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Original Research Article

Correlation of lipid profile of infertile men with abnormal semen parameters

Lovely Singh[1]*, Bindu Bajaj[1], Monika[1], Kumari Usha Rani[1], Megha Panwar[2], Sunil Ranga[3]

[1]Department of Obstetrics and Gynecology, VMMC and SJH, New Delhi, India
[2]Medeor Hospitals, Qutub Institutional Area, India
[3]Department of Pathology, VMMC and SJH, New Delhi, India

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***Correspondence:**
Dr. Lovely Singh,
E-mail: lovelysingh.ls1010@gmail.com

ABSTRACT

Background: Male's inability to impregnate a fertile female is referred as male factor infertility. It accounts for 40-50% of infertile couples and affects almost 7% of all men. Male comorbidities and conditions, which negatively affect men's health, have been repeatedly associated with impaired reproductive functioning. Cholesterol is the main substrate for steroid synthesis and it plays crucial role in formation of sperm plasma membrane and thus in spermatogenesis, highlighting the role of serum lipids in male fecundity. Purpose of the study is to evaluate correlation lipid profile of male partners with abnormal semen parameters in infertile couples.
Methods: A cross sectional study was carried out in the infertility clinic of a tertiary care hospital for over 18 months and 151 infertile men with abnormal semen parameters (as per WHO 2010 criteria) were enrolled. Evaluation of lipid profile was done and its relationship with abnormal semen parameters was analyzed.
Results: Significant positive correlation was seen between LDL and Triglyceride with sperm concentration and total sperm count. However, significant negative correlation was seen between Triglyceride and sperm motility and TMSC. Total and progressive motility was found to be significantly associated with total cholesterol ($p<0.05$). Infertile men having higher total cholesterol were found to have better total and progressive motility compared to men with less total cholesterol.
Conclusions: Our findings demonstrated that lipid profile has significant correlation with semen parameters, specifically sperm concentration, count and motility.

Keywords: Male infertility, Lipid profile, Semen parameters

INTRODUCTION

In a social set up like ours, there is a strong emphasis on child bearing and infertility can have great psychological, economic and medical implications. According to international committee for monitoring assisted reproductive technology (ICMART), world health organization (WHO), infertility is a disease of reproductive system, defined by failure to achieve clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.[1]

Male's inability to impregnate a fertile female is referred as male factor infertility. It accounts for 40-50% of infertile couples and affects approximately 7% of all men.[2] Male fertility and health status are closely related to each other. The prevalence of comorbidities was found to be significantly higher in the infertile men than in the fertile men.[3] Medical comorbidities and conditions, which negatively affect men's health, have been repeatedly associated with impaired reproductive functioning.[4-6]

Etiologic factors in male infertility can be genetic, congenital, endocrinological, infective, vascular,

immunologic, obstructive, effect of antispermatogenic agents or due to coital disorders.[7]

In South India, fertile men showed decline in semen quality and sperm functional parameters over a period of 13 years.[8] Obese men have higher rates of hypogonadotropic hypogonadism and increased rate of sperm DNA or mitochondrial damage compared to normal weight men.[9] The possible decline of semen quality in the past decade have generated intense interest of researchers in risk factors for semen quality, such as biological and environmental factors. Study conducted in Taiwan showed that sperm concentration was statistically positively correlated with triglyceride and very low-density lipoprotein (VLDL). In addition, total sperm motility and progressive motility were statistically increased with increasing low-density lipoprotein and cholesterol levels.[10]

Increased levels of circulating lipids could result in excessive supply of energy substrates to metabolic pathways in adipose and non-adipose cells. Which, in turn, can increase production of ROS (Reactive oxygen species). Elevated level of ROS is thought to be risk factor for development of approximately half of male infertility cases in men diagnosed with sperm dysfunction.[11]

Cholesterol is the main substrate for steroid synthesis plays a crucial role in the formation of sperm plasma membrane and thus in spermatogenesis, highlighting the role of serum lipids in male fecundity. A prospective study conducted across four countries showed that total sperm count had a negative linear association with waist circumference and percentage of men with abnormal volume, concentration and total sperm increased with increasing body size.[12] Some authors have observed negative association of total and free cholesterol and phospholipid concentrations with semen parameters especially morphology, independent of BMI.[13] Studies have also reported statistically significant correlation of total cholesterol levels with total sperm motility and progressive motility.[14]

However, there is paucity of Indian literature evaluating association of lipid profile of male partners with abnormal semen parameters among infertile couples. The present study was planned to find out correlation of lipid profile parameters with abnormal semen parameters of male partners of infertile couples.

Aim

Aim of the study was to study the correlation of lipid profile of male partners with abnormal semen parameters (as per WHO 2010 criteria) in Infertile couples.

METHODS

This was a hospital based cross sectional study carried out in the infertility clinic of VMMC and Safdarjung hospital, new Delhi, INDIA, over a period of 18 months (October 2020 to April 2022) after taking ethical clearance from the institutional ethics committee.

Semen analysis was done as a part of workup of infertile couple. Sample was tested after 3 days of abstinence. All samples examined by same person to exclude interobserver variation. Male partner of infertile couples showing 1/more abnormal finding in semen analysis, such as in volume, concentration, total sperm count, total and progressive motility, vitality, morphology and semen leucocyte count (WHO 2010 criteria), enrolled in study.

A sample size of 151 was calculated taking prevalence of male factor infertility as 40-50% in infertile couples.[2] taking this value as reference, the minimum required sample size with 8% margin of error and 5% level of significance was 151 patients.

A detailed proforma for male infertility was filled for all the participants enrolled in study. A venous sample was collected for lipid profile after 10-12 hours of fasting. The outcome studied correlation of serum total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG) with abnormal semen parameters of male partners of infertile couples.

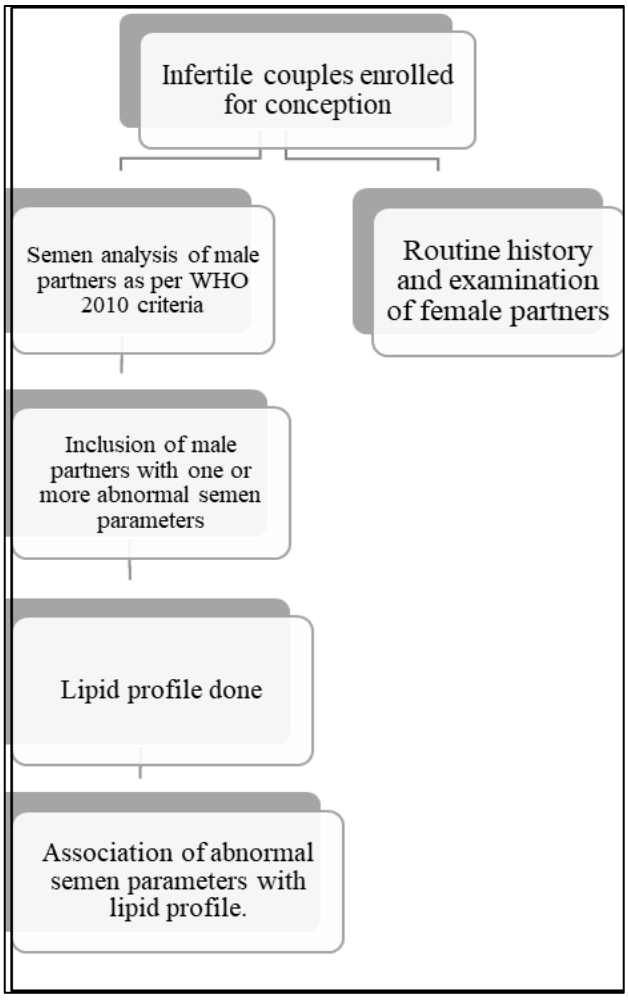

Figure 1: Flow chart of methodology.

Statistical tool

Categorical variables will be presented in number and percentage (%) and continuous variables will be presented as mean ± SD and median. Normality of data will be tested by Kolmogorov-Smirnov test. If the normality is rejected then non parametric test will be used.

Statistical tests will be applied as follows- 1. Quantitative variables will be associated using unpaired t-test/Mann-Whitney test (when the data sets were not normally distributed) with male fertility. 2. Qualitative variables will be associated using Chi-Square test/Fisher's exact test. 3. Pearson correlation coefficient/Spearman rank correlation coefficient will be used to find out correlation of quantitative parameters. A $p<0.05$ will be considered statistically significant. The data will be entered in MS excel spreadsheet and analysis will be done using SPSS version.

RESULTS

In majority (135 (89.40%)) of patients, total cholesterol (mg/dL) was normal (≤200 mg/dL). It was deranged (>200 mg/dL) in only sixteen out of the 151 patients (10.60%).

In majority (135 (89.40%)) of patients, HDL (mg/dL) was normal (≥40 mg/dL). It was deranged (<40 mg/dL) in only 16 out of 151 patients (10.60%).

In majority (111 (73.51%)) of patients, the LDL (mg/dL) was deranged (>130 mg/dL). LDL (mg/dL) was normal (≤130 mg/dL) in only forty out of the 151 patients (26.49%).

In majority (87 (57.62%)) of patients, Triglyceride (mg/dL) was deranged (>150 mg/dL). It was normal (≤150 mg/dL) in only 64 out of 151 patients (42.38%).

Table 1: Distribution of lipid profile of study subjects.

Lipid profile	Frequency	Percentage (%)
Total cholesterol (mg/dL)		
Normal (≤200 mg/dL)	135	89.40
Deranged (>200 mg/dL)	16	10.60
Mean ± SD	178.87±17.62	
Median (25^{th}-75^{th} percentile)	176 (169-183)	
Range	139-246	
HDL (mg/dL)		
Normal (≥40 mg/dL)	135	89.40
Deranged (<40 mg/dL)	16	10.60
Mean ± SD	52.24±10.12	
Median (25^{th}-75^{th} percentile)	54 (45-61)	
Range	23-76	
LDL (mg/dL)		
Normal (≤130 mg/dL)	40	26.49
Deranged (>130 mg/dL)	111	73.51
Mean ± SD	145.23±20.93	
Median (25^{th}-75^{th} percentile)	145 (127-163)	
Range	100-189	
Triglyceride (mg/dL)		
Normal (≤150 mg/dL)	64	42.38
Deranged (>150 mg/dL)	87	57.62
Mean ± SD	155.26±20.36	
Median (25^{th}-75^{th} percentile)	156 (139.5-172)	
Range	101-213	

Table 2: Correlation of lipid profile with semen parameters.

Variables	Sperm conc. (million/ mL)	Total sperm count (×10^6/ ejaculate)	Total motility (%)	Progressive motility (%)	Morphology (%)	Total motile sperm count (×10^6/ejaculate)
Total cholesterol (mg/dL)						
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
HDL (mg/dL)						
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

Continued.

Variables	Sperm conc. (million/ mL)	Total sperm count (×10⁶/ ejaculate)	Total motility (%)	Progressive motility (%)	Morphology (%)	Total motile sperm count (×10⁶/ejaculate)
LDL (mg/dL)						
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
Triglyceride (mg/dL)						
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 rank correlation coefficient

Significant positive correlation was seen between LDL (mg/dL) with sperm concentration (million/mL), total sperm count (×10⁶/ejaculate) with correlation coefficient of 0.231, 0.259 respectively.

Significant positive correlation was seen between triglyceride (mg/dL) with sperm concentration (million/mL), total sperm count (×10⁶/ejaculate) with correlation coefficient of 0.197, 0.204 respectively.

Significant negative correlation seen between triglyceride (mg/dL) with total motility (%), progressive motility (%) with correlation coefficient of -0.186, -0.18 respectively.

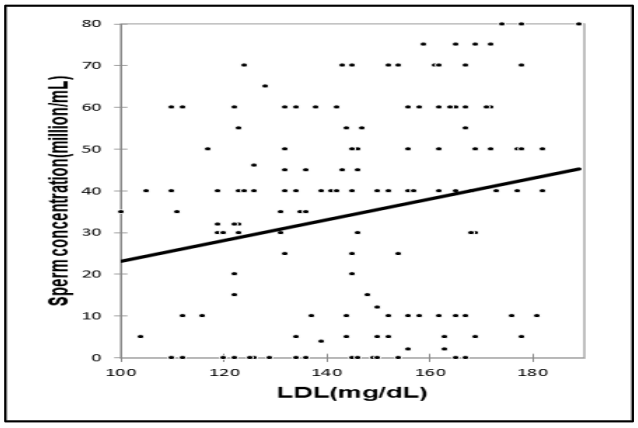

Figure 2: Correlation of LDL (mg/dL) with sperm concentration (million/ml).

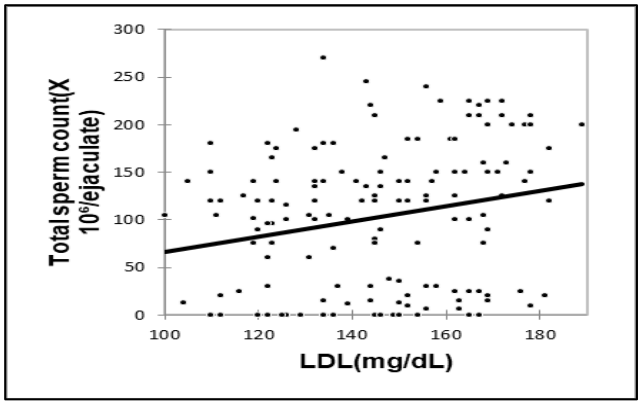

Figure 3: Correlation of LDL (mg/dL) with total sperm count (×10⁶/ejaculate).

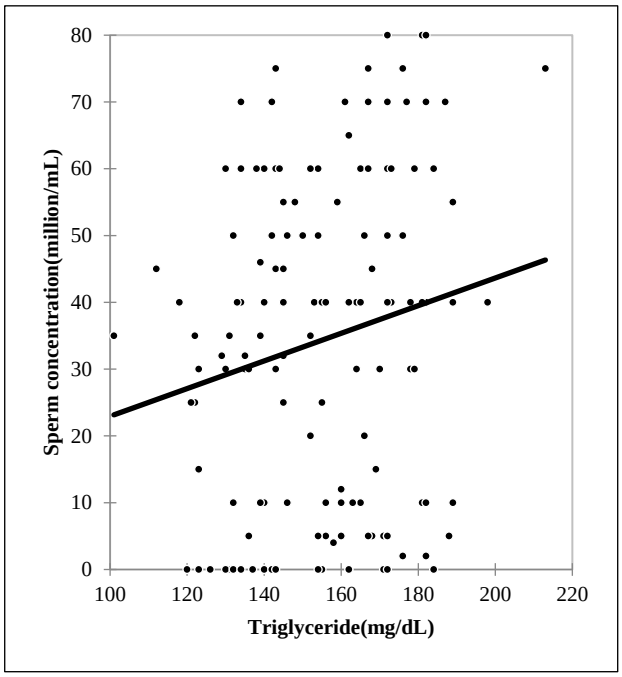

Figure 4: Correlation of triglyceride (mg/dL) with sperm concentration (million/mL).

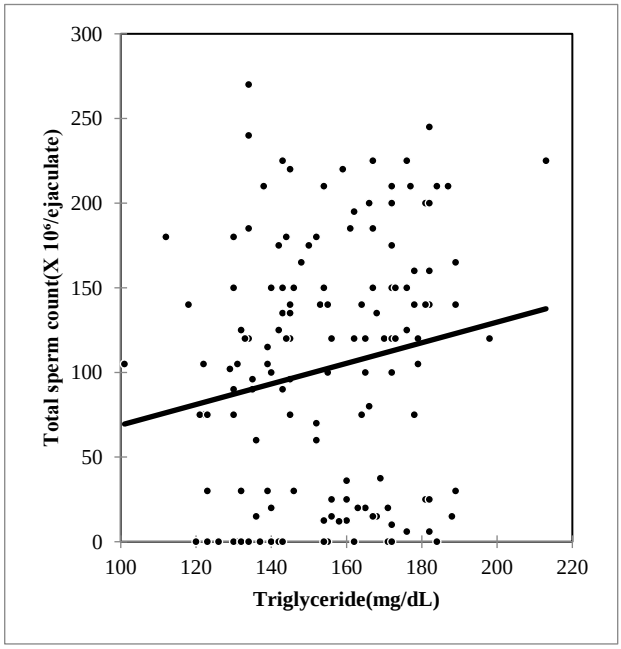

Figure 5: Correlation of triglyceride (mg/dL) total sperm count (×10⁶/ejaculate).

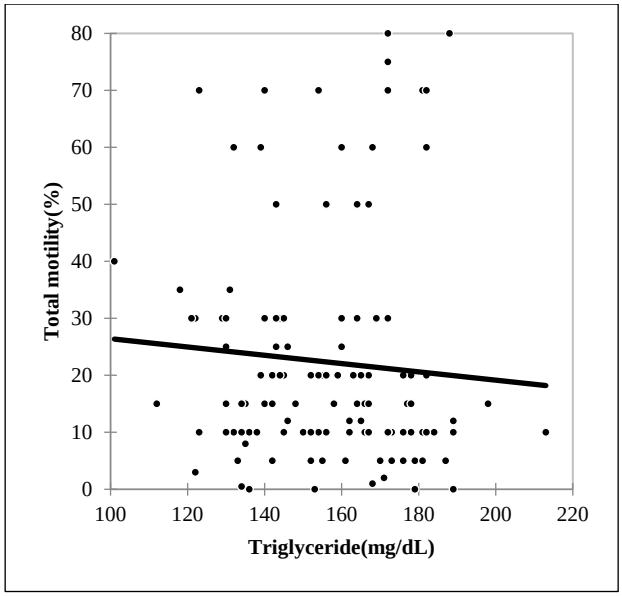

Figure 6: Correlation of triglyceride (mg/dL) with total motility (%).

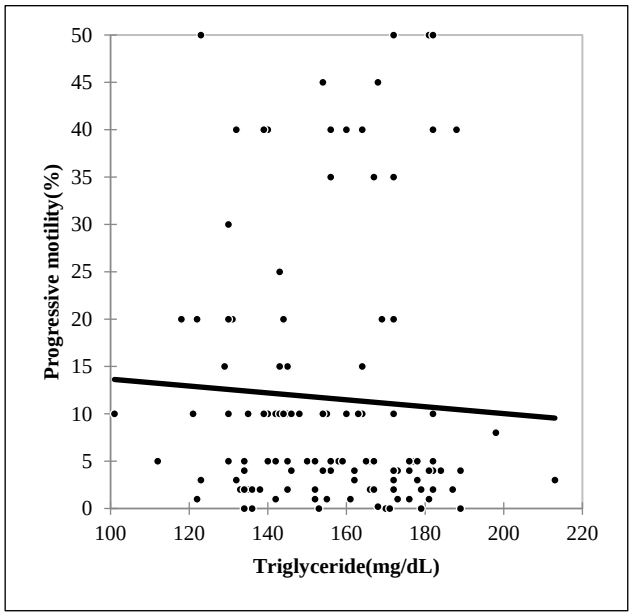

Figure 7: Correlation of triglyceride (mg/dL) with progressive motility (%).

DISCUSSION

The composition and structure of the sperm plasma membrane are essential in the process of spermatogenesis and sperm maturation.[15] It contains about 70% phospholipids, 25% neutral lipids and 5% glycolipids.[16] In contrast to other cell types, the lipid composition of spermatozoa have a higher proportion of neutral lipids, especially diacylglycerol (DAG).[17]

The balance in lipid metabolism is crucial to ensure sperm maturation, motility, capacitation, acrosome reaction or fusion. Sperm maturation occurs in the epididymis where cholesterol sulfate acts as a membrane stabilizer[15]. As the sperm migrates through the female reproductive tract, it loses its asymmetric bilayer distribution of plasma membrane and substantial loss of cholesterol and phospholipids occur during capacitation and acrosomal reaction. The net cholesterol efflux that is observed during capacitation is affected by the capacity of the medium (Reproductive tract) to bind to cholesterol. Several studies also demonstrated that cholesterol influx reduces the rate of acrosomal reaction.[15]

In our study most of the men (90%) had normal total cholesterol and high-density lipoprotein, whereas, low-density lipoproteins and triglycerides were found to be raised in 73% and 57% men, respectively. Most common abnormal semen parameter detected in our study was decreased progressive motility, seen in 85.5% men.

Previous literature is suggestive of significant correlation between lipid profile and semen parameters. Sperm concentration was statistically positively correlated with triglyceride and very low-density lipoprotein (adjusted p=0.001 and p=0.005, respectively). Total sperm motility and progressive motility were statistically increased with increasing low-density lipoprotein and cholesterol levels (both adjusted p=0.008 and p<0.001, respectively).[6]

Higher levels of serum total cholesterol, free cholesterol and phospholipids are associated with a significantly lower percentage of sperm with intact acrosome and smaller sperm head area and perimeter.[5]

Similar results were found in our study as significant positive correlation was seen between LDL with sperm concentration and total sperm count. Significant positive correlation was also seen between Triglyceride with sperm concentration and total sperm count (Table 3).

A complex arrangement of signaling pathways are involved in the regulation of sperm motility. Previous literature is suggestive of negative association of increased serum lipid parameters with sperm motility.

Phosphatidylinositol 3-kinase (PI3K), a lipid and protein kinase, involved in the regulation of several biological aspects of somatic cells was investigated for its role on human sperm motility. The results suggested a negative role for PI3K in the development and maintenance of sperm motility and suggest a possible use of PI3K inhibitors to enhance motility in cases of asthenozoospermia.[18]

Also, studies conducted to investigate the effect of cholesterol lowering agents such as pravastatin, demonstrated reduced sperm motility as a result of reduced total cholesterol and LDL levels with its 6-12 months of use.[19]

In our study, significant negative correlation was seen between Triglyceride and total motility (%) and

progressive motility (%) (Correlation coefficient of -0.186, -0.18 respectively). However, no significant correlation was found between rest of the lipid parameters with reduced sperm motility.

This study depicts correlation of increasing serum lipid levels (may or may not be in normal range) with abnormal semen parameters. Serum lipid levels were not quantified to the upper limit where its adverse effect over semen parameter could be elicitated. Further large scale studies and meta-analysis are needed for the same.

CONCLUSION

This cross-sectional analysis in a small, homogeneous, Asian, cohort of infertile men, offers novel evidence that abnormal semen parameters have significant correlation with lipid profile of infertile men. Higher serum triglyceride levels are the common lipid derangements seen in the male partner of infertile couples and most common abnormal semen parameter was reduced progressive motility.

Our findings demonstrated that serum lipids affect semen parameters, specifically sperm concentration, count and motility, highlighting the importance of cholesterol and lipid homeostasis for male fecundity.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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