelet count (lakhs/mm<sup>3</sup>), urea (mg/dl), serum creatinine (mg/dl) or OGTT [Table 5].

A significant positive correlation was observed between serum uric acid (mg/dl) and sperm morphology (%), with a correlation coefficient of  $0.203$ . However, no significant correlation was found between serum uric acid and the other semen parameters [Table 6].

Additionally, no significant correlation or association was identified between thyroid function tests and semen parameters.

**Table 4:** Correlation of BMI, WC, CRP and BP with semen parameters.

Variables	Sperm concentration (million/ml)	Total sperm count ( $\times 10^6/\text{ejaculate}$ )	Total motility (%)	Progressive motility (%)	Morphology (%)	TMSC ( $\times 10^6/\text{ejaculate}$ )
<b>BMI (kg/m<sup>2</sup>)</b>						
Correlation coefficient	-0.005	0.027	0.004	0.010	0.066	0.050
P-value	0.948	0.743	0.968	0.908	0.456	0.541
<b>WC (cm)</b>						
Correlation coefficient	0.000	0.021	0.019	0.041	0.091	0.080
P-value	0.999	0.799	0.834	0.641	0.301	0.330
<b>CRP (mg/l)</b>						
Correlation coefficient	-0.180	-0.208	0.132	0.104	-0.044	-0.146
P-value	0.027	0.011	0.133	0.235	0.617	0.073
<b>Systolic BP (mmHg)</b>						
Correlation coefficient	0.078	0.058	0.024	0.042	0.168	0.005
P-value	0.339	0.481	0.782	0.631	0.056	0.955
<b>Diastolic blood pressure (DBP) (mmHg)</b>						
Correlation coefficient	-0.161	-0.145	0.062	0.089	0.147	-0.116
P-value	0.049	0.076	0.484	0.313	0.093	0.157

Spearman's rank correlation coefficient was used to calculate the P-value and  $< 0.05$  was considered statistically significant. BMI: Body mass index, TMSC: Total motile sperm count, WC: Waist circumference, CRP: C-reactive protein, BP: Blood pressure.

**Table 5:** Correlation of hemogram with semen parameters.

Variables	Sperm concentration (million/ml)	Total sperm count ( $\times 10^6$ /ejaculate)	Total motility (%)	Progressive motility (%)	Morphology (%)	TMSC ( $\times 10^6$ /ejaculate)
<b>Haemoglobin (g/dl)</b>						
Correlation coefficient	0.044	0.036	-0.096	-0.089	0.090	-0.013
P-value	0.588	0.662	0.273	0.312	0.309	0.870
<b>WBC (cells/mm<sup>3</sup>)</b>						
Correlation coefficient	-0.144	-0.109	-0.017	-0.012	-0.022	-0.104
P-value	0.078	0.181	0.847	0.889	0.801	0.204
<b>Platelet (lakhs/mm<sup>3</sup>)</b>						
Correlation coefficient	-0.074	-0.077	0.107	0.169	0.139	0.026
P-value	0.366	0.346	0.222	0.053	0.114	0.751
<b>Erythrocyte sedimentation rate (ESR) (mm/hour)</b>						
Correlation coefficient	-0.214	-0.198	0.150	0.164	-0.026	-0.035
P-value	0.008	0.015	0.087	0.062	0.768	0.668

Spearman's rank correlation coefficient was used to calculate the P-value and < 0.05 was considered statistically significant. TMSC: Total motile sperm count, WBC: White blood cells.

**Table 6:** Correlation of serum uric acid with semen parameters.

Variables	Sperm concentration (million/ml)	Total sperm count ( $\times 10^6$ /ejaculate)	Total motility (%)	Progressive motility (%)	Morphology (%)	TMSC ( $\times 10^6$ /ejaculate)
<b>Serum uric acid (mg/dl)</b>						
Correlation coefficient	-0.140	-0.118	0.097	0.107	0.203	-0.030
P-value	0.087	0.148	0.271	0.225	0.020	0.715

Spearman's rank correlation coefficient was used to calculate the P-value and < 0.05 was considered statistically significant. TMSC: Total motile sperm count.

**Table 7:** Correlation of lipid profile with semen parameters.

Variables	Sperm concentration (million/ml)	Total sperm count ( $\times 10^6$ /ejaculate)	Total motility (%)	Progressive motility (%)	Morphology (%)	TMSC ( $\times 10^6$ /ejaculate)
<b>Total cholesterol (mg/dl)</b>						
Correlation coefficient	-0.015	0.014	-0.010	0.025	-0.078	0.071
P-value	0.856	0.866	0.914	0.776	0.377	0.387
<b>High density lipoprotein (HDL)(mg/dl)</b>						
Correlation coefficient	-0.031	-0.037	0.068	0.054	0.149	-0.022
P-value	0.703	0.648	0.437	0.538	0.088	0.785
<b>Low-density lipoprotein (LDL) (mg/dl)</b>						
Correlation coefficient	0.231	0.259	-0.056	-0.093	0.063	0.104
P-value	0.004	0.001	0.523	0.293	0.475	0.204
<b>Triglyceride (mg/dl)</b>						
Correlation coefficient	0.197	0.204	-0.186	-0.180	0.085	-0.023
P-value	0.016	0.012	0.034	0.040	0.332	0.779

Spearman's rank correlation coefficient was used to calculate the P-value and < 0.05 was considered statistically significant. TMSC: Total motile sperm count.

A significant positive correlation was found between low density lipoprotein (LDL) and both sperm concentration and total sperm count, with correlation coefficients of 0.231 and 0.259, respectively [Table 7].

Similarly, triglyceride levels showed a significant positive correlation with sperm concentration and total sperm count, with correlation coefficients of 0.197 and 0.204, respectively.

In contrast, triglycerides demonstrated a significant negative correlation with total motility (%) and progressive motility (%), with correlation coefficients of  $-0.186$  and  $-0.18$ , respectively.

## DISCUSSION

We investigated whether abnormal semen parameters in infertile men correlate with lifestyle factors, biochemical markers, and hormonal profiles, thereby assessing the extent to which overall health influences semen quality and quantity. A cohort of 151 Indian men attending an infertility clinic at a tertiary care hospital in Delhi was evaluated. This study aimed to determine the presence or absence of associations between lifestyle, biochemical, and hormonal factors with abnormal semen parameters in this population.

**Table 8:** Correlation of endocrinological profile with semen parameters.

Variables	Sperm concentration (million/ml)	Total sperm count ( $\times 10^6$ /ejaculate)	Total motility (%)	Progressive motility (%)	Morphology (%)	TMSC ( $\times 10^6$ /ejaculate)
<b>FSH (IU/l)</b>						
Correlation coefficient	-0.216	-0.206	-0.006	0.008	-0.044	-0.144
P-value	0.008	0.011	0.943	0.925	0.621	0.078
<b>LH (IU/l)</b>						
Correlation coefficient	-0.123	-0.124	-0.054	-0.014	-0.061	-0.120
P-value	0.133	0.128	0.540	0.870	0.489	0.143
<b>Testosterone (ng/dl)</b>						
Correlation coefficient	0.016	0.020	-0.117	-0.068	-0.149	0.019
P-value	0.841	0.806	0.185	0.440	0.089	0.816
<b>Prolactin (<math>\mu</math>g/l)</b>						
Correlation coefficient	-0.210	-0.264	0.063	0.103	-0.171	-0.191
P-value	0.010	0.001	0.475	0.241	0.051	0.019
<b>Oestrogen (pg/ml)</b>						
Correlation coefficient	-0.387	-0.357	0.137	0.167	-0.110	-0.171
P-value	<0.0001	<0.0001	0.119	0.057	0.212	0.036

Spearman's rank correlation coefficient was used to calculate the P-value and  $< 0.05$  was considered statistically significant. TMSC: Total motile sperm count, FSH: Follicle stimulating hormone, LH: Luteinising hormone.

A significant negative correlation was observed between FSH and both sperm concentration and total sperm count, with correlation coefficients of  $-0.216$  and  $-0.206$ , respectively [Table 8].

Prolactin also showed a significant negative correlation with sperm concentration, total sperm count, and TMSC, with correlation coefficients of  $-0.21$ ,  $-0.264$ , and  $-0.191$ , respectively.

Similarly, oestrogen (pg/ml) was significantly negatively correlated with sperm concentration, total sperm count, and TMSC, with correlation coefficients of  $-0.387$ ,  $-0.357$ , and  $-0.171$ , respectively.

Previous studies have reported a negative correlation between increased BMI and semen quality, particularly with respect to sperm concentration and motility.<sup>[8,9]</sup> In the present study, however, the majority of infertile men (80.13%) were non-obese, with a mean BMI of  $< 25$  kg/m<sup>2</sup>, thereby limiting the variability required to detect such associations. Furthermore, the relatively smaller sample size, compared with larger cohorts from studies conducted predominantly in developed countries, may have further reduced the statistical power. Consequently, no significant associations were observed between BMI, WC, and semen parameters in our cohort.

Several studies suggest that hypertensive men are more likely to exhibit one or more semen abnormalities compared to those with normal BP.<sup>[10]</sup> The prevalence of hypertension was significantly higher among infertile men (17.8%) than among fertile men (9.1%). Furthermore, treatment of hypertension led to a notable improvement in TMSC compared to both baseline levels and men with poorly controlled BP.<sup>[11]</sup> In our study, a significant negative correlation was observed between elevated DBP (mmHg) and sperm concentration (million/ml), with a correlation coefficient of  $-0.161$ . However, no correlation was found between systolic BP and semen parameters.

Elevated ESR and CRP, which are indicators of chronic systemic inflammation, have been linked to an increased risk of disease, morbidity, and mortality in men.<sup>[12]</sup> A 2020 study<sup>[13]</sup> found an association between ESR and abnormal sperm motility, reporting that when ESR is below 9.5, there is a 75% likelihood of normal motility ( $>40\%$ ), whereas an ESR above 9.5 predicts abnormal motility ( $<40\%$ ) with 64.7% accuracy.

In our study, ESR showed a significant negative correlation with both sperm concentration and total sperm count, with correlation coefficients of  $-0.214$  and  $-0.198$ , respectively. Additionally, CRP (mg/l) demonstrated a significant negative correlation with sperm concentration and total sperm count, with correlation coefficients of  $-0.18$  and  $-0.208$ , respectively.

Limited research has been conducted on the relationship between liver function and semen parameters. Similarly, our study did not find any significant association between the two. Although a majority of participants (60.26%) exhibited elevated alkaline phosphatase (ALP) levels ( $>128$  U/l), no significant correlation was observed between ALP and semen parameters.

Uric acid, in moderate concentrations, plays a beneficial role in supporting sperm function by promoting motility, viability, and morphology. This protective effect is primarily achieved through the neutralisation of harmful oxidising and nitrating agents—such as endogenous free radicals and exogenous toxins—and by enhancing the activity of specific bioactive enzymes within spermatozoa. However, elevated uric acid levels may have detrimental effects, potentially impairing sperm function by inhibiting the activity of essential enzymes. In our study, a significant positive correlation was observed between serum uric acid (mg/dl) and sperm morphology (%), with a correlation coefficient of  $0.203$ . Supporting this, previous research has identified high uric acid levels as a potential risk factor for reduced semen quality, concluding that hyperuricemia independently affects semen volume and total sperm count.<sup>[14]</sup>

Balanced lipid metabolism is essential for sperm maturation, motility, capacitation, acrosome reaction, and fusion. The sperm plasma membrane, composed of approximately

70% phospholipids, 25% neutral lipids, and 5% glycolipids, plays a vital role in spermatogenesis and sperm maturation. During epididymal transit, cholesterol sulphate stabilises the membrane, while capacitation in the female tract involves redistribution of the bilayer and efflux of cholesterol and phospholipids. The extent of cholesterol efflux depends on the binding capacity of the reproductive tract, and cholesterol influx has been shown to suppress the acrosome reaction.<sup>[15]</sup>

Phosphatidylinositol 3-kinase (PI3K), a lipid and protein kinase regulating multiple cellular processes, has been implicated in human sperm function, with evidence suggesting a negative role in the development and maintenance of motility. This raises the potential use of PI3K inhibitors to improve motility in asthenozoospermia cases.<sup>[16]</sup> Conversely, cholesterol-lowering agents such as pravastatin have been shown to reduce sperm motility after 6–12 months of use, likely due to decreases in total cholesterol and LDL levels.<sup>[17]</sup>

The LIFE study (2014)<sup>[18]</sup> reported that elevated levels of serum total cholesterol, free cholesterol, and phospholipids were significantly associated with a reduced percentage of sperm exhibiting intact acrosomes, as well as smaller sperm head area and perimeter. A subsequent study in 2017 found a statistically significant positive correlation between sperm concentration and both triglycerides and very low-density lipoprotein (adjusted  $P = 0.001$  and  $P = 0.005$ , respectively). Additionally, total and progressive sperm motility were significantly higher with increased levels of LDL and total cholesterol (adjusted  $P = 0.008$  and  $P < 0.001$ , respectively).<sup>[19]</sup>

Our findings align with these results. We observed a significant positive correlation between LDL levels and both sperm concentration and total sperm count. Triglyceride levels also showed a significant positive correlation with sperm concentration. Conversely, a significant negative correlation was noted between triglyceride levels and both total motility (%) and progressive motility (%) with correlation coefficients of  $-0.186$  and  $-0.18$ , respectively. Furthermore, the proportion of men with impaired total and progressive motility was significantly higher among those with normal total cholesterol levels compared to those with elevated levels ( $P = 0.034$ ).

These observations raise an important question regarding the relationship between lipid homeostasis and semen quality—specifically, whether elevated levels of certain lipid parameters may exert a beneficial effect on semen parameters. Addressing this gap requires a comprehensive evaluation of multiple biochemical and lipid-related markers to clarify their collective influence on male fertility.

Excessive oxidative stress associated with conditions such as diabetes and obesity has been negatively associated with male fertility. A 2019 study reported that sperm motility, progressive motility, and normal morphology were

significantly reduced in obese, non-obese diabetic (Nob-DM), and obese diabetic (Ob-DM) groups compared to healthy controls ( $P < 0.01$ ).<sup>[20]</sup> However, in our study, no significant association was found between abnormal blood glucose levels and semen parameters.

The role of the thyroid gland in the regulation of testicular redox status is well documented. It explains the male factor infertility associated with hypothyroidism. However, no significant association was found between thyroid profile and semen parameters in our study. In the majority [121 (80.13%)] of patients, thyroid stimulating hormone (TSH) was normal (0.35–5 mIU/dl). It was deranged ( $>5$  mIU/dl) in only 30 out of 151 patients (19.87%).

Previous studies have demonstrated that FSH levels increase as overall health declines, concomitant with reductions in testosterone and sperm concentration.<sup>[21]</sup> A 2010 study further reported that obese men with oligozoospermia exhibited significantly higher serum levels of FSH, LH, oestrogen, and prolactin compared with obese fertile controls.<sup>[22]</sup> In alignment with these findings, our study identified a significant negative association between both FSH and LH and total sperm count and sperm concentration ( $P = 0.004$  and  $0.035$ , respectively). Notably, elevation of FSH is widely recognised as a compensatory mechanism reflecting impaired spermatogenesis, testicular damage, or disrupted hypothalamic-pituitary-gonadal feedback. These results indicate that rising FSH and LH levels are accompanied by a decline in sperm count and concentration, thereby reinforcing the inverse relationship consistently reported in prior literature.

### Limitations of the study

This study has certain limitations. First, it included a relatively small cohort of infertile men, which may limit the generalisability of the findings. Second, several key inflammatory markers, such as tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6), which have been shown in previous studies to be associated with semen parameters, were not assessed. Third, semen parameters are known to exhibit day-to-day variability; however, only a single semen sample was analysed for each participant. Finally, given the multiple comparisons performed, the possibility of a Type I error remains despite the application of appropriate statistical tests.

### CONCLUSION

This cross-sectional study, conducted in a small and homogeneous cohort of infertile Asian men, provides new evidence highlighting significant correlations between abnormal semen parameters and various biochemical and endocrinological markers.

Elevated oxidative stress—often resulting from obesity and dyslipidaemia—appears to negatively influence semen quality. Conversely, certain endogenous factors, such as uric acid, may play a protective role by neutralising harmful oxidising and nitrating agents, including ROS and environmental toxins. In our study, uric acid was positively associated with improved sperm viability and morphology, suggesting its potential role in preserving sperm function.

Our findings indicate that serum lipid levels are significantly associated with semen parameters—particularly sperm concentration, total count, and motility—emphasising the critical role of lipid and cholesterol homeostasis in male fertility. Additionally, elevated inflammatory markers, such as ESR and CRP, were associated with poorer semen quality, with both sperm concentration and total sperm count showing negative correlations with these indicators of chronic inflammation. Chronic inflammatory conditions are well-established risk factors for cardiovascular and other long-term health issues.

Semen quality not only reflects male reproductive potential but also serves as a biomarker of overall health, with dyslipidaemia, inflammation, and oxidative stress emerging as key modifiable determinants of male infertility. Recognising male infertility as a clinical marker of systemic health may enable early identification of comorbidities and provide opportunities for timely intervention, ultimately improving both fertility outcomes and long-term health.

**Author contributions:** LS, BB: Conceived and designed the study, critically revised the manuscript; LS, MY: Collected and analysed the data; UK, MS: Contributed to data interpretation and statistical analysis; LS: Drafted the manuscript. All authors read and approved the final version.

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