



ORIGINAL ARTICLE

Correlation between abnormal lipid profile and semen parameters in infertile males: Experience at a Tertiary care hospital.

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ABSTRACT... Objective: To determine the correlation between abnormal lipid profile and semen parameters in infertile males. **Study Design:** Observational Cross-sectional Study. **Setting:** Department of Urology and Pathology, Sheikh Zayed Hospital (SZH), Rahim Yar Khan. **Period:** January 2022 and December 2023. **Methods:** Infertile males between 18 to 45 years of age visiting the outdoor clinic subjected to semen analysis as work up of infertility. Infertile males with high BMI (>25kg/m²), family history of dyslipidemia and family history of high BMI were subjected to the estimation of lipid profile. A total of 127 infertile males with abnormal lipid profile were included. Serum total cholesterol >200 mg/dl, serum triglycerides >150 mg/dl, serum LDL >50 mg/dl, and serum HDL <40 mg/dl were the markers for an abnormal lipid profile. The study examined the correlation between aberrant lipid profile and characteristics related to semen, including sperm concentration (millions/ml), total sperm quantity (millions/ejaculate), morphology (percentage of normal forms), motility (percentage of progressive motility), and vitality (percentage of live). P-value less than 0.05 was deemed significant. **Results:** Mean age of the total 127 study subjects was 33±5.414years. Positive correlation of serum cholesterol has been found with respect to total sperm number (r=1.040), morphology (r=1.622), motility (r=0.832) and vitality(r=1.471). Positive correlation of triglyceride was found with respect to age (r=1.280) and sperm concentration (r=1.729). Positive correlation of HDL-c found with respect to sperm concentration (r=1.116). LDL-c shows positive correlation with respect to age (r=1.342), sperm concentration(r=0.856), total sperm number (r=1.757) and vitality(r=1.347). Statistically significant difference of serum cholesterol with respect to vitality (p value: 0.004), HDL-c with respect to sperm concentration (p value: 0.024), LDL-c with respect to age (p value: 0.037) and total sperm number (p value: 0.049) has been found. **Conclusion:** On the basis of our study, it has been concluded that abnormal lipid profile is positively correlated with semen parameters with significant correlation of LDL-c with total sperm number. Infertile males should have their lipid profile assessed to determine whether it adversely affects the characteristics of their semen parameters.

Key words: Abnormal Lipid Profile, Infertile Males, Semen Parameters.

INTRODUCTION

Male factor infertility is the incapacity of a male to conceive a fertile female. It affects about 7% of all men and accounts for 40–50% of infertile couples. There exists a close relationship between male fertility and health state. It was discovered that the infertile men had a much higher prevalence of comorbidities than the fertile males.¹ It has been frequently observed that medical comorbidities and illnesses that adversely impact men's health are linked to compromised reproductive functioning.² Male infertility can have a variety of etiologic reasons,

including coital problems, infectious diseases, vascular, immunologic, genetic, congenital, endocrinological, obstructive, and the result of antispermatogenic drugs.³ Compared to males of normal weight, obese men had increased rates of hypogonadotropic hypogonadism and increased rates of sperm DNA or mitochondrial damage.⁴

Researchers are now interested in risk factors for semen quality, such as biological and environmental factors, due to the possible decline in semen quality during the past ten years. Lipid metabolism needs to be in balance to

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ensure sperm maturation, motility, capacitation, acrosome response, or fusion. Sperm maturation occurs in the epididymis, where cholesterol sulfate acts as a membrane stabilizer. The sperm's asymmetric bilayer plasma membrane distribution is lost, as it moves through the female reproductive system, and significant losses of phospholipids and cholesterol take place during the acrosomal reaction and capacitation processes. The ability of the reproductive medium to bind to cholesterol has an impact on the cholesterol efflux that is seen in capacitation. Additionally, a number of investigations showed that the inflow of cholesterol lowers the pace of acrosomal response.⁵

Increased levels of circulating lipids can cause both adipose and non-adipose cells' metabolic pathways to receive an excess of energy substrates. As a result, there may be a rise in the production of ROS (reactive oxygen species). Elevated ROS levels are considered a risk factor for the development of nearly half of male infertility cases in males with sperm failure.⁶ Because serum lipids are the main substrate for steroid synthesis and are essential for the sperm plasma membrane's growth and spermatogenesis, they are significant for male fertility. One possible contributing cause to male factor infertility is abnormal lipid metabolism in the male reproductive system.⁷ Changes in seminal plasma oxidative stress, semen quality, and male reproductive hormone levels can all be caused by elevated body mass index (BMI) and are associated with male infertility.^{8,9} However, there isn't enough evidence to conclusively show that male subfertility and high obesity are related. Several studies have shown unfavorable correlations between obesity and body mass index (BMI), waist circumference (WC), hip circumference (HC), and central adiposity as assessed by sperm concentration and quantity.¹⁰

There is, however, a dearth of Pakistani research assessing the relationship between aberrant semen characteristics and the male partner's lipid profile in infertile couples. The goal of the current investigation was to determine whether the aberrant semen parameters of infertile

couples' male partners were correlated with the parameters of their lipid profiles.

METHODS

After taking ethical approval from institutional review board {321/IRB/SZMC/SZH(02-12-21)}, cross sectional observational study conducted in urology and pathology department, Sheikh Zayed Hospital (SZH), Rahim Yar Khan between January 2022 and December 2023. Infertile males between 18 to 45 years of age visiting the outdoor clinic subjected to semen analysis as work up of infertility. Infertile males with high BMI ($>25\text{kg/m}^2$), family history of dyslipidemia and family history of high BMI were subjected to the estimation of lipid profile. A total of 127 infertile males with abnormal lipid profile were included. Serum total cholesterol >200 mg/dl, serum triglycerides >150 mg/dl, serum LDL >50 mg/dl, and serum HDL <40 mg/dl were the markers for an abnormal lipid profile. The sample size was determined by taking into account the 95% confidence interval, the 8% margin of error, and the 30–40% male factor prevalence in infertility.¹² On a predesigned proforma, data was gathered. Samples for lipid profiles were taken following 10 to 12 hours fasting. Data analysis was done with SPSS version 25. Age (years), serum total cholesterol (mg/dl), serum triglyceride (mg/dl), LDL-c (mg/dl), HDL-c (mg/dl), motility (progressive motility %), morphology (% normal forms), and vitality (% live) are examples of continuous variables that are presented in terms of mean and standard deviation. Frequency and percentages were computed in each group once the data was stratified. Additionally, cross tabulation was produced. The link between the aberrant lipid profile and the semen parameters was examined using the Pearson correlation coefficient. Chi square analysis is employed in significance analysis. P-value less than 0.05 was deemed significant.

RESULTS

Of the total 127 study subjects, mean age was 33 ± 5.414 years with 43(33.9%) were having ≤ 30 of age while 84(66.1%) were having >30 years age (Table-I). Mean serum cholesterol was 247.19 ± 36.079 mg/dl with 82(64.6%) were having

≤ 250 mg/dl and 45(35.4%) were having > 250 mg/dl (Table-I). Of the total 127 infertile males, mean serum triglyceride was 198.39 ± 49.969 mg/dl with 80(63%) having ≤ 200 mg/dl and 47(37%) were having serum triglyceride > 200 mg/dl (Table-I). Of the total 127 study subjects, mean LDL was 113.78 ± 28.105 mg/dl and mean HDL was 37.20 ± 6.355 mg/dl (Table-I). Distribution of study subjects with respect to semen parameters has been shown in Table-I with frequency and percentages in each subgroup (Table-I). Correlation of abnormal lipid profile parameters with age and semen parameters has been demonstrated in Table-II. Strong positive correlation of serum Triglyceride and LDL found with respect to age ($r=1.280$ & $r=1.342$) as shown in Table-II. Statistically significant difference of LDL level has been found with respect to age with p value 0.037 (Table-II). Strong positive correlation of serum triglyceride and HDL has been found with respect to sperm concentration ($r=1.729$ & $r=1.116$) as shown in Table-II. Statistically significant difference of HDL level has been found with respect to sperm concentration with p

value 0.024 (Table-II). Strong positive correlation of serum cholesterol and LDL-c has been found with respect to total sperm number (millions/ejaculate) ($r=1.040$ & $r=1.757$) as shown in Table-II. Statistically significant difference of LDL-c has been found with respect to total sperm number with p value 0.049 (Table-II). Serum cholesterol shows positive correlation with respect to morphology (% normal forms) in semen ($r=1.622$) as shown in Table-II. No statistically significant difference of lipid profile with respect to morphology (% normal forms) demonstrated with p value > 0.05 (Table-II). Motility (progressive motility %) shows moderate positive correlation with respect to serum cholesterol ($r=0.832$) as shown in Table-II. No statistically significant difference of lipid profile with respect to motility demonstrated with p value > 0.05 (Table-II). Strong positive correlation of serum cholesterol and LDL-c found with respect to vitality (% live) ($r=1.471$ & $r=1.347$) as shown in Table-II. Statistically significant difference of serum cholesterol found with respect to vitality with p value 0.004 as shown in Table-II.

Variables	Mean \pm SD	Subgroups	Frequency	Percentages
Age (Years)	33 \pm 5.414	≤ 30	43	33.9%
		> 30	84	66.1%
Serum Cholesterol (mg/dl)	247.19 \pm 36.079	≤ 250	82	64.6%
		> 250	45	35.4%
Serum Triglyceride (mg/dl)	198.39 \pm 49.969	≤ 200	80	63%
		> 200	47	37%
LDL(mg/dl)	113.78 \pm 28.105	≤ 120	78	61.4%
		> 120	49	38.6%
HDL (mg/dl)	37.20 \pm 6.355	≤ 30	30	23.6%
		> 30	97	76.4%
Sperm Concentration (millions/ml)	15.44 \pm 4.238	≤ 15	61	48%
		> 15	66	52%
Total Sperm number (million/ejaculate)	35.63 \pm 6.190	≤ 39	47	37%
		> 39	80	63%
Morphology (% normal forms)	3.69 \pm 1.780	≤ 4	81	63.8%
		> 4	46	36.2%
Motility (Progressive motility %)	30.06 \pm 9.305	≤ 32	69	54.3%
		> 32	58	45.7%
Vitality (% live)	52.92 \pm 13.742	≤ 58	70	55.1%
		> 58	57	44.9%

Table-I. Distribution of study subjects with respect to different variables (n=127)

Variable	Sub Groups	Lipid Profile							
		Total Cholesterol (mg/dl)		Triglyceride (mg/dl)		HDL-c (mg/dl)		LDL-c(mg/dl)	
		≤250	>250	≤200	>200	≤30	>30	≤120	>120
Age (Years)	≤30	26	17	30	13	11	32	21	22
	>30	56	28	50	34	19	65	57	27
Pearson Correlation		0.478		1.280		0.138		1.342	
P value		0.489		0.258		0.710		0.037*	
Sperm concentration (millions/ml)	≤15	39	22	42	19	9	52	40	21
	>15	43	23	38	28	21	45	38	28
Pearson correlation		0.021		1.729		1.116		0.856	
P value		0.886		0.189		0.024*		0.355	
Total sperm number (millions/ejaculate)	≤39	49	31	50	30	18	62	44	36
	>39	33	14	30	17	12	35	34	13
Pearson correlation		1.040		0.022		0.151		1.757	
P value		0.308		0.881		0.698		0.049*	
Morphology (% normal forms)	≤4	49	32	50	31	19	62	51	30
	>4	33	13	30	16	11	35	27	19
Pearson correlation		1.622		0.153		0.003		0.225	
P value		0.203		0.695		0.954		0.635	
Motility (Progressive motility %)	≤32	47	22	42	27	16	53	44	25
	>32	35	23	38	20	14	44	34	24
Pearson correlation		0.832		0.292		0.016		0.352	
P value		0.362		0.589		0.900		0.553	
Vitality (% live)	≤58	53	17	43	27	16	54	38	32
	>58	29	28	37	20	14	43	40	17
Pearson correlation		1.471		0.164		0.051		1.347	
P value		0.004*		0.686		0.822		0.067	

Table-II. Cross tabulation and correlation of abnormal lipid profile with respect to Age and Semen parameters such as total sperm number (million/ejaculate), sperm concentration (millions/ml), morphology (% normal forms), motility (progressive motility %) and vitality (% live) (n=127)

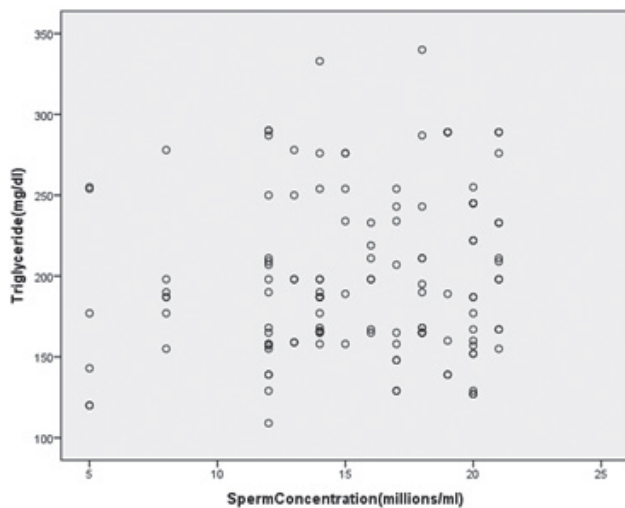


Figure-1. Correlation of serum Triglyceride (mg/dl) with Sperm Concentration (millions/ml)

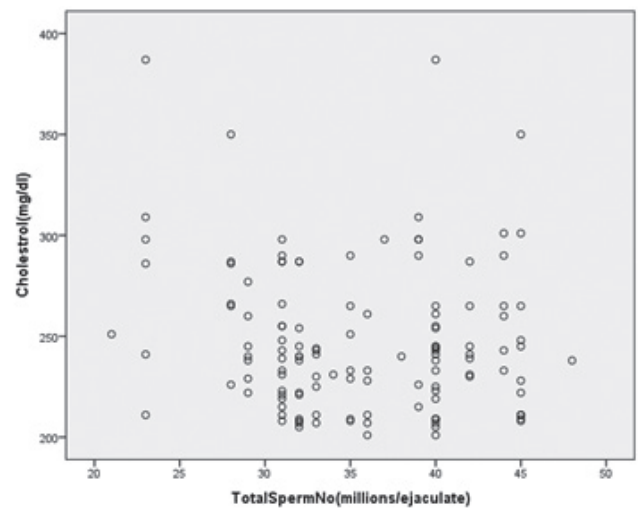


Figure-2. Correlation of Serum Cholesterol (mg/dl) with Total sperm Number (millions/ejaculate)

DISCUSSION

Elevated lipid levels are thought to impair semen quality in addition to occasionally affecting sexual performance. There is a common notion that high cholesterol contributes to infertility. A systematic review conducted by Pakpaphan C et al demonstrated the effect of elevated lipid profile on semen quality and measures the correlation of lipid parameters with semen parameters. This review suggests that lipids have a major effect on sperm quality, even though not all research consistently claim that lipids alter semen quality.

According to this study, maintaining lipid levels is essential for maintaining the quality of sperm and the quality of life.¹² Jian-Xiong Ma et al. looked at the relationships between semen quality, serum reproductive hormones, lipids, and leptin, as well as obesity-associated markers, in another study. They discovered that while there was no significant correlation between BMI and serum reproductive hormones, lipids, leptin, or semen quality, obesity-related markers, such as the waist-to-hip and waist-to-height ratios, showed statistically significant negative correlations with semen parameters, such as sperm concentration, the ratio of progressive motility, and the ratio of non-progressive motility. The percentage of morphologically normal sperm was inversely correlated with serum lipid levels, including total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), leptin, and seminal superoxide dismutase.

In comparison to the normal group, the overweight group exhibited significantly lower values for sperm concentration, the ratio of progressive sperm, and the ratio of morphologically normal sperm.¹³ Findings of the study are consistent with our study as we have found positive correlation of serum cholesterol (mg/dl) with total sperm number (millions/ejaculate), morphology (% normal forms) and vitality (% live). We have found positive correlation of triglyceride (mg/dl), HDL-c and LDL-c with sperm concentration (millions/ml). LDL-c also showed positive correlation with respect to total sperm number (millions/ejaculate) and vitality (% live). Findings of our study are inconsistent with another study conducted by

Lu J.C. et al in which there was no correlation found between lipid parameters and semen parameters.¹⁴

A prospective study conducted in four different countries found that the total sperm count had a negative linear relationship with waist circumference and that the percentage of males with abnormal volume, concentration, and total sperm increased with increasing body size.¹⁵ Independent of BMI, several writers have found a negative correlation between the contents of phospholipids, total and free cholesterol, and semen characteristics, particularly morphology.¹⁶ Tsao TW et al.'s study shown that semen quality and body mass index are related.

Their research led to the conclusion that all four parameters—total motility, progressive motility, normal sperm morphology, and sperm concentration—saw a statistically significant decline with age ($p < 0.001$, $p < 0.001$, $p < 0.001$, and $p = 0.004$). A substantial negative linear association was seen between sperm concentration and BMI ($p = 0.005$), but an inverse relationship was observed between normal sperm morphology, BMI, and waist-to-height ratio ($p < 0.001$ and $p = 0.004$). The frequency of abnormal total sperm motility, progressive motility, normal sperm morphology, and sperm concentration increased with age ($p = 0.011$, $p < 0.001$, $p < 0.001$, and $p = 0.002$). Reduced normal sperm morphology and concentration were connected with an increase in body fat ($p < 0.05$). There was no relationship discovered between obesity and sperm motility.¹⁷ Singh L. et al.'s cross-sectional investigation showed a relationship between semen parameters and lipid profile. Their investigation revealed a strong positive correlation between the total number of sperm and the levels of triglycerides and low-density lipoproteins. Findings are consistent with our study. Nonetheless, a noteworthy inverse relationship was observed between sperm motility and sperm concentration and triglycerides. Total cholesterol was shown to be substantially correlated ($p < 0.05$) with both progressive and total motility. Compared to males with lower total cholesterol, infertile men

with greater total cholesterol showed superior overall and progressive motility. It was concluded that sperm concentration, count, and motility are the three main semen metrics with which the lipid profile is significantly correlated.¹⁸

A Taiwanese study found a statistically significant positive correlation between sperm concentration and very low-density lipoprotein (VLDL) and triglycerides. Furthermore, Elevated low-density lipoprotein and cholesterol levels were accompanied by a significant increase in both total and progressive sperm motility.¹⁹ Compared to other cell types, spermatozoa have a larger concentration of neutral lipids, especially diacylglycerol (DAG).²⁰ Studies looking into the effects of cholesterol-lowering medications, like pravastatin, showed that after 6 to 12 months of use, sperm motility decreased due to lower levels of total cholesterol and LDL.²¹

One of the main limitation of our study was that it was single centered study. Sample size was limited. As the male infertility has become very common in Pakistan, so there is need of more extensive research and meta-analyses to establish the correlation between lipid profile and semen parameters.

CONCLUSION

On the basis of our study, it has been concluded that abnormal lipid profile is positively correlated with semen parameters with significant correlation of LDL-c with total sperm number. Infertile males should have their lipid profile assessed to determine whether it adversely affects the characteristics of their semen parameters.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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




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2	Rukhsana Tumrani	Data analysis, Data interpretation. Manuscript writing.	
3	Madiha Naqvi	Data entry, Data analysis, Proof reading.	
4	Sara Arif	Data analysis, Manuscript writing.	
5	Sana Saleem	Data entry, Discussion, Data interpretation.	
6	Dania Niaz	Data analysis, Manuscript writing.	