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Infertile Women Seeking Conception Through Assisted Reproductive Technology Have Different Lipid Profiles and Atherogenicity Indices

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ABSTRACT
Infertility in women is common over the world, and lipid abnormalities are thought to play a role. The goal of this study was to determine the plasma lipid profile and atherogenicity indices among infertile women who visited assisted reproductive technology clinics. In 140 infertile women and 50 healthy age-matched women of proven fertility, the serum lipid profile (total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and computed indicators of atherogenicity) was assessed.Using reagents provided by Randox Laboratories, Crumlin, Antrim, UK, the lipid profile was determined using the spectrophotometric method. The unpaired Students' test was used to compare the mean values of measured parameters between cases and controls. Age ($p<0.001$), total cholesterol, triglycerides, low-density lipoprotein, AIP, certain cardiac risk ratios, and atherogenic coefficients were considerably greater ($p<0.001$) in infertile women than in control participants, but high-density cholesterol was significantly lower ($p<0.001$). The difference in mean BMI between the patients and controls was not statistically significant. Except for the high density/low-density ratio, all atherogenicity indices were considerably greater in infertile women seeking assisted reproductive technology for conception than in control participants. This group of people has greater atherogenicity indices, which may predispose them to cardiovascular disease. As a result, it is recommended that lipid profiles and atherogenicity indices be evaluated on a regular basis.
Keywords: Female, Fertilization, Infertility, Lipids, Reproductive techniques

INTRODUCTION

The importance of identifying atherosclerotic risk factors and serum indicators in the early identification and prediction of risk for cardiovascular diseases (CVD) is growing. The amount of atherogenic low-density lipoprotein cholesterol (LDL-c) driving the progression of atherosclerosis is calculated using mathematical models (1). The atherogenic coefficient (AC) is calculated by subtracting the value of HDL-c from total cholesterol, all divided by HDL-c value, while the atherogenic index of plasma (AIP) is defined as the logarithm [log] of the ratio of plasma concentration of triglycerides to HDL-C and is strongly correlated with CVD risks (4).However, there is little evidence in the literature about the relationship between atherogenicity indices and infertility in women seeking pregnancy through assisted reproductive technologies (5). Atherogenicity indicators are thought to be key indices that predict cardiovascular risk better than lipid profile parameter values (6, 7). Female infertility is common all throughout the world, causing tremendous financial and emotional hardship for couples. Despite the fact that a variety of factors have been linked to infertility (8), lipid abnormalities have been hypothesised to play a role. According to certain studies, the reproductive potential of couples with aberrant lipids was lower than that of couples with

normal lipids. Both males and females have a high odds ratio (FOR) and have high total cholesterol (9).Because they are given exogenous gonadotropins, infertile women seeking pregnancy through assisted fertility technology may be at an increased risk of cardiovascular disease. Exogenous gonadotropins induce ovulation, which is one of the most common causes of lipoprotein alterations (10). Individualized gonadotropin dosage has been proposed to reduce the negative effects of an overactive ovarian response or a poor response (11). Derangements in lipid concentrations can also have a deleterious impact on the basic function of cholesterol. As a result, dyslipidemia may be a key factor in the advancement of infertility (12). In human in-vitro studies, aberrant maternal serumlipid profiles were linked to lower egg quality, ovarian function, and embryo development, according to some investigators (12).This is a sign of a possible decrease in fertility (13). Dyslipidemia is becoming more common among infertile individuals all over the world. Although many of its causes are unrelated to hormonal imbalance, hyperlipidemia has been linked to a number of hormonal illnesses, including diabetes, polycystic ovarian syndrome, and metabolic syndrome. Dyslipidemia and its related syndromes have also been linked to infertility, in addition to the clinical signs of cardiovascular disease (14, 15).

Atherosclerosis is a chronic, degenerative disease that develops gradually, most likely throughout childhood. It's a condition with a variety of clinical manifestations that might be asymptomatic or progress to cardiovascular disease. The inflammatory process, as well as the oxidative stress it causes, play a role in the development of atherosclerosis (16). The risk of developing atherosclerosis varies depending on the stage of the disease, the patient's race, age, gender, and environmental factors (16). According to a study, Nigerians appeared to have an unfavourable CVD risk profile that was not evident using conventional lipid profile measures (17). The goal of this study was to establish the lipid profile and atherogenicity indices among infertile women who were considering assisted reproductive technologies.

MATERIALS AND METHODS

This is a cross-sectional study of women who are using Assisted Reproductive Technology to conceive. The study included 140 infertile women aged 36.8±0.35, with a body mass index of 24.8±0.01, and 50 healthy women with proven fertility, aged 30.0±0.02, with a body mass index of 24.03±0.01.

INCLUSION CRITERIA

All healthy women who go to an ART facility in the hopes of getting pregnant through ART. Women between the ages of 25 and 45 who did not have menses (anovulatory) or had previous histories of infertility and were not on contraception were enrolled.

EXCLUSION CRITERIA

Those Women < 45 who are still menstruating and are on contraceptives and those above 45 years were excluded.

SAMPLE SIZE DETERMINATION

With a 10% prevalence of female infertility in India, the sample size (N) was estimated using the sample size determination formula for health research (18). (19). As a result, the investigation required a minimum of 140 samples and 50 controls.

SAMPLE COLLECTION

5mL of fasting venous blood was drawn from each participant and placed in a lithium heparin vial under rigorous aseptic conditions. Blood samples were taken at the start of the study, on Days 2-4 of the women's menstrual cycles, and before ovarian stimulation and gonadotropin injection. Plasma was separated by centrifuging the samples at 3000rpm for 5 minutes. The recovered plasma was transferred to a new tube for lipid profile analysis.

STATISTICAL ANALYSIS

SPSS 21.0 software was used for all data analysis (SPSS, Chicago, IL). The independent Student t-test was used to evaluate continuous variables that were reported as means and ±standard deviations. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

The study enlisted the participation of 190 women. There were 140 infertile women seeking assisted reproductive technologies and 50 healthy women with established fertility who served as controls in this study. The demographic features of the study population are listed in Table 1. The study population's mean age was considerably greater ($p<0.001$) than the control group. Between the cases and controls, there was no significant difference in mean body mass index (BMI) or age of commencement of menstruation (Menarche).Table 2 compares the study population's lipid profile and atherogenicity indices to those of the controls. The infertile women's HDL-c levels were considerably lower ($p<0.001$) than the fertile controls. Total cholesterol, triglycerides, LDL-c, VLDL-c, AIP, cardiac risk ratios (excluding HDL-c/LDL-c ratio), and AC were all significantly greater ($p<0.001$) in infertile women compared to control patients.

DISCUSSION

Infertility in women is a social problem with economic, social, and psychological consequences for both the individual and society. Infertile women undergoing assisted reproductive procedures are given recombinant follicle-stimulating hormone and human chorionic gonadotropins to stimulate the production of oocytes in their ovaries (hCG). Exogenous hormones have been shown to raise lipid levels in the body. To forecast cardiovascular risk and fecundity potential, it is critical to understand lipid profile levels and atherogenicityindices.

Table 2: Comparison of Lipid profile parameters and atherogenic indices between infertile and fertile women

Parameters	Infertile Women (n=140)	Fertile Women (n=50)	P Value
Triglycerides(mmol/L)	1.72±0.02	1.60±0.07	0.001
Total Cholesterol(mmol/L)	5.70±0.01	5.46±0.02	0.001
HDL-c(mmol/L)	0.89±0.02	1.16±0.02	0.001
LDL-c(mmol/L)	3.90±0.02	3.60±0.02	0.001
VLDL-c(mmol/L)	082±0.02	0.73±0.02	0.001
AIP	0.52±0.001	0.29±0.001	0.001
Cardiac Risk Ratios			
TC/HDL-c	6.38±0.04	4.69±0.03	0.001
LDL-c/HDL-c	4.35±0.05	3.11±0.04	0.001
HDL-c/LDL-c	0.22±0.06	0.32±0.04	0.5
AC	5.39±0.06	3.72±0.04	0.001

HDL-c=High Density Lipoprotein cholesterol; LDL-c= Low-Density Lipoprotein cholesterol; VLDL-c=Very Low-Density Lipoprotein cholesterol; AIP=atherogenic index of plasma lipid; atherogenic coefficient

Table 1: Demographic characteristics of study population

Variables	Infertile women (n=140)	Controls (n=50)
Age(years)	35.9±0.35	30.0±0.01
Body mass index(Kg/m^2)	24.8±0.5	24.03±0.2
Menarche (Years)	13.1±1.0	13.0±0.2
Irregular menstruation	40(28.6%)	0(0%)
Gynecological surgery	50(35.7%)	03(06%)
Physical activity	120(85.7)	32(64%)
Cigarette smoking	02(1.4)	0(0%)
Alcohol Consumption	10(7.1%)	15(30%)

In this investigation, plasma concentrations of triglycerides, total cholesterol, LDL-c, VLDL-c, and atherogenicity indices were considerably greater in infertile women than controls, except for HDL-c/LDL-c ratio, which was significantly lower. The findings are consistent with earlier research (8, 10, 12). Infertile women's lipid profiles were studied, and their levels were linked to oocyte and embryo quality, according to Wang et al. (12. Infertile females' lipid problems may be linked to the quality of their embryos, according to the scientists. They discovered a link between triglycerides, total cholesterol, and LDL-c levels and embryo quality.The amount of HDL-c in the blood was linked to the quality of the embryo (12). In knockout (SR-BI KO) female mice, the importance of HDL cholesterol in the process of mammalian female reproduction was clearly highlighted. Exencephaly with female bias was found to be related with aberrant HDL metabolism in embryos missing SR-BI in anexperimental research (21). Furthermore, HDL-c has been shown to have a critical cytoprotective effect on oocytes and surrounding granulosa cells (22). According to the findings of Wang et al (12), an acceptable level of HDL-c is essential for the development of oocytes into embryos.This protective effect of HDL-c may be due to both HDL-c and LDL-c delivering cholesterol to the corpus luteum as a substrate for progesterone production (23).

It has been observed that the detrimental impact of a higher BMI on IVF outcomes is becoming more common (24, 25). There was no significant difference in BMI between infertile women and control patients in this study. BMI, on the other hand, has been linked to a lower frequency of properly fertilised oocytes, cleavage embryos, and good quality embryos. It has been suggested that having a high BMI can affect the success rate of IVF in women with endometriosis (12). The involvement of lipids in ovarian steroidogenesis is the physiologic mechanism through which lipids and lipoproteins affect effective reproduction (8, 23). Others have proposed that insulin dysregulation, which impairs ovarian function, could be to blame (26). From the ages of 20 to 35 years, women with menstrual abnormalities had a 50% greater risk of myocardial infarction or coronary heart disease compared to those who had regular cycles (27). Infertile women have much greater triglycerides than control women, according to the findings. According to several researchers, both fat and non-obese women suffering from infertility had high triglyceride levels (28). Infertile women with high serum levels of total cholesterol and LDL-c may be experiencing disproportionate steroidogenesis, which could be the cause of infertility. This is in line with a research that found women with various causes of infertility had higher overall cholesterol levels (29).

It was hypothesised that lipid may be employed as a fertility marker. Adults over the age of 20 years should have their lipid profiles checked every 5 years in India, since this will allow for the detection of diminished fecundity (30). Despite the fact that cholesterol is a precursor to steroid hormones, it can induce infertility in women (31). In certain cases of infertility, abnormalities of LDL-c had not been consistently recorded. VLDL-c levels were higher in those with normal LDL-c levels than in the control group (32). When compared to the fertile group, infertile women had a considerably greater index of atherogenicity.This means that infertile women are more likely than fertile women to acquire cardiovascular problems. This is especially noteworthy because Black Africans' lipid levels are known to be lower than Caucasians' (33). As a result, using lipid levels to diagnose cardiovascular disease in Africans could be deceiving. Using cardiac risk ratios, Glew et al. (17) claimed that they were able to distinguish patients with stroke from healthy people. The need of identifying potential CVD-affected women seeking assisted reproductive technology treatments cannot be overstated.

CONCLUSION

Plasma triglycerides, total cholesterol, LDL-c, and atherogenicity indices (except HDL-c/LDL-c ratio) were significantly greater in infertile women seeking conception via assisted reproduction, but HDL-c was significantly lower. Periodic lipid profiles and indices of

atherogenicity determination for fertility potential and/or CVD risk assessments are indicated for this group of women.

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