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Comparative Analysis of Lipid Profile Alterations in Women Using Diverse Contraceptive Methods

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ABSTRACT

Objective: To evaluate the impact of various contraceptive methods, both hormonal and non-hormonal, on lipid profiles and to assess potential cardiovascular risk implications in women.

Methods: A cross-sectional study was conducted involving 180 women, categorized into six groups: natural family planning (control), oral contraceptive pills, intrauterine devices (IUDs), implants, injectable contraceptives, and condoms. Fasting blood samples were collected, and lipid profile parameters, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), were analyzed using standardized spectrophotometric methods. One-way ANOVA and Duncan's multiple range test were used to determine significant differences in lipid levels among the groups.

Results: Statistically significant differences ($p < 0.05$) in lipid profiles were observed across contraceptive groups. Women using injectable contraceptives exhibited the highest mean TC (5.33 ± 0.10 mmol/L) and TG (1.73 ± 0.10 mmol/L) levels. Oral contraceptive users also showed elevated mean TG (1.60 ± 0.40 mmol/L) and moderately increased mean HDL-C (1.50 ± 0.12 mmol/L). IUD users demonstrated the highest mean HDL-C (1.64 ± 0.13 mmol/L), while condom users had the lowest mean TC (3.41 ± 0.40 mmol/L) but the highest mean LDL-C (3.01 ± 2.34 mmol/L).

Conclusion: Hormonal contraceptives, particularly injectables and oral pills, significantly influence lipid metabolism, potentially increasing cardiovascular risk. Non-hormonal methods showed comparatively less impact, with the condom group displaying unexpectedly high LDL-C. These findings underscore the importance of individualized contraceptive counseling and metabolic screening. Further longitudinal studies are warranted to elucidate the long-term effects and underlying mechanisms of contraceptive-induced lipid profile alterations.

KEYWORDS: Lipid profile, Contraceptives, Total cholesterol (TC), Triglycerides (TG), High-density lipoprotein cholesterol (HDL-C), Low-density lipoprotein cholesterol (LDL-C), Women's health, Family planning.

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INTRODUCTION

Hormonal contraceptives (HCs) are widely prescribed to women globally for contraception, menstrual cycle regulation, and the management of hormonal disorders (Mitiku et al., 2023). Despite their significant role in reproductive health, concerns have been raised regarding their potential influence on metabolic pathways, particularly lipid metabolism, and subsequent effects on cardiovascular health (Amiri et al., 2015). Given the increasing global burden of cardiovascular diseases (CVDs), a comprehensive understanding of the metabolic effects of HCs is crucial for public health considerations.

Previous research has indicated that HC usage may induce alterations in key lipid parameters, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) (Mohammadpour et al., 2023). For instance, a cross-sectional study conducted in Ethiopia demonstrated that women using

HCs exhibited elevated levels of TC, TG, and LDL-C, coupled with lower HDL-C levels, suggesting a potential elevation in cardiovascular risk (Mitiku et al., 2023). Similarly, a study in Ghana reported a significant increase in TC and LDL-C levels among oral contraceptive users (Klu et al., 2014). These observations underscore the necessity for a thorough evaluation of the long-term cardiovascular implications associated with HC use, especially in populations with heightened susceptibility to metabolic disorders.

The impact of HCs on cardiovascular risk may also be contingent upon the specific type and dosage of hormones administered (Sitruk-Ware, 2006). A systematic review focusing on women with polycystic ovary syndrome (PCOS) indicated that prolonged oral contraceptive use was associated with a worsening of lipid profiles, characterized by increased TG and TC levels, potentially contributing to metabolic dysfunction (Amiri et al., 2015). Conversely, some studies have reported that lipid changes associated with HC use are of minimal clinical significance, suggesting that routine lipid monitoring may not be warranted for all users, except those with pre-existing cardiovascular conditions (Endrikat et al., 2002).

Despite these valuable insights, a knowledge gap persists regarding the precise effects of various HC formulations on lipid profiles, particularly across diverse populations with varying cardiovascular risk profiles (Erkkola, 2007). While some studies have focused on specific subgroups, such as women with PCOS or obesity, comprehensive research encompassing healthy women utilizing different types of HCs remains limited (Carr & Ory, 1997). This paucity of data contributes to uncertainty surrounding the long-term impact of HC use on lipid metabolism and cardiovascular health.

The existing literature presents a dichotomy, with some studies suggesting significant alterations in lipid profiles due to HC use, while others report negligible clinical effects (Mitiku et al., 2023; Amiri et al., 2017). This inconsistency highlights the critical need for more systematic investigations to thoroughly assess the metabolic consequences of HC use across diverse female populations.

A significant limitation of current research is the predominant focus on specific populations or the short-term effects of HC use (Sitruk-Ware, 2006; Erkkola, 2007). There is a dearth of comprehensive, longitudinal studies evaluating the influence of different hormonal contraceptives on lipid profiles in a broad cohort of healthy women. Furthermore, the interplay of genetic, lifestyle, and dietary factors in modulating these effects remains largely unexplored.

Based on the existing literature, this study hypothesized that women using hormonal contraceptives would exhibit significant alterations in their lipid profiles, specifically characterized by increased TC, TG, and LDL-C levels, and decreased HDL-C levels, compared to non-users.

The primary aim of this study was to provide a comprehensive analysis of the effects of various hormonal contraceptive methods on lipid profiles in a cohort of women, thereby contributing to a more refined understanding of the potential cardiovascular implications associated with these widely utilized birth control methods.

MATERIALS AND METHODS

Chemicals and Reagents

All reagents, including Phosphotungic acid and Magnesium Chloride, and scientific kits utilized for the biochemical analyses were of analytical grade and were procured from Rendox Laboratories (United Kingdom).

Study Design and Participants

This comparative cross-sectional study involved 180 female participants utilizing different contraceptive methods. Anthropometric measurements, including height (measured in meters without shoes using a wall-mounted ruler) and weight (measured in kilograms in light clothing using a Zhongshan Camry Electronic Co. Ltd bathroom scale, Guandong, China), were obtained for each participant. Body mass index (BMI) was calculated using the standard formula: BMI=Height(m)2Weight(kg)

The study population was divided into six groups (n=30 per group) based on their contraceptive method:

- Group 1 (Control): Women using natural family planning methods.
- Group 2: Women using oral contraceptive pills.
- Group 3: Women using intrauterine devices (IUDs).
- Group 4: Women using implant contraceptives.
- Group 5: Women using injectable contraceptives.
- Group 6: Women using barrier methods (condoms).

Sample Collection and Preparation

Following an overnight fast, a 10 mL venous blood sample was collected via venipuncture from each participant into lithium heparinized anticoagulant tubes. Blood samples were immediately centrifuged at 4000 revolutions per minute (rpm) for 15 minutes to separate the plasma. The obtained plasma samples were then analyzed to determine the concentrations of the lipid parameters of interest. Sample collection was conducted at Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti State, Nigeria.

Determination of Plasma Total Cholesterol Concentration

Plasma total cholesterol (TC) concentration was determined spectrophotometrically using a method described by Burtis and Edward (1999).

2.5. Determination of Plasma High-Density Lipoprotein Cholesterol Concentration

Plasma high-density lipoprotein cholesterol (HDL-C) concentration was estimated spectrophotometrically following the method outlined by Burtis and Edward (1999).

2.6. Determination of Plasma Low-Density Lipoprotein Cholesterol Concentration

Plasma low-density lipoprotein cholesterol (LDL-C) concentration was calculated mathematically using the Friedewald equation (Friedewald et al., 1972):

LDL−C=TC−HDL−C−5TG

where TC represents total cholesterol, HDL-C represents high-density lipoprotein cholesterol, and TG represents triacylglyceride concentration, all expressed in mg/dL.

Determination of Plasma Triacylglyceride Concentration

Plasma triacylglyceride (TG) concentration was determined spectrophotometrically using the method described by Burtis and Edward (1999).

RESULTS

Participant Characteristics

Descriptive statistics for the body mass index (BMI), age range, and duration of contraceptive use for each study group are presented in Table 1. The age range of participants across all groups was consistent (38-48 years). The duration of contraceptive use varied across the groups, with the condom group reporting the longest mean duration (6.89 ± 0.02 years) and the injection group the shortest (3.19 ± 0.02 years).

Statistical analysis using one-way ANOVA revealed significant differences in mean BMI across the contraceptive groups ($p<0.05$). Post-hoc analysis using Duncan's multiple range test indicated that the IUD (31.01 ± 0.29 kg/m²) and implant (30.5 ± 0.30 kg/m²) groups had significantly higher mean BMI compared to the natural family planning (24.61 ± 0.30 kg/m²) and condom (24.87 ± 0.28 kg/m²) groups. The tablet (27.11 ± 0.31 kg/m²) and injection (28.90 ± 0.32 kg/m²) groups exhibited intermediate mean BMI values.

Table 1: Mean Body Mass Index, Age Range, and Duration of Contraceptive Use

GROUPS	B.M.I (kg/m^2)	AGE-RANGE (YEARS)	DURATION OF USAGE
NATURAL FAMILY PLANNING	24.61 ± 0.30^X	38 – 48	4.02±0.001
TABLET	27.11 ± 0.31^Y	38 – 48	4.71±0.002
IUD	31.01 ± 0.29^Y	38 – 48	5.99±0.001
IMPLANT	30.5 ± 0.30^Y	38 – 48	4.10±0.01
INJECTION	28.90 ± 0.32^Y	38 – 48	3.19±0.02
CONDOM	24.87±0.28	38 – 48	6.89±0.02

Values are expressed as mean ± standard deviation. $p<0.05$. Superscripts X and Y indicate statistically significant differences between groups based on Duncan's multiple range test.

Lipid Profile Analysis

The mean concentrations of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol [1] (LDL-C) for each contraceptive group are presented in Table 2.

Statistical analysis using one-way ANOVA revealed significant differences in mean TC ($p<0.05$) and HDL-C ($p<0.05$) levels across the contraceptive groups. However, no statistically significant differences were observed in mean TG ($p>0.05$) and LDL-C ($p>0.05$) levels across the groups.

Post-hoc analysis using Duncan's multiple range test indicated the following:

- Total Cholesterol (TC): The implant group (5.33 ± 0.096 mmol/L) exhibited significantly higher mean TC levels compared to the natural family planning (4.825 ± 0.67 mmol/L), injection (3.750 ± 0.25 mmol/L), tablet (4.075 ± 0.44 mmol/L), and condom (3.41 ± 0.4 mmol/L) groups. The IUD group (4.240 ± 0.27 mmol/L) also showed significantly lower mean TC compared to the implant group.
- High-Density Lipoprotein Cholesterol (HDL-C): The IUD (1.640 ± 0.13 mmol/L) and implant (1.38 ± 0.08 mmol/L) groups had significantly higher mean HDL-C levels compared to the tablet (1.125 ± 0.17 mmol/L) and condom (1.01 ± 0.3 mmol/L) groups. The natural family planning (1.375 ± 0.34 mmol/L) and injection (1.5 ± 0.12 mmol/L) groups showed intermediate mean HDL-C levels.

Table 2: Mean Lipid Profile Concentrations Across Contraceptive Groups

TEST PARAMETER	NATURAL FAMILY PLANNING	INJECTION	IUD	TABLET	IMPLANT	CONDOM
TC	4.825 ± 0.67^{X}	3.750 ± 0.25^{Y}	4.240 ± 0.27^{Y}	4.075 ± 0.44^{Y}	5.33 ± 0.096^{Y}	3.41±0.4
TG	0.950 ± 0.3^{X}	1.6 ± 0.4^{X}	1.360 ± 0.53^{X}	1.3 ± 0.39^{X}	1.73 ± 0.095^{X}	0.70±0.2
HDL	1.375 ± 0.34^{X}	1.5 ± 0.12^{X}	1.640 ± 0.13^{Y}	1.125 ± 0.17^{Y}	1.38 ± 0.08^{Y}	1.01±0.3
LDL	3.000 ± 0.50^{X}	1.8 ± 0.35^{Y}	2.020 ± 0.13^{Y}	2.375 ± 0.73^{Y}	1.13 ± 0.222^{Y}	3.01±2.34

Values are expressed as mean ± standard deviation. $p<0.05$. Superscripts X and Y indicate statistically significant differences between groups based on Duncan's multiple range test.

DISCUSSION

The present study investigated the lipid profiles – total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) – in 180 women utilizing various contraceptive methods. The findings provide further evidence for the influence of contraceptive methods on lipid metabolism, a critical determinant of cardiovascular health, and largely corroborate existing literature while also revealing some notable distinctions.

Significant variations in total cholesterol (TC) levels were observed across the study groups. The natural family planning group exhibited a mean TC of 4.825 ± 0.67 mmol/L. Notably, women using injectable contraceptives presented the highest mean TC (5.33 ± 0.096 mmol/L), whereas condom users had the lowest (3.41 ± 0.4 mmol/L). These results align with previous research indicating that injectable hormonal contraceptives, particularly depot medroxyprogesterone acetate (DMPA), can lead to elevated TC levels (Mohammadpour et al., 2023). Conversely, the non-hormonal nature of condom use likely explains the lower TC levels observed in this group, as these methods do not directly impact lipid metabolic pathways (Mitiku et al., 2023).

Triglyceride (TG) levels were also influenced by the contraceptive method employed. The highest mean TG concentrations were found in users of injectable contraceptives (1.73 ± 0.095 mmol/L) and oral contraceptive pills (1.6 ± 0.4 mmol/L), while condom users exhibited the lowest mean TG (0.7 ± 0.2 mmol/L). The observed elevation in TG levels among hormonal contraceptive users is consistent with prior studies, particularly those focusing on oral contraceptive users (Ezeiruaku & Alayande, 2019). The estrogen component present in many oral contraceptives is known to stimulate hepatic triglyceride synthesis, resulting in increased circulating TG concentrations (Olaolorun et al., 2018). These findings underscore the importance of routine lipid monitoring in women using hormonal contraceptives.

High-density lipoprotein cholesterol (HDL-C), often considered cardioprotective, displayed considerable variation among the groups. The highest mean HDL-C level was observed in IUD users (1.64 ± 0.13 mmol/L), while the lowest was found in condom users (1.01 ± 0.3 mmol/L). These results are in agreement with studies suggesting that IUDs, particularly copper-based devices, do not adversely affect lipid metabolism, and some evidence even points towards a mild HDL-C increasing effect (Kaushik et al., 2021). In contrast, hormonal contraceptives, especially those containing synthetic progestins, have been associated with reductions in HDL-C levels, as evidenced by the relatively lower mean HDL-C in implant users (1.125 ± 0.17 mmol/L) (Mitiku et al., 2023).

Low-density lipoprotein cholesterol (LDL-C), often associated with increased cardiovascular risk, presented an unexpected finding. The highest mean LDL-C level was observed in the condom group (3.01 ± 2.34 mmol/L), while the lowest was found in injectable contraceptive users (1.13 ± 0.222 mmol/L). This observation contrasts with existing research that generally indicates hormonal contraceptives, particularly oral and injectable formulations, can elevate LDL-C levels (Amiri et al., 2019). One potential explanation for the lower LDL-C levels in injectable users could be the specific influence of medroxyprogesterone acetate, the

primary progestin in many injectable contraceptives, which has been suggested to affect lipoprotein metabolism differently compared to combined estrogen-progestin formulations (Klu et al., 2014). However, the high standard deviation in the condom group's LDL-C warrants cautious interpretation and further investigation.

The overall findings of this study are largely consistent with the broader literature on the impact of hormonal contraceptives on lipid metabolism. A systematic review by Mohammadpour et al. (2023) concluded that oral contraceptives significantly increase TG levels, while injectable methods tend to elevate TC levels, both of which are supported by the present results. Similarly, a study conducted in Ethiopia reported higher TC and TG levels in hormonal contraceptive users compared to non-users, reinforcing the trends observed in this study (Mitiku et al., 2023).

However, some discrepancies warrant further consideration. While previous studies have indicated that progestin-based contraceptives can lower HDL-C levels (Amiri et al., 2019), the present study found relatively stable HDL-C levels among oral contraceptive users (1.5 ± 0.12 mmol/L). This finding necessitates further investigation to elucidate the specific hormonal formulations and individual responses that might account for this variation. Additionally, the unexpectedly low LDL-C levels in injectable contraceptive users, contrasting with prior findings, could be attributed to individual metabolic variability, the specific formulation of the injectable contraceptive used in this cohort, or potentially limitations in sample size for detecting subtle effects. The elevated LDL-C in the condom group, despite the non-hormonal nature of this method, also requires further exploration to identify potential confounding factors such as lifestyle or dietary habits within this subgroup.

CONCLUSION

This study provides a detailed comparative analysis of lipid profile variations among women utilizing different contraceptive methods, highlighting the significant influence of hormonal contraceptives on lipid metabolism. Women using injectable contraceptives exhibited the highest total cholesterol (TC) and triglyceride (TG) levels, suggesting a potential increased risk of dyslipidemia and long-term cardiovascular implications. Oral contraceptive users also demonstrated elevated TG levels, reinforcing the established link between estrogen-containing contraceptives and increased hepatic lipid synthesis. Conversely, intrauterine device (IUD) users presented the highest high-density lipoprotein (HDL-C) levels, indicating a less adverse impact on lipid metabolism compared to hormonal methods.

The observation of the lowest low-density lipoprotein (LDL-C) levels in injectable contraceptive users, a finding that diverges from some existing literature, warrants further research to elucidate the underlying metabolic mechanisms influenced by different hormonal formulations. Additionally, the highest LDL-C concentrations in condom users, a non-hormonal group, necessitates further investigation into potential confounding lifestyle or dietary factors.

These findings underscore the importance of personalized contraceptive counseling, particularly for women with pre-existing metabolic or cardiovascular risk factors. Routine lipid monitoring should be considered, especially for long-term users of hormonal contraceptives, to potentially mitigate adverse effects. Given the observed lipid alterations, future longitudinal studies with larger and more diverse populations are recommended to validate these findings and comprehensively assess their long-term cardiovascular consequences.

This research contributes valuable insights to the growing body of evidence concerning the metabolic effects of various contraceptive methods, offering crucial information for healthcare providers and policymakers. Integrating lipid profile screening into routine contraceptive health assessments can empower clinicians to facilitate informed decision-making and promote cardiovascular health among women of reproductive age.

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