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Research Article

Hyperlipidemia Is Not Related to Semen Quality, but to Serum Testosterone Levels

Jiajie Bi,[1] Jing Ma,[2] Chaoju Yang,[3] Yuanjing Li,[4] Xuan Liu,[5] Yanqing Tie,[3] and Shusong Wang[1,2,4,5]

[1]*Chengde Medical University, Chengde 067000, China*
[2]*Hebei Key Laboratory of Reproductive Medicine, Hebei Reproductive Health Hospital, Shijiazhuang 050071, China*
[3]*Hebei General Hospital, Shijiazhuang 050051, China*
[4]*School of Chemistry and Materials Science, Hebei Normal University, Shijiazhuang 050024, China*
[5]*Graduate School of Hebei Medical University, Shijiazhuang 050017, China*

Correspondence should be addressed to Shusong Wang; wshsong@126.com

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Background. Currently, there are few studies on the effects of hyperlipidemia on semen parameters and serum hormones in men. In this study, we divided the study subjects into two groups of normal and hyperlipidemia according to the criteria, and observed the differences between semen parameters and serum reproductive hormones in hyperlipidaemic men and normal men, to explore the potential associations between the indicators. *Materials and Methods*. Eight hundred eighty five men attending infertility clinics in six hospitals from September 2016 to June 2017 were selected. Their lipid levels, semen parameters, and serum reproductive hormone levels were tested, and a total of 480 men with normal lipids and 405 men with hyperlipidemia were selected according to the criteria, and the relationship between semen quality, serum reproductive hormones, lipids and semen parameters, and serum hormones was statistically analyzed. *Results*. There was no significant difference in semen parameters between hyperlipidaemic men and normal men ($P > 0.05$), serum testosterone levels were significantly lower in hyperlipidaemic men ($P < 0.05$), and there was a negative correlation between triglycerides (TG) and testosterone in the blood ($P < 0.05$).*Conclusion*. Hyperlipidemia does not affect male semen parameters, and changes in testosterone in hyperlipidaemic men may be related to triglycerides.

1. Introduction

Hyperlipidemia is a metabolic disorder caused by abnormal lipid levels, with total cholesterol, triglycerides, low-density lipoproteins, and high-density lipoproteins as the typical clinical indicators. Disorders of lipid metabolism are most evident in the development of hyperlipidemia [1]. Lipid metabolism homeostasis is related to male reproductive [2, 3] in the control of male testicular function and fertility [4, 5]. Abnormal blood lipid levels can jeopardize male reproductive function, affecting male testicular development and sperm quality [6]. A systematic meta-analysis points out that hyperlipidemia can damage testicular and epididymal structures, affect the quality of male semen, and affect male hormone levels, thus reducing male fertility and even causing infertility [7].

Reproductive hormones as potential markers of spermatogenesis, including follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), estradiol (E2), and testosterone (T), are critical for the initiation and maintenance of spermatogenesis [8]. Studies have shown that reduced male fertility may be the result of decreased testosterone concentrations due to impaired testicular functions [9]. Testosterone is the main component of androgens, and testosterone levels are closely related to the development of the male reproductive system and male reproductive function [10–12]. When lipid metabolism is disturbed, testosterone synthesis is inhibited, resulting in limited spermatogenesis [13].

Lipid homeostasis is inextricably linked to both semen parameters and reproductive hormone levels. There have been many studies in recent years regarding the correlation between lipid levels and semen parameters, but the results

Table 1: General information on participants.

	n	Mean (SD)	Range
Age (years)	885	27.00 (5.00)	20–45
BMI (kg/m^2)	885	25.64 (6.61)	16.90–42.44
Height (cm)	885	173.00 (6.00)	151–195
Weight (kg)	885	75.00 (21.00)	50–140
WC (cm)	885	88.00 (17.75)	64–123.50
Semen volume (mL)	885	3.00 (1.50)	1.20–9.80
Sperm concentration (10^6 per mL)	885	66.13 (65.16)	2.72–351.9
Total sperm count (10^6 per ejaculate)	885	203.96 (197.42)	5.37–1488.32
Progressive motility (%)	885	45.50 (24.22)	1.00–91.70
Nonforward-moving sperm (10^6 per ejaculate)	885	9.17 (6.23)	0.00–87.08
Immortal spermatozoa (10^6 per ejaculate)	885	43.08 (25.43)	2.47–97.00
TC (mmoL/L)	885	4.37 (1.06)	1.39–8.17
TG (mmoL/L)	885	1.17 (1.04)	0.26–12.16
HDL-C (mmoL/L)	885	1.19 (0.43)	0.49–3.02
LDL-C (mmoL/L)	885	2.45 (0.88)	0.80–5.71
Apo A (mmoL/L)	885	1.28 (0.19)	0.75–2.19
Apo B (mmoL/L)	885	0.85 (0.20)	0.41–1.78
FSH (mIU/mL)	169	4.50 (2.35)	0.77–17.08
LH (mIU/mL)	169	3.28 (2.04)	1.13–8.88
PRL (ng/mL)	169	7.90 (4.30)	1.02–35.55
E2 (pg/mL)	169	34.13 (13.65)	13.27–86.35
T (ng/mL)	169	4.01 (0.11)	0.51–7.31

have been inconsistent. Ergun et al. [9] found a significant negative correlation; Liu et al. [7] considered a positive correlation [7, 14]. However, other studies did not find a correlation between the two [15, 16]. This research is a retrospective cohort study based on male reproduction and endocrinology. By analyzing 885 men, the aim was to assess the differences between semen parameters and serum hormones in hyperlipidemia men and men with normal lipids and to explore the factors influencing semen parameters and hormone levels.

2. Objects and Methods

2.1. Research Population. Men aged 20–45 years old who attended infertility clinics in six hospitals in Hebei Province, China, from September 2016 to June 2017; the exclusion criteria for the study population were as follows: Subjects with erectile dysfunction, ejaculatory disorders, and the inability to obtain a semen specimen; patients with lives or work environments that may affect spermatogenesis (e.g., high temperatures, occupation, and toxic substances) and smoking and alcohol abuse; infectious and other systemic diseases; history of prolonged medication (e.g., weight-loss pills); and factors associated with male infertility. A total of 885 (hormone 169) named men were included in this study and semen samples were collected by masturbation. The study was conducted according to the guidelines of the Declaration of Helsinki. All experiments on clinical specimens were approved by the Ethics Committee of the Hebei Provincial Reproductive Health Hospital (2022-006).

2.2. Semen Analysis. Participants collected semen samples by masturbation method after 2–7 days of abstinence. Sperm concentration and viability of fresh semen samples were analyzed for routine semen analysis mainly according to the 2010 World Health Organization Laboratory Manual for the Examination and Processing of Human Semen (5th edition). Semen parameters were analyzed using the CASA system.

2.3. Blood Sample Collection and Serum Hormone Determination. Fasting blood samples were drawn from the study subjects, centrifuged and lipid levels (total cholesterol (TC), triglycerides (TG), low-density lipoproteins (LDL), high-density lipoproteins (HDL), apolipoprotein A (Apo A), apolipoprotein B (Apo B)) were measured using Toshiba/Toshiba Automatic Biochemistry Analyser Accute TBA-40 FR. T, LH, FSH, E2, and PRL levels were measured by electrochemiluminescence using an automated Unicel Dxi 800 Access Immunoassay System (Beckman Coulter, Inc., USA).

2.4. Grouping. Based on the lipid levels obtained from the test, they were divided into normal lipid group and hyperlipidemia group [17–19]. In the normal group, the lipid criteria were as follows: TC < 5.18, LDL-C < 3.37, HDL-C < 4.14, and TG < 1.70. Hyperlipidemia includes the following four types: (1) hypercholesterolemia is TC ≥ 6.22 mmoL/L; (2) hypertriglyceridemia is TG ≥ 2.26 mmoL/L; (3) LDL-C ≥ 4.14 mmoL/L; and (4) HDL-C ≤ 1.04 mmoL/L. Hyperlipidemia can be diagnosed when any of the above items is met.

2.5. Statistics. Samples of differences between the two groups were analyzed using the independent samples t-test (normal

Table 2: Comparison of indicators of hyperlipidemia with normal men in 885 cases.

	Normal	Hyperlipidaemia	
N	405	480	*P*
Age	28.01(4.35)	28.19(4.79)	0.062
BMI	24.03(3.91)	27.18(4.25)	**<0.001**
Weight	72.28(13.18)	81.52(14.41)	**<0.001**
WC	84.80(10.11)	91.94(11.28)	**<0.001**
H	173.17(5.18)	173.06(5.10)	0.773
Semen volume	3.08(1.26)	3.09(1.20)	0.605
Sperm concentration	74.25(48.35)	79.70(53.55)	0.112
Total sperm count	235.33(170.35)	238.93(181.74)	0.761
Progressive motility	43.60(16.10)	45.07(16.09)	0.178
TC	4.14(0.53)	4.90(1.10)	**<0.001**
TG	0.94(0.32)	2.28(1.47)	**<0.001**
HDL-C	1.41(0.27)	1.14(0.37)	**<0.001**
LDL-C	2.28(0.48)	2.93(0.92)	**<0.001**
Apo A	1.32(0.15)	1.22(0.19)	**<0.001**
Apo B	0.79(0.13)	0.96(0.22)	**<0.001**

The values are shown as the mean ± standard deviation. Independent samples *t*-test for normality, Wilcoxon rank-sum test for non-normality. Bolding indicates significant difference.

Table 3: Comparison of indicators of hyperlipidemia with normal men in 169 cases.

	Normal	Hyperlipidaemia	
N	93	76	*P*
TC	4.22(0.50)	4.87(1.14)	**<0.001**
TG	1.00(0.32)	2.44(1.51)	**<0.001**
HDL-C	1.45(0.28)	1.21(0.38)	**0.013**
LDL-C	2.21(0.43)	2.90(1.06)	**<0.001**
Apo A	1.31(0.13)	1.27(0.23)	**0.010**
Apo B	0.81(0.12)	0.98(0.23)	**<0.001**
Semen volume	3.48(1.32)	3.02(1.07)	0.069
Sperm concentration	61.04(37.47)	73.55(49.74)	0.552
Total sperm count	211.85(160.63)	214.47(138.82)	0.271
Progressive motility	44.67(17.25)	45.55(14.72)	0.086
FSH	4.99(2.40)	4.91(2.05)	0.806
LH	3.85(2.10)	3.50(1.38)	0.187
PRL	8.91(4.56)	8.25(3.31)	0.295
E2	37.80(13.60)	35.35(10.44)	0.200
T	4.32(1.43)	3.66(1.21)	**0.002**

Bolded text indicates significant differences.

Table 4: Correlation between lipid indices and serum testosterone.

		Serum				
		FSH	LH	PRL	E2	*T*
Semen	Semen volume	0.094	−0.076	0.023	−0.111	**0.185** *
	Sperm concentration	−0.030	0.017	0.056	0.082	0.083
	Total sperm count	0.020	−0.024	0.074	0.026	0.131
	Forward motion ratio	−0.039	0.033	0.107	0.028	−0.026

*Indicates a significant correlation at the 0.05 level of *P*. Bolded text indicates significant differences.

distribution) or the Wilcoxon rank-sum test (non-normal distribution). The Shapiro–Wilk normality test was used to evaluate whether the analyzed parameters obeyed a normal distribution. If the parameters conformed to a normal distribution, the Pearson test was used. If the parameters conformed to non-normal distribution, Spearman's rho test was used. All analyses were performed using SPSS 26.0.

Table 5: Correlation between lipid indices and serum testosterone.

	TC	TG	HDL	LDL	Apo A	Apo B
T	−0.037	**−0.259** **	0.082	−0.096	0.003	−0.135

**Indicates a significant correlation at the 0.01 level of *P*. Bolded text indicates significant differences.

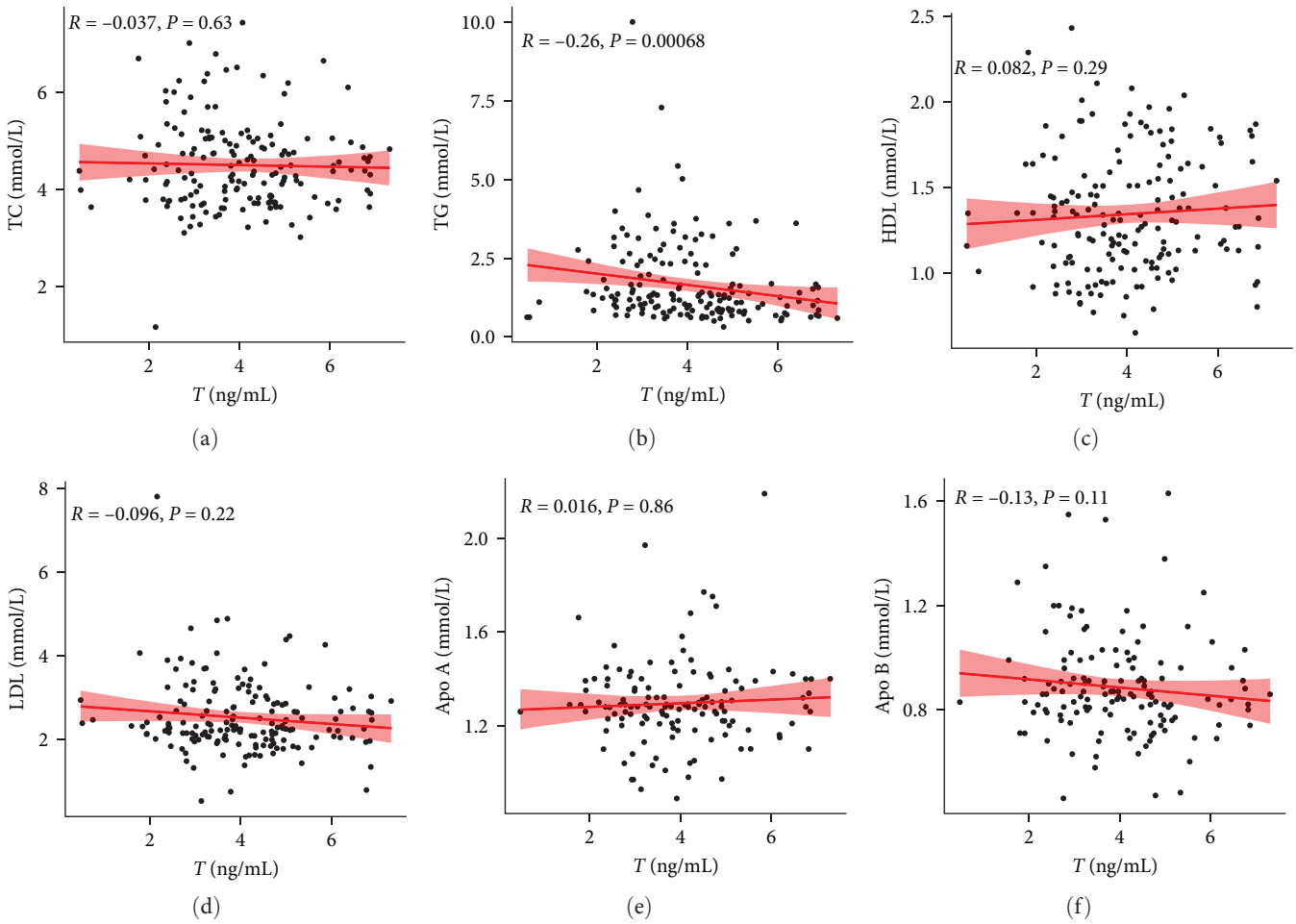

Figure 1: Correlation of lipid indices with serum testosterone: (a) correlation of TC with serum testosterone; (b) correlation of TG with serum testosterone; (c) correlation of HDL with serum testosterone; (d) correlation of LDL with serum testosterone; (e) correlation of Apo A with serum testosterone; and (f) correlation of Apo B with serum testosterone.

3. Result

3.1. General Information on Participants. A total of 885 men were included in this study and further tabulation of the study sample is shown in Table 1.

3.2. Relationship between Hyperlipidemia and Semen Parameters/Serum Reproductive Hormones. First, we analyzed the differences between age, semen parameters, and the lipid indices in 405 male specimens from the hyperlipidemia group and 480 male specimens from the normal lipid group. The results showed that there was a significant difference in lipid indicators between the two groups ($P < 0.05$). However, there was no significant difference ($P > 0.05$) in semen volume, sperm concentration, total sperm count, and sperm viability (Table 2).

Next, for the 169 serum hormone specimens and their corresponding semen parameters analyzed, there was a significant difference between the serum testosterone levels of hyperlipidemia and normal lipid men ($P < 0.05$), whereas there was no significant difference in the semen parameters ($P > 0.05$), which was statistically the same as for the data of 885 cases (Table 3).

4. Correlation Analysis Semen Parameters and Serum Hormones

We correlated serum hormones with semen parameters in 169 subjects and found that there was a significant positive correlation between semen volume and serum testosterone, while no significant correlation was seen between the rest of the hormones and semen parameters (Table 4).

Table 6: Literature overview.

Author	Study population (n)	Impact of lipids on semen parameters	Impact of lipids on reproductive hormone levels
Ergun et al. [9]	18	Lipids negatively correlate with sperm motility	Lipids negatively correlate with T
Attaman et al. [33]	99	Lipids negatively correlate with sperm count and concentration	Unstudied
Schisterman et al. [6]	491	Lipids are negatively correlated with sperm head morphology	Unstudied
Pons-Rejraji et al. [34]	17	Lipids are negatively correlated with semen parameters	Lipids have no effect on reproductive hormone levels
Hagiuda et al. [35]	167	No significant relationship between blood lipids and sperm concentration and viability	Lipids negatively correlate with T
Eisenberg et al. [15]	456	No significant relationship between lipids and semen quality	Unstudied
Lu et al. [16]	631	No significant relationship between blood lipids and semen parameters	Unstudied
Liu et al. [7]	7,601	Lipids positively correlate with sperm motility	Unstudied
Chen et al. [14]	8,395	Lipids positively correlate with sperm quality	Unstudied
Ma et al. [36]	181	Lipids positively correlate with sperm PR ratio, sperm concentration	Lipids positively correlate with FSH, LH
Osadchuk et al. [37]	90	No significant relationship between blood lipids and semen parameters	Unstudied
Andrade et al. [31]	278	Lipids negatively correlate with semen volume	Lipids negatively correlate with T

Literature in the table is sorted by year.

5. Correlation Analysis between Lipid Indices and Serum Testosterone

The results of correlation analysis used showed that there was a significant negative correlation between TG and T (Table 5 and Figure 1).

6. Discussion

With the improvement of economic standards and changes in human living habits, the occurrence of many metabolic diseases such as obesity and diabetes is becoming more and more common, and the basis of these diseases is hyperlipidemia [20]. In this study, we analyzed the relationship between lipid levels and semen parameters and serum reproductive hormones in 885 men. By dividing the samples into hyperlipidemia and normal lipid groups, it was found that there was a significant difference in serum testosterone levels between the two groups, but there was no significant difference in semen parameters, which shows that hyperlipidemia has no effect on male semen parameters to some extent, which is in agreement with the study of Keskin et al. [21].

Reproductive hormones can reflect the status of male fertility to a certain extent. A clinical study showed that changes in lipid levels can affect the secretion of reproductive hormones T, FSH, and LH, with T being the most serious [22]. Testosterone is an important hormone for the maintenance of male characteristics and has a very important role in spermatogenesis and development as well as in the maintenance of sexual function and is involved in a variety of physiological pathways in men [23–25]. Reduced testosterone levels can lead to disorders in spermatogenesis, which in turn reduces the total number of spermatozoa. Abnormal lipid metabolism can affect the synthesis and secretion of reproductive hormones [22]. Current research on lipid metabolism and reproductive hormones in men has focused on the relationship between testosterone and lipid metabolism. Hyperlipidemia leads to lower testosterone levels, our study showed that serum testosterone levels in hyperlipidemia patients were significantly lower than those of normal men, which was consistent with the findings of Sung et al. [26, 27] TG have been shown to correlate negatively with T levels, with decreased testosterone levels increasing lipid accumulation, leading to hypertriglyceridemia [28, 29]. In order to investigate the real cause of changes in serum testosterone due to hyperlipidemia, we analyzed the correlation between lipid indicators and testosterone and the results showed a significant negative correlation between TG and T, which is consistent with the findings of Lee et al. [30, 31]

Reproductive hormones determine semen parameters and fertility in men. Despite disturbed testosterone levels in hyperlipidemia men, their sperm production process is not affected. There are a number of possible explanations for this situation, including the absence of a specific quantifiable role in T levels in sperm and semen production, or the presence of other adaptive factors that maintain homeostasis in the body [32]. To put it another way, there may be a progressive relationship between serum reproductive hormone levels, lipids and semen parameters, i.e., lipids—reproductive hormones—semen parameters. In the present study, we found that T levels were reduced in hyperlipidemia patients and no changes in semen parameters were seen. In other words, to some extent, hyperlipidemia can affect male reproductive hormone levels (endocrine levels), but not spermatogenic function and sperm quality.

There have been many studies in recent years regarding the correlation between lipid levels and semen parameters, but the available data on this topic are conflicting and

partially inconsistent. An overview of the current literature is presented in Table 6. Some authors hypothesized that changes in lipid levels would lead to a decrease in ejaculate volume, total number of spermatozoa and motility, and sperm concentration [6, 9, 31, 33, 34]; some studies found a positive correlation [7, 14, 36]; and some studies could not show any association between lipid levels and sperm concentration, total number of spermatozoa, and sperm motility [15, 16, 35, 37]. In addition, abnormal lipid levels lead to changes in reproductive hormones.

There are some potential limitations of this study. The age of the samples we collected was concentrated in the reproductive age, so the results of the study are not representative of all populations, and hyperlipidemia is more prevalent in middle-aged and older adults; hyperlipidemia varies in severity depending on the duration of the disease, and the long-term effects of hyperlipidemia on semen parameters have not been studied. In addition, the sample areas were distributed in different regions of Hebei, and the results may also be biased due to geographical differences. Our study only deals with the relationship between lipid indices, reproductive hormones, and semen parameters in blood samples and did not analyze the semen for lipid-related indices, reproductive hormones, sperm function, and energy metabolism indices associated with normal sperm activity. Hyperlipidemia may affect semen quality through abnormal lipid metabolism or abnormal sperm function in the male reproductive system. In addition, sperm DNA breakage, which is a direct factor affecting semen quality, was a limitation for multiple reasons, and we did not test for sperm damage. In future studies, large-sample, multicentre studies should be conducted to obtain more valuable conclusions for early clinical intervention in lipid metabolism disorders and reproductive health in men.

7. Conclusion

In conclusion, the present study is a retrospective study based on male reproduction and endocrinology to elucidate the relationship between lipid indicators and T in men and the effect of hyperlipidemia diseases on semen parameters. It was found that TG levels in blood were negatively correlated with testosterone. And hyperlipidemia may not affect semen parameters in men. These findings provide new insights into clinical interventions for hyperlipidemia in men.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval

The study was conducted according to the guidelines of the Declaration of Helsinki. All experiments on clinical specimens were approved by the Ethics Committee of the Hebei Provincial Reproductive Health Hospital (2022-006).

Conflicts of Interest

The authors have no relevant financial or nonfinancial interests to disclose.

Authors' Contributions

All authors contributed to the study conception and design. Jiajie Bi and Yuanjing Li analyzed the data. Chaoju Yang and Yanqing Tie collated the data. Jing Ma and Jiajie Bi wrote the manuscript. Xuan Liu checked the manuscript for grammar. Jing Ma and Shusong Wang conceived the idea, designed the study, collected the funds, and revised the manuscript. All authors commented on previous versions of the manuscript. All authors read and approved the final version of the manuscript.

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