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Serum Lipids and Plasma Glucose in Women on Hormonal-Based ContraceptivesAbdullahi, H.L.*¹, Saleh, A.A.², Mohammed, I.Y.³, Yahaya, I.S.⁴, Abdullahi, T.M.⁵

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Author for Correspondence*: hadeezahlawal@gmail.com/+234-803-705-2469**Abstract**

Hormonal-based contraceptives (HCs) available as oral (OCs) and injectable (ICs), have gained wide acceptance worldwide including developing countries like Nigeria due to their high efficacy in preventing pregnancy. However, they are associated with increased risks for certain metabolic diseases. In this study, a total of 200 participants were randomly recruited for the study made up of 100 women on contraceptive (subjects) and 100 non-contraceptive users (controls) The mean age and BMI of the subjects was 28.97 ± 7.18 years and 24.61 ± 5.30 respectively. There were significant differences ($p < 0.05$) between the mean values of fasting glucose (FG) (4.58 ± 1.10 mmol/L vs. 3.9 ± 0.57 mmol/l), total cholesterol (TC) (4.75 ± 0.68 mmol/L vs. 3.98 ± 0.74 mmol/L), triglyceride (TG) (1.16 ± 0.28 mmol/L vs. 1.35 ± 0.31 mmol/L), high density lipoprotein (HDL-C) (1.62 ± 0.35 mmol/L vs. 1.13 ± 0.33 mmol/L) and low density lipoprotein (LDL-C) (2.65 ± 0.45 mmol/L vs. 2.14 ± 0.59 mmol/L) of women on HCPs and that of control group. No significant differences ($p > 0.05$) were observed between the mean values of plasma FG (6.94 ± 6.85 mmol/L vs. 5.15 ± 1.20 mmol/L), serum TC (5.72 ± 1.53 mmol/L vs. 5.23 ± 1.24 mmol/L), serum TG (1.19 ± 0.98 mmol/l vs. 1.14 ± 0.82 mmol/l) as well as serum LDL-C (3.47 ± 1.28 mmol/l vs. 3.41 ± 1.21 mmol/L) of OC and IC users respectively. However, a significant difference was observed between mean values of serum HDL-C (1.70 ± 0.73 mmol/l vs. 1.37 ± 0.37 mmol/l respectively) between OC and IC users. No significant difference ($p < 0.05$) was observed on the basis of duration of use of HCs. The results of this study further emphasize the need for caution and routine regular check-up when using HCs in order to prevent complications and the adverse side effects associated with their use.

Keywords: Hormonal contraceptive, plasma glucose, serum lipid profile.

Introduction

Contraception is defined as the deliberate use of artificial methods to prevent pregnancy that may result following sexual intercourse (Oxford, 2014). The World Health Organization defines contraceptives as agents or devices used to prevent conception (WHO, 2016). The use of contraceptive methods in developing countries has helped to reduce the number of maternal deaths by 40% with about 27000 deaths prevented in 2008 (Cleland *et al.*, 2012). It is estimated that if full demands for birth controls are met, 70% of maternal deaths would be avoided (Ahmed *et al.*, 2012).

Birth control methods include hormonal birth controls (oral, injectable, implants and vaginal rings), sterilization (cream and jelly), behavioral methods (withdrawal and abstinence, rhythm and cervical mucus), barriers (condoms and diaphragm) and permanent method (vasectomy and tubal ligation).

Evidence from the recent Nigeria demographic and health survey indicates that only about 30 percent of sexually active Nigerian women currently practice effective contraception (Nwachukwu and Obasi, 2008). Although higher in the Southern part of the country, the figure varies from region to region. The prevalence of modern contraceptive use of 12.5% has been reported among married women in the Southern part compared to a prevalence rate of 5.3% among married women in the Northern part of the country. The same pattern follows for fertility rate where the northern part of the country has a higher fertility rate of 6.6% compared to 4.5% in the south and a higher maternal mortality rate of 1,287 per 100,000 live birth in the north compared to 225 per 100,000 live births in the South (Emmanuel *et al.*, 2010). The use of injectable hormonal contraceptives has continued

to rise rapidly in many countries (Lande and Richey, 2006). From 1995 to 2005, the estimated numbers of injectable users doubled to more than 32 million worldwide (Lande and Richey, 2006).

Some studies indicate that the intake of oral contraceptives could cause metabolic changes in carbohydrate, protein, and lipid macromolecules (Obisesan *et al.*, 2002). Progestins exert an adverse influence on lipid metabolism, they have the ability to counteract the estrogen-induced changes in low density lipoprotein and high-density lipoprotein levels (Klipping and Marr, 2005). Women are also at high risk of dyslipidemia due to long-term use of hormonal contraceptives (Santos *et al.*, 2008).

The high efficacy of oral contraceptives has led to their wide acceptance in Northern Nigeria. However, several studies have indicated that oral contraceptives use is associated with increased risks of cardiovascular disease and other adverse side effects. Hence, this study aimed at studying the pattern of these effects in oral contraceptive users in Kano, Nigeria.

Materials and Method

Study Population

A total of 100 females on contraceptive were recruited for the study as subjects while 100 women who were not on any form of contraceptive were recruited as controls.

Anthropometric Measurement

Height and weight of all subjects were measured and recorded and the body mass index (BMI) was calculated from the formula:

$BMI = \text{weight in kilogram} / (\text{height in meters})^2$ Blood pressure was measured using a mercury sphygmomanometer (cuff width 12.5cm) and a Littman stethoscope.

Specimen Collection and Processing

Five (5) milliliter of blood was collected from peripheral vein (antecubital venipuncture) with

minimal application of tourniquet after disinfecting the skin with methylated spirit. Sterilized 5ml syringes with 22-G needle were used. Samples from the fluoride oxalate and plain bottle were used for determination of glucose and lipid respectively. Plasma for glucose estimation and serum for lipid estimation were obtained by centrifugation at 3500rpm for 5minutes and stored frozen at -20°C until required for analysis

Analysis of Data

Data was summarized and entered into a Microsoft Excel 2013 worksheet. Data analysis was carried out using Statistical Package for Social Sciences (SPSS) software package version 16.0. Data was expressed as mean and standard error of mean (mean \pm SEM). Student's t -test was used for the comparison of quantitative variables. Correlation between variables was assessed using paired sample t-test. A p value ≤ 0.05 was considered significant.

Results

There were significant differences between the mean values of fasting glucose, total cholesterol, triglyceride, high density lipoprotein and low-density lipoprotein of women on contraceptives and those in the control group ($p = 0.01$, $p = 0.00$, $p = 0.00$, $p = 0.00$, $p = 0.00$) respectively as shown in Table 1.

Comparison of oral and injectable contraceptives showed non-statistically significant difference in the glucose ($p = 0.12$), total cholesterol ($p = 0.27$), triglyceride ($p = 0.86$) as well as low density lipoprotein ($p = 0.85$). The high-density lipoprotein was statistically elevated in oral contraceptive women compared to injectable contraceptive women ($p = 0.04$) as shown in Table 2.

Table 3 shows the results of plasma glucose and serum lipids among the study subjects based on the duration of contraceptive use. There were no statistically significant differences in all the parameters at different duration of the contraception ($p = 0.25$, $p = 0.23$, $p = 0.14$, $p = 0.07$ and $p = 0.08$).

Table 1: Comparison of plasma glucose and serum lipid levels of Contraceptive users versus control group

Parameters (mmol/L)	Contraceptive users (50) (SEM)	Non-contraceptive users (50) (SEM)	p- value
Glucose	4.58 ± 1.10	3.97 ± 0.57	0.01
Total Cholesterol	4.75 ± 0.68	3.98 ± 0.74	0.00
Triglyceride	1.16 ± 0.28	1.35 ± 0.31	0.00
HDL-cholesterol	1.62 ± 0.35	1.13 ± 0.33	0.00
LDL-cholesterol	2.64 ± 0.45	2.14 ± 0.59	0.00

Significant at p≤0.05

Table 2: Comparison of plasma glucose and serum lipids of oral versus injectable Contraceptive users

Parameters (mmol/L)	Oral Contraceptives (23) (SEM)	Injectable Contraceptives (27) (SEM)	p -value
Glucose	6.94 ± 1.85	5.15 ± 1.20	0.12
Total Cholesterol	5.72 ± 1.53	5.23 ± 1.24	0.27
Triglycerides	1.19 ± 0.98	1.14 ± 0.82	0.86
HDL-cholesterol	1.70 ± 0.73	1.37 ± 0.37	0.04
LDL-cholesterol	3.47 ± 1.28	3.41 ± 1.21	0.85

Significant at p≤0.05

Table 3: Comparison of plasma glucose and serum lipid levels based on Duration of use

Parameters (mmol/L)	≤5years (45) (SEM)	>5years (5) (SEM)	p value
Glucose	5.55 ± 3.50	5.50 ± 1.76	0.25
Total Cholesterol	5.27 ± 1.27	5.88 ± 1.68	0.23
Triglycerides	1.15 ± 0.89	1.14 ± 0.33	0.14
HDL-cholesterol	1.46 ± 0.51	1.22 ± 0.84	0.07
LDL-cholesterol	3.34 ± 1.16	4.18 ± 1.64	0.08

Significant at $p \leq 0.05$

Discussion

In this study, glucose and lipid profile of women on contraceptives were compared with that of control group (non-contraceptive users). The results obtained showed a statistically significant differences in the lipid profile of women on hormonal contraceptives compared to non-contraceptive users (Total cholesterol triglyceride, high density lipoprotein, and low-density lipoprotein levels in contraceptive women are higher than non-contraceptive users) (Table 2). The major health risks of oral and injectable contraceptives are glucose impairment and cardiovascular diseases particularly coronary artery disease, stroke and venous thrombosis (De Abood *et al.*, 1997).

Total cholesterol level above 5.2 mmol/L has been repeatedly shown as an independent risk factor for development of peripheral vascular disease (PVD) and coronary artery disease (CAD). Hypercholesterolemia is associated with endothelial

cell dysfunction, elevated oxidation stress, and creation of strongly pro-inflammatory conditions (Stapleton *et al.*, 2010). The findings in this study is in agreement with the findings of Yesmin *et al.* (2013) who reported increased total cholesterol and low-density lipoprotein cholesterol in contraceptive users.

The finding in this study however contradicts the finding of Asare *et al.* (2014) who stated that there is decrease of total cholesterol and low-density lipoprotein cholesterol in contraceptive users compared to non-contraceptive users. The differences in this finding could be attributed to the fact that increased serum triglyceride might be due to increased production and transport of very low-density lipoproteins that lead to synthesis of triglyceride in the liver. Also, the significant difference found between the values of high density lipoprotein cholesterol in contraceptive users and non-users in this study is in accordance with findings of Naz *et al.* (2012).

Plasma glucose was also found to be significantly increased in contraceptive users compared to non-contraceptive users. Our finding is in agreement with the findings of Berenson *et al.* (2011). This may be due to compensation for increased insulin resistance and glucocorticoid-like activity of progesterone. Plasma glucose levels were slightly higher in oral contraceptive users than injectable contraceptive users but this difference was not statistically significant.

The total cholesterol, triglyceride, and low-density lipoprotein cholesterol values were slightly higher in oral contraceptive users than in injectable contraceptive users but differences were also not statistically significant. High density lipoprotein cholesterol was significantly increased in oral contraceptive users compared to injectable contraceptive users (Table 3). This may be due to the effect of estrogen contained in combined oral contraceptive pills on high density lipoprotein causing it to be elevated. These findings are consistent with the findings of Hogan *et al.* (2010) and Sitruk *et al.* (2006) whose studies revealed high levels of high density lipoprotein cholesterol in oral contraceptive users.

Conclusion

The study concluded that there is a significantly increased level of fasting glucose, total cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein in women using contraceptives as opposed to women who are not on contraceptives.

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