Mekelle University

College of Health Sciences,

Institute of Biomedical Sciences

Department of Medical Biochemistry and Molecular Biology

Assessment of Blood Glucose Level and Lipid Profiles among Hormonal Contraceptive Users in Ayder Comprehensive Specialized Hospital, Tigray, Northern Ethiopia, 2024.

By

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A Thesis submitted to the Department of Medical Biochemistry and Molecular Biology, College of Health Sciences, Mekelle University in Partial Fulfilment of the Requirements for the Master's Degree in Clinical Biochemistry.

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Master's thesis research submission form

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Mekelle University College of Health Science

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Adviser‘s Approval Sheet

This is to certify that, the thesis entitled "Assessment of blood glucose level and lipid profile among hormonal contraceptive users at Ayder Comprehensive Specialized Hospital, Tigray, Northern Ethiopia, 2023/2024", is submitted in partial fulfillment of the requirements for the Degree of Master of Science (MSc.) with specialization in Clinical Biochemistry to the Graduate Program of the Department of Medical Biochemistry and Molecular Biology of the College of Health Sciences at Mekelle University and has been carried out by: SEARE TEKLAY ID: CHS/PR168870/12 under my supervision. The student has fulfilled the thesis requirements and hence hereby can submit the thesis to the Department.

Name of Principal Supervisor	Signature	Date
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Examiners' Approval Sheet

We, the undersigned, members of the Board of Examiners of the final open defense by "SEARE TEKLAY" have read and evaluated his thesis entitled "“Assessment of blood glucose level and lipid profile among hormonal contraceptive users at Ayder Comprehensive Specialized Hospital, Tigray, Northern Ethiopia", and evaluated the candidate. This is therefore to certify that, the thesis has been accepted in partial fulfillment of the requirements for the MSc. Degree in Clinical Biochemistry.

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Declaration

I the undersigned to declare that, this thesis is my original work in partial fulfillment for the requirements for the Degree of Master of Clinical Biochemistry. All the sources of the materials used for this thesis and all people and institutions who gave support for this work are fully acknowledged.

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This thesis work has been submitted for examination with my approval as university adviser.

____________________________________ _______________________

Adviser's Name Signature

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Abbreviations and acronyms

BMI: ——— Body mass index

CVD: ——— Cardiovascular disease

CHD: ——— Coronary heart disease

COC: ——— Combination oral contraception

DMPA: ——— Depo medroxyprogesterone acetate

EDTA ——— Ethylene diamine tetra acetic acid

EE: ——— Ethinyl estradiol

EMDHS: ——— Ethiopian mini demographic health survey

ENG: ——— Etonogestrel

ETB: ——— Ethiopian birr

FSH: ——— Follicle stimulating hormone

GnRH: ——— Gonadotropin releasing hormone

HC: ——— Hormonal contraceptive

HDL-c: ——— High density lipoprotein cholesterol

HRT: ——— Hormonal replacement therapy

IM: ——— Intramuscular

IUCD: ——— Intra-uterine contraceptive device

LAM: ——— Lactational amenorrhea method

LDL-c: ——— Low density lipoprotein cholesterol

LH: ——— Luteinizing hormone

NET-EN: ——— Norethisterone oenanthate

RBS: ——— Random blood sugar

TC: ——— Total cholesterol

TG: ——— Triglyceride

vLDL-c: ——— Very Low-Density Lipoprotein Cholesterol

Table of Contents

List of Tables

List of figures

Abstract

Background: Hormonal contraceptives have been observed to affect and induce changes in blood glucose level and lipid profiles. Studies have been shown that hormonal contraceptive is suggested to trigger changes in blood glucose level and lipid profiles.

Objective: To assess blood glucose level and lipid profile among hormonal contraceptive users at Ayder Comprehensive Specialized Hospital, Tigray, Northern Ethiopia, 2023/2024.

Methods: Comparative cross-sectional study design was carried out on 57 hormonal contraceptive users and 57 age-matched non-users, in Ayder Comprehensive Specialized Hospital from July 2023 to October 2024. Fasting blood samples for the estimation of TC, TG, HDL-c, LDL-c and FBS levels were collected. Data was entered using Epi-data software version 4.5 and analyzed using SPSS software version 25. Student's independent t-test was used to compare the results**.** A one-way ANOVA was used to identify the variation in the lipid profile and FBS between oral contraceptive pills, DMPAs and implant users. Simple linear regression was used to determine the changes in blood glucose and lipid profile in relation to the duration of hormonal contraceptive use.

Results: The mean serum levels of TC, TG, LDL-c, and FBS were significantly greater in hormonal contraceptive users than in non-users ($P = 0.005$, $P = 0.000$, $P = 0.003$, and $P = 0.012$, respectively), and the mean serum HDL-c level was significantly lower than that in controls ($P = 0.002$). The mean serum levels of TG, LDL-c, and HDL-c were significantly different between DMPA, implant, and OCP users ($P = 0.000$, $P = 0.031$, and $P = 0.001$, respectively). Compared with OCP and implant users, DMPA users had the highest mean serum levels of TC, TG, and LDL-c but had the lowest mean serum levels of HDL-c. As the duration of oral contraception and DMPA use increased the serum levels of TG and LDL-c increased ($P = 0.017$ and $P = 0.014$ respectively), whereas the serum level of HDL-c decreased ($P = 0.01$). The serum levels of LDL-c increased as the duration of implant use increased ($p = 0.017$). As the duration of DMPA use increases, the serum level of FBS moderately increases ($p = 0.000$).

Conclusions: Over all, hormonal contraceptive use results in changes in the mean serum lipid profile and FBS level. DMPA produces more change on mean serum lipid profiles and FBS than the other types are, and implants have a minimal effect on the level of all lipid profiles.

Key words: *Hormonal contraceptive, Lipid profile, Blood glucose*

1. Introduction

1.1. Background

Hormonal contraceptives affect fat and carbohydrate metabolism, cardiac function and blood clotting, and have direct effects on the vascular wall (1). The resultant effect of hormonal contraceptives on lipid metabolism depends on the type and dose of the compounds, the route of administration and the duration of treatment (2).

Contraceptives are a means of family planning and hormonal contraceptives are agents or drugs used to prevent pregnancy (3).Hormonal contraceptives are distinguished based on their hormone content into two categories: combined contraceptives (with estrogen and progesterone content) and progesterone contraceptives (4).

Contraceptive methods have been implemented as a birth restrictions among couples as overpopulation has become a severe problem for the world in recent decades (5). In 2019, about 49% of women in the world between the ages of 15 and 49 who were sexually active (i.e., 922 million women) used some type of contraception, up from 42% (i.e., 554 million women) in 1990. In sub-Saharan Africa, the prevalence of contraception among women of reproductive age grew from 13% in 1990 to 29% in 2019 (6).

In Ethiopia the percentage of women aged 15-49 years who used contraceptives was 39.7%, which increased from 35% in 2016. Hormonal contraception is currently the most widely used kind of birth control. According to the Ethiopia Mini Demographic and Health Survey, 39.7% of Ethiopian women used hormonal contraceptives in July 2019. Injection (27.2%), implant (8.5%), and oral/pill (2% of all hormonal contraceptives used) are the most popular methods. A total of 37.3% of women in Tigray use hormonal contraceptives, with 16% opting for injections, 15.4% choosing implants, and 10.11% choosing oral pills (3).

Modifications have been made to improve the effectiveness, acceptability, and tolerability of hormonal contraceptives. Initially, the doses of the estrogen and progestin components were lowered, and formulations containing only progestin were developed. Subsequently, new progestins have been developed to decrease androgenic side effects, and more recently, alternative delivery systems have been introduced to improve tolerability, continuance, and convenience of use (7, 8).

Changes in glucose metabolism are related to hormonal contraceptive techniques. These changes may be brought on by impaired glucose tolerance and elevated insulin resistance, which are risk factors for cardiovascular disease (CVD) and noninsulin-dependent diabetic mellitus (NIDDM). Both estrogen-containing and progestin-only contraceptives have been associated with these issues (9).

Hormonal contraceptives affect lipid profiles, particularly high- and low-density lipoprotein levels (10). Numerous studies, such as those performed in Uganda on women's dyslipidemias, have investigated the impact of hormonal contraception on lipid profiles. Insufficient use of hormonal contraceptives (HCs) revealed that 16% of women were obese, which was linked to changes in lipid profile levels (11).

According to the World Health Organization (WHO), lipid profile abnormalities contribute to almost 9% of deaths in Ethiopians from coronary heart disease (CHD) (12).

1.2. Statement of problem

One-third of ischaemic heart diseases in the world are secondary to hypercholesterolaemia, and it is estimated that hypercholesterolaemia is responsible for 2.6 million (4.5%) deaths worldwide. The burden of cardiovascular disease (CVD) secondary to dyslipidemia is a challenging task in sub-Saharan African countries, including Ethiopia (13).

A systematic review conducted in Ethiopia indicates that of the 9% of coronary heart disease deaths due to dyslipidemia, 5.2% were women of reproductive age who used hormonal contraceptives (14). The effect of oral contraception on the elevation of triglyceride levels depends on the estrogen dosage and is affected by the increase in VLDL, which is caused by the elevated production of triglycerides in the liver (15). Furthermore, hypertriglyceridaemia secondary to hormonal contraceptive use is the cause of up to 7% of all cases of acute pancreatitis (16).

Previous studies have shown that synthetic progesterone has a variety of effects on both catabolism and anabolism of lipids (17). The metabolic process of glucose is affected where it increases with the occurrence of the dominance of progesterone(18). Manufactured steroidal hormones cause lipid metabolism impairment but also inhibit ovulation via feedback mechanisms of end-product cascades of the brain master, pituitary gland (19). Because HC alters the lipid profile, it is understood that HC leads to dyslipidemia and subsequently increases CVD risk (20).

Even though there were different changes in the formulation of the hormonal contraceptive drugs, including a decrease in dosage, studies still showed that there were derangements in lipid profiles and blood glucose levels (21). Although a number of studies have been conducted on the relationship between hormonal contraceptives, lipid profiles, and glucose worldwide, the results are inconsistent across studies. Reports in the literature on lipids and glucose in hormonal contraceptive users are inconsistent. Some studies reported a reduction in HDLC (22) and no change was reported in another study (23). Another study reported statistically significant increases in glucose, cholesterol, triglycerides HDLc and LDLc concentrations (24) However, study in Norplant, there was a significant monthly decrease ($p<0.05$) in the level of glucose (25). Another study on Depo Medroxyprogesterone Acetate (DMPA) reported that the LDL-c and TC levels significantly increased but, neither HDL-c nor TG levels were affected by DMPA use (26). Studies performed among different ethnic groups have shown diverse results and the change in lipid profiles may be due to genetic predisposition and the active ingredients of the hormonal compounds (27, 28).

In Ethiopia, there are still limitations in access and an information gap concerning the exact effects of hormonal contraceptives on lipid profiles and blood glucose. To date in Tigray, no studies have investigated the effects of hormonal contraceptives on lipid profiles and blood glucose. Blood glucose levels and lipid profiles are not routinely measured in women using HCs.

Therefore, the purpose of this study was to assess blood glucose levels and lipid profiles among hormonal contraceptive users to fill this gap.

1.3. Significance of the study

Hormonal contraceptives generally increase the rate of noncommunicable diseases such as hypertension, cardiovascular disease, and diabetes mellitus. They alter several metabolic pathways that lead to the derangement of some biochemical parameters, resulting in an unwanted increase in body weight and increasing the rate of noncommunicable disease (29).

Generally, the results of studies conducted on the relationship between hormonal contraceptives and lipid profiles are not consistent. The present study aimed to assess derangements in blood glucose level and lipid profiles of hormonal contraceptive users and provide information for the users as well as for clinicians and family planning service providers, for early medical screening and evaluation of blood glucose and lipid profiles prior to the provision of hormonal contraceptives. Therefore, the findings are critical for ensuring the optimum delivery of comprehensive follow-up services before they result in serious complications and death. Furthermore, this study identified lipid profiles and glucose derangements among different hormonal contraceptives used as imputes for policymakers. This study will also provide baseline data for further investigations by researchers who want to do more on the effects of hormonal contraceptives on blood glucose and lipid profiles.

2. Literature review

2.1. Reproductive hormone and its biological effects

2.1.1. Steroid hormone actions

Estrogens and progesterone's are the two types of ovarian sex hormones. Estradiol, a hormone, is by far the most significant estrogen, whereas progesterone, a hormone, is by far the most significant progestin. To produce the majority of secondary sexual traits in females, some cells in the body must proliferate and expand. The primary roles of progestins are to prepare the uterus for pregnancy and the breasts for nursing (30).

2.1.1.1. Estrogen and its biological effect

The steroid hormone estrogen is generated from cholesterol. (First activated by luteinizing hormone), theca cells produce testosterone. Androstenedione diffuses to adjacent granulosa cells, which contain the enzymes 17-hydroxysteroid dehydrogenase and aromatase, which turn androstenedione into testosterone and 17-estradiol (induced by follicle stimulating hormone), respectively (31). Estrogens' main purposes are to control the menstrual cycle, help with the hormonal management of pregnancy and lactation, and keep female libido levels high (32). Orally administered estrogens increase hepatic triglyceride synthesis and VLDL secretion. Estrogens increase the rates of elimination of LDL, VLDL and chylomicrons; suppress the synthesis of key enzymes of lipoprotein metabolism, hepatic and lipoprotein lipase, and increase synthesis of the principal apoprotein of HDL, apoAI (33).

2.1.1.2. Progesterone and its biological effect

Repetitive cycles of follicle development and ovulation are necessary for normal menstrual function. The ovarian alterations during the sexual cycle are entirely dependent on alveolar cells in the breast proliferating, expanding, and developing secretory characteristics as a result of the promotion of the growth of the lobules and alveoli by progesterone. The breasts enlarge as a result of progesterone. The secretory growth in the lobules and alveoli, as well as the increased fluid in the subcutaneous tissue, are both responsible for some of this swelling (32).

All currently used synthetic progestogens decrease circulating levels of HDL, which is one of the key metabolic changes that can be linked to an increase in the incidence and severity of cardiovascular disease, particularly ischemic heart disease (34).

2.2. Hormonal contraceptives

2.2.1. Oral contraceptive pills

Oral contraceptive pills are the most commonly used hormonal contraceptive methods due to their simplicity of use and effectiveness. A big part of how estrogen and progestogens work together to avoid pregnancy is by selectively inhibiting pituitary activity, which prevents ovulation (35).With reductions in both the estrogen and progestin components, the creation of multiphasic formulations, and the availability of progestin-only OCs, OCs have undergone tremendous change over the past 40 years (36).

Hormonal components include ethinyl estradiol (EE; low-dose OCs must contain less than 50 g of EE), one of the eight progestins, and progestin alone. Low-dose combinations make up the currently offered products. A woman takes Seasonal for 84 consecutive days (12 weeks), then an inactive tablet for seven days, during which she develops vaginal bleeding. A low-dose combination OC with levonorgestrel and 0.03 mg of EE is FDA-approved for prolonged use. (37). A monthly contraceptive estrogen/progestin injection (Lunelle) is highly effective, with a first-year failure rate of <0.2%, but it may be less effective in obese women. Its use is associated with bleeding irregularities that diminish over time (38).

2.2.2. Depo-medroxyprogesterone acetate (DMPA)

Depo-Provera (DMPA), which is now on the market, has a contraceptive dose of 150 mg administered intramuscularly every three months (39). In order to prevent pregnancy, Depo-Provera is a progestin hormone birth control pill that is administered intravenously. Medroxyprogesterone acetate, a progesterone derivative, is the active component of the drug Depo-Provera(39).Depo-Provera (medroxyprogesterone acetate), when administered at the recommended dose to women every 3 months, inhibits the secretion of gonadotropins, which, in turn, prevents follicular maturation and ovulation and results in endometrial thinning. These actions produce the contraceptive effect (38).

adverse effects that are specific to this medication's administration include weight gain, about 50% of women using DMPA experience weight gain, especially those who are overweight or sedentary or who have irregular menstrual cycles. Almost all women experience changes to their menstrual cycle, including spotting, irregular flow, and occasionally excessive bleeding. After around six months, amenorrhea is more common and severe or frequent bleeding is less common. Up to 70% of women have amenorrhea within one year (40).

2.2.3. Implanon NXT (Etonogestrel)

Implanon NXT is a contraceptive implant that comes preloaded in a single-use applicator. In women between the ages of 18 and 40, safety and efficacy have been proven. The implant is a tiny, flexible, soft plastic rod that is 2 mm in diameter and 4 cm long. It contains 68 milligrams of the active ingredient etonogestrel (41).Metabolic effects on carbohydrate and lipid metabolism: Although progestagens may affect peripheral insulin resistance and glucose tolerance, there is no evidence that diabetics taking progestagen-only contraceptives should change their treatment plan. However, while using progestagen-only contraceptives, diabetic women should be closely monitored. If a woman decides to use Implanon NXT while receiving treatment for hyperlipidemia, they should be continuously monitored. Some progestagens may increase LDL levels and make it more challenging to treat hyperlipidemia (42).

2.2.4. Norplant (Levonorgestrel-releasing implant)

Sold under the brand name Jadelle among others, are devices that release levonorgestrel for birth control (43). The device is placed under the skin and lasts for up to five years and it contains levonorgestrel 36 mg (44)

2.3. Hormonal contraceptive and lipid profiles

Although the formulation of many hormonal contraceptives has greatly changed and the dose has decreased, there is still a measurable effect on the lipid profile.

A case-control study of 99 women in the United Arab Emirates revealed statistically significant differences between COCP users and nonusers.TC increased significantly (198.0 ± 33.0 mg/dl vs. 176.7 ± 28.2 mg/dl; $p=0.001$). High-density lipoprotein (HDL-C) (60.1 ± 19.6 mg/dl vs. 53.1 ± 13.7 mg/dl; $p=0.04$) and Triglyceride (TG) (112.4 ± 54.6 mg/dl vs. 98.1 ± 54.4 mg/dl; p 0.05) were not statistically significant. Low density lipoprotein (LDL-C) levels increased statistically significantly over the course of COCP ingestion (102.1 ± 31.8 mg/dl vs. 123.9 ± 23.1 mg/dl; $p=0.017$) (45).

A cross-sectional study conducted to investigate the effects of hormonal contraceptives (HCs) on lipid profiles among women attending family planning services in Rwanda (2023) revealed a high risk of developing abnormal lipid profiles among the exposed group compared with the control group. An association was found for LDL-cholesterol (LDL-C) (odds ratio [OR] = 11 > 1), TC (OR = 14 > 1), and TG (OR = 2.8 > 1). A greater risk of developing an abnormal lipid profile among users than among controls was observed for LDL-C and TC. HDL-C (OR = 0.8 < 1) revealed that there is no risk of developing an abnormal lipid profile among users and controls. The implant ($\chi2 = 10$, df = 3, P = 0.018397 < 0.05) significantly affected all the studied lipid profile parameters, whereas the TC ($\chi2 = 20.88$, df = 3, P = 0.000111) was significantly affected by all the HCs studied among the users (46).

In a cross-sectional analytical study conducted in Bangladish (2018), combined oral contraceptive use was associated with increased levels of total cholesterol ($p \leq 0.001$), low-density lipoprotein cholesterol ($p \leq 0.001$), and triglycerides ($p \leq 0.001$), as well as decreased high-density lipoprotein cholesterol (HDL-c) (p =.408) in comparison with controls (47).

Similarly, in a study performed on women in Keffi, Nasarawa State, Nigeria (2019), a study group consisting of 400 women and 50 control groups revealed a significant increase in the mean values of total cholesterol (4.82±0.46), triglycerides (1.67±0.11), and LDL cholesterol (2.37±0.23) in the test group compared with those in the control groups, with total cholesterol (3.34±0.12), triglycerides (0.89±0.04), and LDL cholesterol (1.89±0.05). The results also revealed a significant monthly increase ($p<0.05$) in the levels of total cholesterol, triglyceride, and LDL cholesterol following the administration of Noriesterate, Depo-Provera, and oral pills, whereas the level of HDL cholesterol significantly decreased ($p<0.05$) within the duration of contraceptive use compared with that in the control group. However, for women taking Norplant, there was a significant monthly decrease ($p<0.05$) in the levels of glucose, total cholesterol, triglyceride and LDL-cholesterol, whereas HDL-cholesterol levels were significantly increased (25).

In a longitudinal study of 54 women in Nigeria (2018), after Implanon insertion, each woman was followed up monthly for a period of 12 months at the 1st, 3rd, 6th, 9th, and 12th months of follow-up. Total cholesterol (TC) levels generally tended to increase. The increase was, however, significant only in the 3rd and 12th months of use. The serum triglyceride level tended to decrease, but the difference was significant only at the 6th and 9th months of use. High-density lipoprotein (HDL) levels were consistently and significantly elevated above baseline levels. Beyond the 3rd month, low-density lipoprotein (LDL) levels are lower but not significantly different from baseline levels (48).

In contrast, a cross-sectional study was performed on 54 young Pakistani females aged 26–32 years in 2012 to compare the extent of cardiovascular atherosclerotic risk associated with lipid metabolism in women using hormonal contraceptives: oral contraceptives, DMPA, norethisterone oenanthate (NETEN), implants, and nonhormonal intrauterine contraceptive devices (IUCDs). It was suggested that

DMPA has beneficial effects, as the DMPA group had the lowest TC, TG, and LDL-c values (next to the implant) compared with the other methods of contraception. Compared with the other methods, the DMPA group also presented the highest HDL-c value (next to oral contraceptives). The Castelli indices revealed that the use of OCs was associated with the highest atherogenic index, followed by NET-EN, IUCD, DMPA and implantation (49).

A case–control study conducted in Brazil in 2008 involving 100 women and fifty women who had not used hormonal contraception (control group) was conducted. The DMPA group had lower values of total cholesterol (TC) and low-density lipoprotein (LDL-C) than did the COC group and the control group (TC: DMPA=139.9±21.5 mg/dL vs. controls=167.1±29.2 mg/dL vs. COC=168.2±37.5, p=.001; LDL-C: DMPA=85.3±20.1 mg/dL vs. controls=102±24.5 mg/dL vs. COC=106.7±33.3 mg/dL, p=.01). The control group had higher levels of high-density lipoprotein (HDL-C) than the DMPA and COC groups did (controls=52.4±14.1 mg/dL vs. DMPA=42.2±7.2 mg/dL vs. COC=45.4±9.1 mg/dL, p=.001) (50).

A case–control study performed in Brazil in 2018 involving one hundred fifty-four participants revealed that oral contraceptive users had higher serum levels of triglycerides, total cholesterol, and HDL cholesterol (HDL-C) than did controls (24).

A study of the effects of long-term use of DMPA on lipid metabolism was conducted among 60 DMPA users and 100 control groups of Nepalese women. They reported that LDL-c and TC levels in DMPA users were significantly greater (P =.001, P =.001, respectively) than those in controls, but neither HDL-c nor TG levels were affected by DMPA use (51).

A study conducted on One hundred and three women. They were taken hormonal contraceptives including oral contraceptive pills or injection for a period not less than 6 months up to 12 years. Another group consisting of one hundred non-contraceptive users taken from the same population participated in the study as a control group. A highly significant values of serum glucose concentrations, total cholesterol, triglycerides and LDL- cholesterol were obtained in contraceptive users as compared with contraceptive non-users. Whereas a nonsignificant values of HDL cholesterol were obtained (52).

A study conducted on DMPA users (2011) reported a significant increase in serum TG levels after 6 months of DMPA use. However, there was no significant change in the mean serum TC, HDLc, or LDLc among DMPA users compared with nonusers (23)

A study performed in Ghana on forty-seven and 19 cases involved oral contraceptives (OCs) and injectable contraceptives (ICs), respectively; five involved subdermal implants. Twenty-four nonusers served as controls. The Castelli indices I and II were calculated. The TC levels in the control and case groups were 3.35±0.62 mmol/L and 4.07±0.91 mmol/L, respectively (P=0.002). The LDLC levels for the control and case groups were 1.74±0.57 mmol/L and 2.38±0.84 mmol/L, respectively (P=0.003). The Castelli indices I (TC/HDLC) and II (LDLC/HDLC) were significantly different between the control and OC groups (P=0.026 and P=0.014, respectively). Spearman's rho correlation revealed a significant influence of HC use on TG (P=0.026), TC (P=0.000), LDLC (P=0.004), and VLDLC (P=0.026) over time(20).

Purposive random sampling was performed in Ghana to select women on various forms of contraceptives and aged-matched controls for the study. Statistically significant differences were observed for high-density lipoprotein (HDL) levels (p=0.001) and the atherogenic index (p=0.0101) between the cases and the controls (53).

On the other hand, a case–control study carried out in women attending the Sudanese Family Planning Society in Atbara city, Sudan (2019), to measure the lipid profile in a total of 117 participants revealed that the mean serum cholesterol level was 156.16±5.52 mg/dl, the mean serum triglyceride level was 126.89±12.84 mg/dl, the mean serum LDL-C was 88.75±2.95 mg/dl, and the mean serum HDL-C level was 48.06±4.54 mg/dl, indicating that there was no effect of the OCP on the lipid profile, except for HDL-C, which was significantly lower than that in the control group (54).

A descriptive, case–control study conducted in Khartoum State, Sudan (2016), on a hundred eighty premenopausal women using progestogen-only contraceptive treatment revealed that there was a significant increase in total cholesterol among women using oral contraceptive pills, injectables, and subdermal implants (p value of 0.000); a significant increase in triglycerides among women using oral contraceptive triglyceride injectables (p value of 0.000); and a significant increase in LDL-c among women using oral contraceptive pills, injectables, and subdermal implants (p value of 0.000) compared with women who are not. The results also revealed a significant decrease in HDL-c among women who used oral contraceptive pills, injectables, and subdermal implants (p value of 0.000) compared with women who were not (55).

In one study investigating the effects of DMPA on 80 average Egyptian women (2005), DMPA was shown to induce a gradual increase (but not significant) in the LDL-to-HDL ratio in comparison with the control group; however, neither TC nor TG were affected by the drug (56).

A comparative cross-sectional study conducted in Ethiopia on the effects of hormonal contraceptives on the lipid profile from September to November 2022 revealed that the mean serum levels of TC, TG, and LDL-c were significantly greater in hormonal contraceptive users than in nonusers. The mean serum levels of TC, TG, LDL-c, and HDL-c were significantly different between DMPA, Implanon, and POP users. The mean serum levels of TC, TG, and LDL-c in Implanon users were lower than those in DMPA and POP users. As the duration of DMPA and POP use increases, the serum levels of TC, TG, and LDL-c significantly increase. However, the serum level of HDL-c was significantly decreased. LDL-c significantly increased with the duration of Implanon use (22).

Similarly, a study investigating the effects of DMPA on 50 healthy women who had been using DMPA while attending the family planning unit and another 50 age-matched healthy controls who were not using any hormonal contraceptives while attending the family planning unit and other units at Addiss Ababa Health Centers in 2015 revealed that the serum TC and LDL-c levels in DMPA users were significantly greater than those in controls (P =.003 and P =.001, respectively); on the other hand, the serum HDL-c levels in DMPA users were significantly lower (P =.001) than those in controls. The serum TG level in DMPA users was greater than that in the control group; however, the difference was not statistically significant (P =0.24) (57).

2.4. Hormonal contraceptives and blood glucose

A cross-sectional study conducted in Pakistan (2019) revealed that compared with other contraceptives, OCs and implants presented below-normal levels of fasting blood sugar and hence progesterone-containing injectables, which presented slightly elevated FBS (58).

On the other hand, a study performed in 2019 on women in Keffi, Nasarawa State, Nigeria, with a study group consisting of 400 women and 50 control groups, revealed a significant monthly increase ($p > 0.05$) in the levels of glucose following the administration of Noriesterate, Depo-Provera, and oral pills.

However, for women taking Norplant, there was a significant monthly decrease ($p<0.05$) in the level of glucose. The levels of glucose in this study significantly increased as the age range of the users increased from 18–23 years to 36–41 years, indicating that age has a direct influence on contraceptive use (59).

An analytic observational study with a cross-sectional design was conducted by Surakarta (2016). Women of childbearing age who used hormonal contraceptives had an average blood glucose level 26 mg/dL higher than nonusers of hormonal contraceptives did (b = 26.18; 95% CI = 15.03--37.33; $p <0.001$) (60).

A case–control study performed in Iraq revealed highly significant differences in serum glucose concentrations between contraceptive users and nonusers of contraceptives (52).

2.5. Hypotheses of the study

- **Null hypothesis (Ho):** Hormonal contraceptives have no effect on blood glucose level and lipid profiles.
- **Alternative hypothesis (HA):** Hormonal contraceptives have effect on blood glucose level and lipid profiles.

3. Objectives

3.1. General objective

- To assess blood glucose level and lipid profiles among hormonal contraceptive users attending family planning services at ACSH, Tigray, Northern, Ethiopia, 2024

3.2. Specific objectives

- To determine lipid profiles (TC, TG, LDL-c, and HDL-c) and blood glucose level (FBS) of hormonal contraceptive users and controls.
- To compare lipid profiles (TC, TG, LDL-c, and HDL-c) and blood glucose level (FBS) of hormonal contraceptive users and controls.

4. Methodology and materials

4.1. Study area

The study was conducted at Ayder Comprehensive Specialized Hospital (ACSH). ACSH is found in Mekelle town, which is the capital city of the Tigray region, located 783 km from Addis Ababa. ACSH is one of the leading comprehensive specialized hospitals found in Tigray. ACSH commenced rendering its referral and non-referral services to 8 million populations in its catchment areas of the Tigray, Afar and North-eastern parts of the Amhara Regional States and Eritrean refugees. It provides a broad range of medical services to both inpatient and out patients. It is also a teaching hospital and research center for the College of Health Sciences, under Mekelle University.

4.2. Study Design and Period

An institutional-based comparative cross-sectional study was carried out to assess blood glucose level and lipid profiles among hormonal contraceptive users attending family planning services. The study was conducted from October/2023 -December30/2024 G.C.

4.3. Source population

The source population was all women between the ages of 15 and 49 who visited the family planning clinic of ACSH for contraceptives.

4.4. Study population

The study population consists of all healthy women between the ages of 15 and 49 who have been on hormonal contraceptives attending the family planning unit in ACSH.

4.5. Study subjects

The study subjects were healthy women who have been using hormonal contraceptives and gave consent.

4.6. Inclusion and exclusion criteria

4.6.1. Inclusion criteria

- Apparently healthy women between 15- and 49- years of age who have been using oral pills, DMPA, Implanon or Norplant for at least 3 or more months (for users)
- Another apparently healthy volunteer women who have been using nonhormonal IUCD that were came for follow up, new visitors those plans to use any type of contraception and family

care givers who have not been using any hormonal contraceptives as age-matched controls.

4.6.2. Exclusion criteria

- Hormonal contraceptive use within the past 12 months (for controls)
- Breastfeeding
- Women on contraceptives but with known chronic disease (diabetes, hypertension, liver dysfunction, cardiovascular disorders); women with chronic alcohol use; BMI ≥ 30 or obesity; and those currently using medication known to affect lipid profiles and blood glucose (including corticosteroids, antipsychotics, diuretics, and anticonvulsants) were excluded by reviewing their medical records and/or by measuring and asking.

4.7. Sample size and sampling technique

4.7.1. Sample size

The sample size was determined on the basis of a double population mean formula with the following assumption: the value of the outcome variable was taken from a previous study performed in Ethiopia (61). After all the values of the lipid profile and blood glucose components were calculated, the component with the highest value (triglyceride) was taken. The reported mean ± SD value of triglycerides for users was 134.64 ± 18.31, whereas it was 124.5 ± 18.38 for nonusers. By assuming a significance level = 95% and 80% power of the test, type of test = two-sided, Z α\2 = the critical value at the 95% confidence level of certainty (1.96). The sample size was calculated via the following formula:

$$n_1 = \frac{(Z_{\alpha/2} + Z_{\beta})^2 * ({\sigma_1}^2 + {\sigma_2}^2)}{\Delta^2}$$

where: n_1= sample size for each group

Z_α= Z-score for two-tailed test based on α-level

Z_β= Z-score based on β level of 80% power

σ^2= Standard deviation

$\Delta^2 = (\mu_1 - \mu_2)^2 = (mean_1 - mean_2)^2$

Therefore, the sample size calculated was 52. Since an equal number of cases and controls were used, n × 2 = 52 × 2 =104. The nonresponse rate was 10% =10/100 × 104 = 10. The total sample size was 114 (104 + 10). Therefore, a total of 114 participants, 57 hormonal contraceptive users who fulfilled the inclusion criteria of the case and 57 non-users who fulfilled the inclusion criteria of the controls, were included in this study.

4.7.2. Sampling technique

Systematic random sampling techniques were used to select 57 hormonal contraceptive users, and convenient sampling techniques were used to recruit 57 age-matched controls. Since there are about 810 hormonal contraceptive users per month in ACSH, every seventh visit was taken from the study population during the study period.

4.8. Study variable

4.8.1. Dependent variables

Lipid profiles (TC, TG, LDL-c, HDL-c), and FBS level.

4.8.2. Independent variables

Socio-demographic characteristics, anthropometric measurement, duration of use of hormonal contraceptives.

5.0. Data collection tools and techniques

The techniques that were used to obtain information from the participants were an interview using a structured questionnaire adapted from previous studies, anthropometric measurements, and blood glucose and lipid profile laboratory assessments. The questionnaire included questions related to sociodemographic status and clinical data. Trained nurses had collected the data on sociodemographic and clinical status.

5.1. Blood Specimen Collection and Sample Analysis

5 ml of venous blood samples from women who were hormonal contraceptive users and non-users were drawn by a phlebotomist into standard sampling tubes (SST). TC/HDL-c ratio (Castelli index I) and LDL-c/HDL-c (Castelli index II) were calculated to determine the CVD risk. Weight and height were measured by using weight scale and stadiometer respectively. BMI was calculated from weight in kg/ height in m^2.

5.1.1. Estimation of serum lipid profiles

5.1.1.1. Determination of total cholesterol

Principles: was carried out using an enzymatic colorimetric test. Cholesterol esterase converted esterified cholesterol into cholesterol. Following this, the cholesterol is oxidized by cholesterol oxidase, resulting in the production of hydrogen peroxide and cholestenone. Following the addition of peroxidase, the hydrogen peroxide and 4-aminophenazone combine to form a colorful product that can be detected at 505 nm (secondary wavelength = 700 nm).

$$\text{Cholesteryl ester} + H_2O \xrightarrow{\text{Cholesteryl ester hydrolase}} \text{Cholesterol} + \text{Fatty acid}$$

$$\text{Cholesterol} + O_2 \xrightarrow{\text{Cholesterol oxidase}} \text{Cholestenone} + H_2O_2$$

$$2H_2O_2 + \text{4aminophenazone} + \text{Phenol} \xrightarrow{\text{Peroxidase}} \text{Quinonimine} + 4H_2O$$

Procedure: Ten microliters (10µL) of serum was added to the sample cups and put on the sample disk, which rotates to bring the desired sample cup into the position next to the sample probe for specimen sampling. 1000µL reaction reagent (4-aminophenazone, phenol, peroxidase, cholesterol esterase, and cholesterol oxidase) were pipetted into reagent bottles leveled for TC and put on a reagent disk, and then on the screen menu of the machine, TC was entered as a parameter to be tested. The sample probe was pipetted from the sample disk and transferred to the reaction disk, which contains cuvettes.

Calculations: The COBAS 6000 system automatically calculates the total cholesterol concentration of each sample(62).

5.1.1.2. Determination of plasma triglycerides

Principle: based on an enzymatic colorimetric test be carried out. quickly and completely hydrolyze triglycerides to glycerol using a lipoprotein lipase, then oxidize the glycerol to produce dihydroxyacetone phosphate and hydrogen peroxide. Under the catalytic influence of peroxidase, the hydrogen peroxide thus created combines with 4-aminophenazone and 4-chlorophenol to produce a red dye. A photometric measurement was made of the red dye's color intensity, which is directly proportional to the triglyceride concentration.

Triglyceride +H_20 $\xrightarrow{\text{lipase}}$ glycerol + fatty acid

Glycerol + ATP $\xrightarrow{\text{Gk}}$ glycerol -3- phosphate +ADP

Glycerol -3- phosphate +O_2 $\xrightarrow{\text{GPO}}$ dihydroxyacetone phosphate +H_2O_2

$2H_2O_2$ + 4- amino phenazone + 4 chlrophenolquinoneimine + HCI + $4H_2O$

Procedure: Ten microliters (10µL) of serum was added to the sample cups and put on the sample disk, which rotates to bring the desired sample cup into the position next to the sample probe for specimen sampling. 1000µL reaction reagent (4-aminophenazone, phenol, peroxidase, lipoprotein lipase, glycerol kinase, and glycerol phosphate oxidase) were pipetted into reagent bottles leveled for TC and put on a reagent disk, and then on the screen menu of the machine, TC was entered as a parameter to be tested. The sample probe was pipetted from the sample disk and transferred to the reaction disk, which contains cuvettes.

Calculations: The COBAS 6000 system automatically calculates the triglyceride concentration of the sample(62).

5.1.1.3. Determination of HDL- cholesterol

Principle: Was done using enzymatic colorimetric assay. HDL-cholesterol ester is converted to HDL cholesterol by PEG-cholesterol esterase. The HDL-cholesterol is acted upon by PEG-cholesterol oxidase, and the hydrogen peroxide produced from this reaction combines with 4-amino-antipyrine and

HSDA under the action of peroxidase to form a purple/blue pigment that was measured photometrically at 600 nm (secondary wavelength = 700 nm).

Procedure: Ten microliters (10µL) of serum was added to the sample cups and put on the sample disk, which rotates to bring the desired sample cup into the position next to the sample probe for specimen sampling. 1000µL reaction reagent (4-aminophenazone, phenol, peroxidase, lipoprotein lipase, glycerol kinase, and glycerol phosphate oxidase) were pipetted into reagent bottles leveled for HDLc and put on a reagent disk, and then on the screen menu of the machine, HDLc was entered as a parameter to be tested. The sample probe was pipetted from the sample disk and transferred to the reaction disk, which contains cuvettes.

Calculation: Concentration of HDL cholesterol = A sample ⁄ A standard × 8.27mmol (62).

5.1.1.4. Determination of low-density lipoprotein cholesterol

LDLc was calculated from the measured values of total cholesterol, triglycerides, and HDLc according to the Friedewald equation:

LDLc = TC - [HDLc + (TG/5)]. where [TG]/5 is an estimate of vLDLc, all values are expressed in mg/dL. The equation is derived from another equation, [Total Cholesterol] = [vLDLc] + [LDLc] + [HDLc].

5.1.1.5. Determination of blood glucose

Principle: Was done using the enzymatic colorimetric method. Glucose was converted to glucose-6-phosphate (G-6-P) by hexokinase in the presence of ATP, a phosphate donor. Glucose-6-phosphate dehydrogenase then converted the G-6-P to gluconate-6-P in the presence of NADP+. As the NADP+ was reduced to NADPH during this reaction, the resulting increase in absorbance at 340 nm (secondary wavelength = 700 nm) was measured.

$$\text{Glucose} + \text{ATP} \xrightarrow{\text{HK}} \text{G-6-P} + \text{ADP}$$

$$\text{G-6P} + \text{NADP}^{+} \xrightarrow{\text{G-6-PDH}} \text{Gluconate-6-P} + \text{NADPH} + \text{H}$$

Procedure: Ten microliters (10µL) of serum was added to the sample cups and put on the sample disk, which rotates to bring the desired sample cup into the position next to the sample probe for specimen sampling. 1000μL reaction reagents (hexokinase, glucose-6-phosphate dehydrogenase, and NADP+) were pipetted into reagent bottles leveled for glucose and put on a reagent disk, and then on the screen menu of the machine, glucose was entered as a parameter to be tested. The sample probe was pipetted from the sample disk and transferred to the reaction disk, which contains cuvettes (62).

5.2. Materials and reagents

5.2.1. Materials

- Glove, needle, alcohol, pipette, test tube, centrifugation, sample rack, cuvette, centrifuge tube, COBAS 6000 Automated Chemistry Analyzer machine and Computer loaded with COBAS 6000 Automated Chemistry Analyzer machine software.

5.2.2. Reagents

- Hexokinase, glucose-6-phosphate dehydrogenase, 4-aminophenazone, Phenol, peroxidase, lipoprotein lipase, glycerol kinase, glycerol phosphate oxidase, cholesterol esterase, cholesterol oxidase, hydrogen peroxide (H_2O_2), peroxidase, lipase, glycerol kinase, glycerol -3- phosphate oxidase and 4-chlorophenol.

5.3. Data management and Quality control

A questionnaire prepared in English was translated into Tigrigna by an individual who has good ability in language translation. To ensure reliability, it was translated back to English by another individual fluent in both languages. Data collectors, supervisors, and phlebotomists were trained for one day to maintain uniformity in the data collection process, blood specimen collection, processing, and analysis. Questionnaires and laboratory results were checked for completeness on a daily basis by the immediate supervisor and the principal investigator. Questionnaires with missing values were sent back to the respective data collector and laboratory technologist for correction. Complete questionnaires were rechecked repeatedly by the principal investigator to maintain the quality of the data. Pretest of the questionnaire was conducted in 5% study participant at Semen health center for one week prior to actual data collection to check tool's reliability. The blood sample was collected with precaution using the right procedures of sample collection for blood glucose and lipid profile analysis, and both were determined by the COBAS 6000 automated chemistry analyzer machine after being calibrated to an adequate temperature and appropriate wavelength to conduct the standard procedure. Also, indiscriminate results were repeated.

5.4. Ethical consideration

Ethical clearance was obtained from the Institution Review Board (Ref No. MU-IRB 2105/2023) of College of Health Sciences, Mekelle University. Prior to data collection, general agreement was asked to the hospital family planning unit focal person through a letter written from Department of Medical Biochemistry and Molecular Biology (Ref No: DMB/202/2023) and Department of Obstetrics and Gynecology (Ref No: GYN/OBS/2294/16). Subjects were informed that the information collected would keep anonymous to protect individual privacy and the objective of the study was explained to the study participants prior to obtaining their informed consent. The subjects were briefed about the confidentiality of their response and the importance of providing correct information. The selection of subjects and the collection of samples from the study participants were done after prior notice and approval for all protocols involved, and made clear that the participants under study had the right to refuse participation or quit participation at any point of the interview, data collecting, and laboratory test if they so wish.

5.5. Data process and analysis

The data obtained was entered using Epidata software and analyzed using SPSS software version 25. During analysis, standard statistical methods were used to determine the mean, standard deviation (SD) and the range. A student's independent t-test was used to compare the results of the blood glucose level and lipid profiles of hormonal contraceptive users and the control group. A one-way ANOVA was used to identify the variation of lipid profile and FBS between oral contraceptive pills, DMPA and implant users. Simple linear regression was used to determine the change in blood glucose and lipid profile in relation to the duration of hormonal contraceptive use. The normality and homoscedasticity of the data were checked by using the kolmogrov-smirnov test and Levene’s test respectively. All values were quoted as the means ± SD Variables with P-value < 0.05 was considered as a statistically significant. Finally, the result was present using text, table and graph.

6. Results

6.1. Sociodemographic and anthropometric characteristics

A total of 114 study participants (57 hormonal contraceptive users and 57 nonusers (controls) women) were enrolled in this study. Among the hormonal contraceptive users, 15 were oral contraceptive pill users, 22 were DMPA users, and 20 were implant users. The mean age (in years) of the hormonal contraceptive users was 30.89 ± 5.99, while that of the control participants was 30.77 ± 6.11. The age range of hormonal contraceptive users was 18–45 years, and the age range of controls was 19–45 years.

The majority of the study participants (31 (54.4%) hormonal contraceptive users and 32 (56.1%) nonusers—were aged 20–30 years. The majority of the study participants (31 (54.4%) hormonal contraceptive users and 23 (40.4%) nonusers) were housewives, whereas 14 (24.6%) hormonal contraceptive users and 23 (40.4%) nonusers were merchants.

The mean BMI (kg/m2) of the hormonal contraceptive users was 24.84 ± 2.83, while that of the control participants was 24.56 ± 2.35. (Table 1).

Table-1: Sociodemographic characteristics and anthropometric data of participants in Ayder comprehensive and specialized hospital, Tigray, North Ethiopia, 2024.

Variables		**Hormonal contraceptives**		**P value**
		User n (%) (n=57)	Nonuser n (%) (n=57)	
Age in years	<20	1 (1.8)	1 (1.8)	
	20-30	31 (54.4)	32 (56.1)	
	>30	25 (43.9)	24 (42.1)	0.91
Marital status	Single	…	4 (7)	
	Married	42 (73.7)	40 (70.2)	
	Divorced	12 (21.1)	9 (15.8)	
	Widowed	3 (5.3)	4 (7)	0.20
Educational level	Illiterate	12(21.1)	6(10.5)	
	Able to read and write	6(10.5)	13(22.8)	0.11
	Elementary school	7(12.3)	13 (22.8)	
	Secondary and preparatory school	16 (28.1)	14 (24.6)	
	College and above	16 (28.1)	14 (24.6)	
Occupation	House wife	31(54.4)	23 (40.4)	
	Governmental employee	10(17.5)	8(14)	
	Farmer	2(3.5)	3(5.3)	
	Merchant	14(24.6)	23(40.4)	0.28
Religion	Orthodox	37 (64.9)	39 (68.4)	
	Protestant	7 (12.3)	7 (12.3)	
	Muslim	13 (22.8)	11 (19.3)	0.90
BMI	<18.5 (Underweight)	1 (1.8)	1 (1.8)	
	18.5-24.9 (Normal)	26 (45.6)	33 (57.9)	
	25-29.9 (Overweight)	30 (52.6)	23 (40.4)	0.22
Where BMI: Body Mass Index				

6.2. Lipid Profile of the Study Participants

The mean serum TC level in hormonal contraceptive users was 171.56 ± 35.18 mg/dl, which was significantly (P = 0.005*) higher than that in nonusers (150.63 ± 41.87 mg/dl) by 20.93 mg/dl. The maximum serum TC levels among hormonal contraceptive users and nonusers were 246 mg/dl and 215 mg/dl, respectively, whereas the minimum serum TC levels among hormonal contraceptive users and nonusers were 96 mg/dl and 75 mg/dl, respectively.

There was a 20.74 mg/dl increase in the mean serum TG level among hormonal contraceptive users (133.67 ± 32.26 mg/dl) compared with nonusers (112.93 ± 27.52 mg/dl), and the difference was statistically significant (p = 0.000*). The maximum serum TG level was 231 mg/dl in hormonal contraceptive users and 162 mg/dl in nonusers. The minimum serum TG level in hormonal contraceptive users was 63 mg/dl, which alike with that of nonusers.

The results of our study indicated that the mean serum LDL-c level in hormonal contraceptive users (93.17 ± 38.66 mg/dl) was significantly greater (p = 0.003*) than that in nonusers (71.06 ± 39.65 mg/dl). The maximum serum LDL-c level among hormonal contraceptive users was 175.4 mg/dl, and that of nonusers was 130 mg/dl. However, the minimum serum LDL-c level among hormonal contraceptive users was 14.4 mg/dl, whereas that of nonusers was 5.6 mg/dl.

Compared with those in nonusers, serum HDL-c levels in hormonal contraceptive users decreased by 5.49 mg/dl. The mean serum HDL-c level was 52.02 ± 10.80 mg/dl in hormonal contraceptive users and 57.51 ± 7.33 mg/dl in nonusers, which was statistically significant (p = 0.02*). The ranges were 30–74 mg/dl and 40–69 mg/dl for hormonal contraceptive users and the control group, respectively.

6.3. Glucose Status of the Study Participants

The mean serum FBS level in hormonal contraceptive users was 100.04 ± 14.03 mg/dl, which was significantly (P = 0.012*) higher by 6.67 mg/dl than that of nonusers (93.37 ± 13.71 mg/dl). The maximum serum FBS levels among hormonal contraceptive users and nonusers were 133 mg/dl and 129 mg/dl, respectively, whereas 70 mg/dl and 66 mg/dl were the minimum serum TC levels among hormonal contraceptive users and nonusers, respectively (Table 2).

Table- 2: Mean serum levels and mean differences in TC, TG, HDL-c, LDL-c and FBS in hormonal contraceptive users and controls, in Ayder Comprehensive Specialized Hospital, 2024.

Lipid profile and Glucose level	**Hormonal contraceptive**		**Mean difference**	**P Value**
	Users (n=5)	Nonusers (n=57)		
TC	171.56 ± 35.18	150.63 ± 41.87	+20.93	0.005*
TG	133.67 ±32.26	112.93 ± 27.52	+20.74	0.000*
LDL-c	93.17 ± 38.66	112.93 ± 27.52	+22.11	0.003*
HDL-c	52.02 ± 10.80	57.51 ± 7.33	-5.49	0.02*
FBS	100.04 ± 14.03	93.37 ± 13.71	+6.67	0.012*

Where: (-) = Decreased from controls, (+) = Increased from controls, values are represented as M ± SD, *=statistically significant, P values were obtained by student's independent t-test. TC: Total Cholesterol, TG: Triglyceride, LDL-c: Low Density Lipoprotein Cholesterol, HDL-c: High Density Lipoprotein Cholesterol, FBS: Fasting Blood Sugar

6.4. Lipid Profile of Hormonal Contraceptive Users

Our study revealed a significant difference (p = 0.000*) in the mean serum TG levels among the three groups of hormonal contraceptive users. Compared with the OCP (126.93 ± 29.57 mg/dl) and implants (118.05 ± 30.05), there was a significant increase in TG among women using DMPA (152.45 ± 27.23 mg/dl).

There was a significant difference (p = 0.031*) in the mean serum level of LDL between the three groups of hormonal contraceptive users. There was a 23.84 mg/dl increase in the serum LDL-c level in DMPA users (109.60 ± 48.12 mg/dl) and a 6.8 mg/dl decrease in the serum LDL-c level in OCP users (78.95 ± 22.64 mg/dl) compared with implant users (85.76 ± 30.60 mg/dl). Moreover, there was a 30.65 mg/dl increase in the serum LDL-c level in the DMPA group compared with the OCP group.

There was a significant difference (p = 0.001*) in the mean serum level of HDL-c among the three groups of hormonal contraceptive users. There was a 12.27 mg/dl increase in the serum HDL-c level in

OCP users (58.13 ± 12.43 mg/dl) and an 8.34 mg/dl increase in the serum HDL-c level in implant users (54.20 ± 6.69 mg/dl) compared with DMPA users (45.86 ± 9.83 mg/dl).

There was a nonsignificant difference (p = 0.051) in the mean serum level of total cholesterol (TC) among the three groups of hormonal contraceptive users. There was a nonsignificant increase in TC among women who used DMPA (185.77 ± 43.55 mg/dl) compared with those who used OCP (162.47 ± 20.11 mg/dl) or implants (162.75 ± 29.55). The mean difference between DMPA and OCP users was 23.31 mg/dl, that between OCP and implant users was 0.28 mg/dl, and that between DMPA and implant users was 23.02 mg/dl.

6.5. Glucose Status among hormonal contraceptive users

There was a nonsignificant difference (p = 0.65) in the mean serum level of FBS between the three groups of hormonal contraceptive users. (Table 3).

Table -3: Mean serum lipid profile and glucose level among hormonal contraceptives user, in Ayder Comprehensive Specialized Hospital, 2024.

Lipid profile and Glucose level	**Hormonal contraceptive**			**P Value**
	OCP (n=15)	DMPA (n=22)	Implanon/Norplant (n=20)	
TC	162.47 ± 20.11	185.77 ± 43.55	162.75 ± 29.55	0.051
TG	126.93 ± 29.57	152.45 ± 27.23	118.05 ± 30.05	0.000*
LDL-c	78.95 ± 22.64	109.60 ± 48.12	85.76 ± 30.60	0.031*
HDL-c	58.13 ± 12.43	45.86 ± 9.83	54.20 ± 6.69	0.001*
FBS	100.07 ± 15.96	101.95 ± 13.91	97.90 ± 13.03	0.65
Values are represented as M ± SD (mg/dl), *=statistically significant, p values were obtained by One-way ANOVA. DMPA: Depo-Medroxyprogesterone Acetate, OCP: Oral Contraceptive Pill. TC: Total Cholesterol, TG: Triglyceride, LDL-c: Low Density Lipoprotein Cholesterol, HDL-c: High Density Lipoprotein Cholesterol, FBS: Fasting Blood Sugar				

6.6. Lipid Profile in relation to the duration of hormonal contraceptive use

As the duration of OCP use increases by one month, the serum total cholesterol level of women increases by 1.37 mg/dl. There was a nonsignificant, moderate, and positive ($r = 0.49$) relationship between the duration of OCP use and total cholesterol. As the duration of OCP use increases by one month, the serum triglyceride level of women increases by 2.46 mg/dl. There was a significant ($p = 0.017$), moderate, and positive ($r = 0.60$) relationship between the duration of OCP use and triglycerides. As the duration of OCP use increases by one month, the serum LDL-c level of women increases by 1.93 mg/dl. There was a significant ($p = 0.014$), moderate, and positive ($r = 0.62$) relationship between the duration of OCP use and LDL-c. As the duration of OCP use increases by one month, the serum HDL-c level of women decreases by 1.05 mg/dl. There was a significant ($p = 0.015$), moderate, and negative ($r = -0.61$) relationship between the duration of OCP use and HDL-c (Figs. 1-4).

As the duration of DMPA use increases by one month, the serum total cholesterol level of women increases by 3.47 mg/dl. There was a significant ($p = 0.000$), moderate, and positive ($r = 0.72$) relationship between the duration of DMPA use and total cholesterol. As the duration of DMPA use increases by one month, the serum triglyceride level of women increases by 2.54 mg/dl. There was a significant ($p = 0.000$), strong, and positive ($r = 0.84$) relationship between the duration of DMPA use and triglyceride. As the duration of DMPA use increases by one month, the serum LDL-c level of women increases by 3.8 mg/dl. There was a significant ($p = 0.000$), moderate, and positive ($r = 0.71$) relationship between the duration of DMPA use and LDL-c. As the duration of DMPA use increases by one month, the serum HDL-cl level of women decreases by 0.84 mg/dl. There was a significant ($p = 0.000$), moderate, and negative ($r = -0.77$) relationship between the duration of DMPA use and HDL-c (Figs. 1-4).

As the duration of implant use increases by one month, the serum total cholesterol level of women increases by 0.56 mg/dl. There was a nonsignificant, weak, and positive ($r = 0.43$) relationship between the duration of implant use and total cholesterol. As the duration of implant use increases by one month, the serum triglyceride level of women increases by 0.23 mg/dl. There was a non-significant, weak, and positive ($r = 0.18$) relationship between the duration of implant use and triglyceride. As the duration of implant use increases by one month, the serum LDL-c level of women increases by 0.71 mg/dl. There was a significant ($p = 0.017$), weak, and positive ($r = 0.53$) relationship between the duration of implant use and total LDL-c. As the duration of implant use increases by one month, the serum HDL-c level of women decreases by 0.16 mg/dl. There was a significant, weak, and negative ($r = -0.56$) relationship between the duration of implant use and HDL-c (Figs. 1–4).

6.7. Glucose level (FBS) in relation to the duration of hormonal contraceptive use

As the duration of OCP use increases by one month, the serum FBS level of women increases by 0.35 mg/dl. There was a nonsignificant, weak, and positive ($r = 0.16$) relationship between the duration of OCP use and FBS.

As the duration of DMPA use increases by one month, the serum FBS level of women increases by 1.10 mg/dl. There was a significant ($p = 0.000$), moderate, and positive ($r = 0.71$) relationship between the duration of DMPA use and serum FBS.

As the duration of implant use increases by one month, the serum FBS level of women increases by 0.14 mg/dl. There was a nonsignificant, weak, and positive ($r = 0.25$) relationship between the duration of implant use and the serum FBS concentration (Fig. 5).

6.8. Castelli risk index

There was a significant ($p = 0.000$) difference in the Castelli risk index I between hormonal contraceptive users (3.57 ± 1.49) and nonusers (2.65 ± 0.75). There was also a significant ($p = 0.000$) difference in the Castelli risk index II between hormonal contraceptive users (2.03 ± 1.23) and nonusers (1.25 ± 0.72). A ratio of < 3 indicates a below average, but not absent risk. A ratio of 3–5 indicates average risk. Ratios > 9 clearly pose a marked elevation in risk according to Framingham study (65).
The Castelli risk index (I) indicates an average risk factor for the development of cardiovascular disease in hormonal contraceptive users. These findings indicate that the use of hormonal contraceptives is associated with the development of CVD. The Castelli risk index II indicates that there are no risk factors for the development of cardiovascular disease in hormonal contraceptive users (Table 4).

Table -4: Castelli Risk Index I and Castelli Risk Index II of Hormonal Contraceptive users and non-users in Ayder comprehensive and specialized hospital, 2024.

Castelli Risk Index	**Hormonal contraceptive**		**Mean difference**	**P Value**
	Users (n=57)	Nonusers (n=57)		
LDL-c/HDL-c	2.03 ± 1.23	1.25 ± 0.72	+0.78	0.000*
TC/HDL-c	3.57 ± 1.49	2.65 ± 0.75	+0.93	0.000*
Where: (+) = Increased from controls, values are represented as M ± SD, *=statistically significant, P values were obtained by student's independent t-test. LDL-c: Low Density Lipoprotein Cholesterol, HDL-c: High Density Lipoprotein Cholesterol				

There was a significant difference (p = 0.02*) in the mean serum level of total cholesterol (TC)/high-density lipoprotein cholesterol (HDL-c) between the three groups of hormonal contraceptive users. There was a 1.47 mg/dl decrease in the serum TC/HDL-c level in OCP users (2.95 ± 0.84 mg/dl) and a 1.32 mg/dl decrease in the serum TC/HDL-c level in implant users (3.10 ± 0.86 mg/dl) compared with DMPA users (4.42 ± 1.87 mg/dl). There was also a significant difference (p = 0.03*) in the mean serum level of LDL/HDL-c among the three groups of hormonal contraceptive users. There was a 1.23 mg/dl decrease in the serum LDL/HDL-c level in OCP users (1.48 ± 0.65 mg/dl) and a 1.02 mg/dl decrease in the serum LDL/HDL-c level in implant users (1.69 ± 0.77 mg/dl) compared with DMPA users (2.71 ± 1.59 mg/dl) (Table 5).

Table -5: Castelli risk index I and Castelli risk index II of hormonal contraceptive users in Ayder Comprehensive Specialized Hospital, 2024.

Castelli Risk Index	**Hormonal contraceptive**			**P Value**
	OCP (n=15)	DMPA (n=22)	Implanon/Norplant(n=20)	
TC/HDL-c	2.95 ± 0.84	4.42 ± 1.87	3.10 ± 0.86	0.02
LDL-c/HDL-c	1.48 ± 0.65	2.71 ± 1.59	1.69 ± 0.77	0.03

Values are represented as M ± SD (mg/dl), *=statistically significant, P values were obtained by One-way ANOVA. DMPA: Depo-Medroxyprogesterone Acetate, OCP: Oral Contraceptive Pill. TC: Total Cholesterol, TG: Triglyceride, LDL-c: Low Density Lipoprotein Cholesterol, HDL-c: High Density Lipoprotein Cholesterol

7. Discussion

Both the hormonal contraceptive users and nonusers had similar socio-demographic and BMI statistical result. This explains that the differences in lipid profile values between these two groups were not caused by socio-demographic characteristics.

The mean serum TC level in hormonal contraceptive users was 171.56 ± 35.18 mg/dl, which was significantly (P = 0.005*) higher than that in nonusers (150.63 ± 41.87 mg/dl) by 20.93 mg/dl. The findings from the present study suggests that the mean serum TC level of hormonal contraceptive users was significantly increased by 20.93 mg/dl in comparison with that of nonusers. This study is comparable to a previous study done in the United Arab Emirates, which reported that the TC level of COCP users was significantly higher (P =.001) than controls (45). Similar to the present study, a study conducted in Rwanda, reported a high risk of developing an abnormal lipid profile among users compared with controls in TC (46). The present study is in accordance with a study performed in Sudan, that revealed women using POP treatment had a significant increase in TC compared with women who were not (55).The present study is also consistent with the previous study performed in Ethiopia, in which the mean serum levels of TC were significantly increased in hormonal contraceptive users in comparison with nonusers (22).Unlike the findings of the present study, there was no significant change in mean serum TC among DMPA users in comparison to nonusers (27) and no significant change in mean serum TC among OCP users in comparison to the nonusers according to the study done in Sudan (54). The present study was in contrast to the results found in a study conducted in Pakistan, where it was suggested that DMPA has beneficial effects on serum TC (49). The discrepancy among the studies may be due to differences in the age of the study participants, sample size, and study design.

In the present study, there was no significant difference in the mean serum level of TC among the OCP, DMPA, and implant groups. There was no a significant increase in TC among women who used DMPA compared with OCP and implant. The mean difference between DMPA and OCP users was 23.31 mg/dl; in OCP and implant users was 0.28 mg/dl; and DMPA and implant users was 23.02 mg/dl. This result is comparable to a prior study conducted in Nigeria that reported a significant monthly increase in the levels of total cholesterol in Noriesterate, Depo-Provera, or oral pills. However, for women taking Norplant, there was a significant monthly decrease in the levels of total cholesterol (25). However, another study reported the beneficial effects of DMPA, in which the DMPA group had lower values of TC than COC users and the control group (50).

There was a 20.74 mg/dl increase in the mean serum TG level among hormonal contraceptive users (133.67 ± 32.26 mg/dl) compared with nonusers (112.93 ± 27.52 mg/dl), and the difference was statistically significant (p = 0.000*). The present study revealed that users of hormonal contraceptives had significantly increased mean serum TG levels by 20.74 mg/dl in comparison with the nonusers. The finding of our study is similar to the finding of the study done in Brazil (24). Another study suggested that there was a significant increase in the mean value of triglyceride in the test group when compared with the control groups (25). A similar study revealed that DMPA users had a significant increase in serum TG levels in comparison with the nonusers (23).The present study is also consistent with a study performed in Ethiopia where the mean serum levels of TG is significantly increased in hormonal contraceptive users in comparison with nonusers (22). In contrast, another study reported that the serum triglyceride level tended to decrease but was significant only at the 6th and 9th months of Implanon use (48). Other studies done in Nepal showed that, compared to controls, TG levels were not affected by DMPA use (51). Similarly, in a in a study done in Sudan, there was no effect of using OCP on the TG level compared to the control group (54). This discrepancy may be a result of differences in the age of the study participants, genetic differences, food habits.

In the present study, there was a significant increase in TG among women treated with DMPA (152.45 ± 27.23 mg/dl) compared with those treated with OCP (126.93 ± 29.57 mg/dl) or implants (118.05 ± 30.05). The mean difference between DMPA and OCP users was 25.52 mg/dl, that between OCP and implant users was 8.88 mg/dl, and that between DMPA and implant users was 34.41 mg/dl. This finding revealed a significant difference in the mean serum TG levels among the three groups of hormonal contraceptive users. This result is comparable to that of a study performed in Nigeria: women taking Norplant presented a significant monthly decrease in triglycerides, whereas OCP and DMPA significantly increased monthly (25). The finding of the present study is consistent with a study performed in Pakistan that found POP had higher mean serum TG levels than Implanon users (49). This finding is also in line with a previous study done in Ethiopia where the mean serum levels of TG in Implanon users were lower than those of DMPA and POP users(22). Depo-Provera has a contraceptive dose of 150 mg of progesterone. Progesterone-only pills are composed of 75 mg of progesterone; COC contains 150 mcg of levonorgestrel and 30 mcg of ethinylestradiol; Implanon contains 68 mg of synthetic progesterone, which decreases its release over time; and Norplant contains 36 mg of synthetic progesterone, which decreases its release over time (40,39, 42, 45,). Thus, the variation in progestin composition among different hormonal contraceptives may affect lipid profiles differently.

The finding of the present study suggests that the mean serum LDL-c level of hormonal contraceptive users was significantly increased by 22.11 mg/dl in comparison with nonusers. The present finding is similar with a study performed in Bangladesh, Nepal, and Ethiopia that revealed that the mean serum levels of LDL-c were significantly greater in COC and DMPA of hormonal contraceptive users respectively in comparison with the non-users (22, 47, 51). However, a study performed in Sudan reported no effect of using OCP on the level of mean serum LDL-c (54). In addition to this in a study performed in the UAE, the LDL-c level of COC users did not significantly differ with nonusers (45).This discrepancy may be due to different in study design and sample size.

The results of our study indicated that the mean serum LDL-c level in hormonal contraceptive users (93.17 ± 38.66 mg/dl) was significantly greater (p = 0.003*) than that in nonusers (71.06 ± 39.65 mg/dl). There was a 23.84 mg/dl increase in the serum LDL-c level in DMPA users and a 6.8 mg/dl decrease in the serum LDL-c level in OCP users compared with implants. There was a 30.65 mg/dl increase in the serum LDL-c level in the DMPA group compared with the OCP group. This finding is comparable to that of a study performed in Ethiopia; the mean serum levels of LDL-c in Implanon users were lower than those in DMPA and POP users (22). In contrast to the present findings, a study performed in Brazil suggested that the DMPA group had lower values of LDL-c than COC users and the control group (50). This discrepancy could be due to the difference in ethnic groups and physical activity.

The mean serum HDL-c level was 52.02 ± 10.80 mg/dl in hormonal contraceptive users and 57.51 ± 7.33 mg/dl in nonusers, which was statistically significant (p = 0.02*). In the present study, Serum HDL-c level in hormonal contraceptive users decreased by 5.49 mg/dl in comparison with nonusers. This finding supports the results reported by a study performed in Sudan and Ethiopia, which showed that the mean serum levels of HDL were significantly decreased in hormonal contraceptive users in comparison with the nonusers (22, 54, 55, 57).Whereas, other studies reported that there was no significant change in mean serum HDLc among DMPA users in comparison with the nonusers (23, 51). In contrast to our study, studies performed in Brazil and Nigeria on OCP and Implanon, respectively, showed higher serum HDLc among the users compared to non-users (24, 48). This disparity may be due to different ethnic groups. This difference may also be due to differences in lifestyle.

There was a 12.27 mg/dl increase in the serum HDL-c level in OCP users (58.13 ± 12.43 mg/dl) and an 8.34 mg/dl increase in the serum HDL-c level in implant users (54.20 ± 6.69 mg/dl) when compared with DMPA users (45.86 ± 9.83 mg/dl). This finding is in line with other studies; the DMPA group had a lower HDL-c level than the control and COC groups did (50).

The present study is comparable to a study performed in Ethiopia and the mean serum HDL-c level of Implanon users was significantly higher than that of DMPA and POP users (22).Whereas, another study reported that the DMPA group showed the highest HDL-c value compared with the other methods (next to oral contraceptives) (49).

The mean serum FBS level in hormonal contraceptive users was 100.04 ± 14.03 mg/dl, which was significantly (P = 0.012*) higher by 6.67 mg/dl than that of nonusers (93.37 ± 13.71 mg/dl). In the present study, the mean serum FBS levels in hormonal contraceptive users were significantly higher by 6.67 mg/dl than those of nonusers. This result is in line with findings in Surakarta and it was revealed that hormonal contraceptives had a higher blood glucose level than nonusers of hormonal contraceptives (63).The present study, which is also consistent with a study performed in Iraq, showed that highly significant serum glucose concentrations were obtained in contraceptive users as compared with contraceptive nonusers (52). Another study revealed, highly significant values of serum glucose concentrations were obtained in contraceptive users as compared with contraceptive nonusers (52). In the present study, there was a 2.17 mg/dl non-significant increase in FBS among women using DMPA and 4.06 mg/dl OCP compared to implants. This is comparable to other studies performed in Pakistan that reported progesterone-containing injectables, which showed slightly elevated FBS in comparison to other contraceptives (58).

There was a significant (p = 0.000) difference in the Castelli risk index I between hormonal contraceptive users (3.57 ± 1.49) and nonusers (2.65 ± 0.75). There was also a significant (p = 0.000) difference in the Castelli risk index II between hormonal contraceptive users (2.03 ± 1.23) and nonusers (1.25 ± 0.72). Castelli indices I and II were significantly higher in hormonal contraceptive users than in nonusers. The Castelli risk index (I) indicates an average risk factor for the development of cardiovascular disease in hormonal contraceptive users. These findings indicate that the use of hormonal contraceptives is associated with the development of CVD. The Castelli risk index II indicates that there are no risk factors for the development of cardiovascular disease in hormonal contraceptive users. These findings indicate that the use of hormonal contraceptives is associated with the development of CVD. The findings of the present study were similar to previous findings in Ghana, and the Castelli indices I and II were significantly different between the control and OC groups (20). Similarly, another study performed in Ghana reported statistically significant differences were observed for the atherogenic index between the cases and the controls (53). However, in a study performed in Egypt, it was shown that DMPA induces a gradual increase (but not significant) in the LDL-to-HDL ratio in comparison to the control group (56).Variations in findings could also be due to differences in life styles and food habits. Most Ethiopians usually utilize imported edible palm oil containing a large proportion of saturated fatty acids that raise the TC/HDL-c and LDL-c/HDL ratios.

There was a significant difference ($p = 0.02^*$) in the mean serum level of the Castelli index I among the three groups of hormonal contraceptive users. There was a 1.47 mg/dl decrease in the serum Castelli index I level in OCP users (2.95 ± 0.84 mg/dl) and a 1.32 mg/dl decrease in the serum Castelli index I level in implant users (3.10 ± 0.86 mg/dl) compared with DMPA users (4.42 ± 1.87 mg/dl). There was also a significant difference ($p = 0.03^*$) in the mean serum level of the Castelli index II among the three groups of hormonal contraceptive users. There was a 1.23 mg/dl decrease in the serum Castelli index II in OCP users (1.48 ± 0.65 mg/dl) and a 1.02 mg/dl decrease in the serum Castelli index II in Castelli index II users (1.69 ± 0.77 mg/dl) compared with DMPA users (2.71 ± 1.59 mg/dl). Castelli risk indices revealed that the use of DMPA was associated with the highest risk (atherogenic index) of CVD, followed by OCP and implants. However, in Pakistan, Castelli indices revealed that use of OCs was associated with the highest atherogenic index, followed by NET-EN, IUCD, DMPA and implantation (49).

In the present study, the serum levels of TC, TG, and LDL-c greatly increased as the duration of DMPA use increased, whereas the serum level of HDL-c decreased. The serum levels of TG and LDL-c moderately increased as the duration of OCP use increased, whereas the serum level of HDL-c moderately decreased. There was a nonsignificant increase in TC as the duration of OCP increased. The serum levels of LDL-c slightly increase as the duration of implant use increases, whereas the serum level of HDL-c slightly decreases. There was a nonsignificant slight increase in TC and TG as the duration of implantation increased. This result is comparable to that of a study performed in Ethiopia, in which the blood levels of TC, TG, and LDL-c greatly increased as the duration of DMPA and POP use increased, whereas the serum level of HDL-c dramatically decreased. The duration of Implanon use had no effect on the serum levels of TC, TG, or HDL-c; nevertheless, the serum level of LDL-c dramatically increased with increasing Implanon usage time (22). study performed Ghana similarly showed, significant influence of HC use on TG, TC, LDL-c, and VLDL-c over time (20). Another study done in

Nigeria showed a significant monthly increase in the levels of TC, TG, and LDL cholesterol following administration of Depo-Provera and oral pills, while the level of HDL cholesterol significantly decreased within the duration of contraceptives used when compared with the control group. However, for women taking Norplant, there was a significant monthly decrease in the TC, TG, and LDL cholesterol levels, whereas the HDL- cholesterol levels were significantly increased (25).The age of study participants, eligibility criteria, and study setting could have contributed to the discrepancy between the present and prior results.

In the present study, as the duration of DMPA use increased by one month, the serum FBS level of women significantly increased by 1.10 mg/dl. The duration of implant and OCP use had no effect on the serum levels of FBS. This result is comparable to a study conducted in Nigeria, which reported a significant monthly increase in the levels of glucose following the administration of Depo-Provera and oral pills. However, for women taking Norplant, there was a significant monthly decrease in the level of glucose (25).

8. Conclusions

Compared with controls, users of hormonal contraceptives had higher mean serum levels of TC, TG, LDL, and FBS and lower mean serum HDL-c levels. The mean serum lipid profiles differed among DMPA, implant, and OCP users. However, the mean serum levels of FBS did not differ among DMPA, implant, and OCP users. Compared with OCP and implant users, DMPA users had the highest mean serum levels of TC, TG, and LDL-c but had the lowest mean serum levels of HDL-c.

With increased duration of oral contraceptive use, TG and LDL-c increased, whereas HDL-c decreased. No change in TC was detected. With increasing duration of DMPA use, TC, TG, and LDL-c strongly increased, whereas HDL-c strongly decreased. With increasing duration of implant use, LDL-c slightly increased, whereas HDL-c slightly decreased. No change in TC or TG was detected. With increased duration of DMPA use, the serum level of FBS moderately increased. The duration of implantation and OCP use had no effect on the serum levels of FBS.

There was also a significant difference in the Castelli risk indices I and II between hormonal contraceptive users and nonusers. There was a significant difference in the mean serum levels of the Castelli index I and Castelli index II among the three groups of hormonal contraceptive users. Compared with those in DMPA users, serum Castelli index I and Castelli index II levels were lower in OCP users, and serum Castelli index I and Castelli index II levels were lower in implant users.

The results of this study revealed that hormonal contraceptive use produces changes in mean value of serum lipid profile and FBS level. Among the types of hormonal contraceptives, DMPA had the greatest ability to increase TC, TG, LDL-c, the Castelli index I, and the Castelli index II and the greatest ability to decrease HDL-c. These findings indicate that DMPA produces more changes in mean value of serum lipid profile and FBS level than the other methods are. Implants have a minimal effect on the level of all lipid profiles. Thus, implantation seems to be the best form of family planning. A shorter duration of hormonal contraceptive use may lead to minimal change on mean serum value of lipid profiles.

9. Recommendations

On the basis of findings of the present study, we recommend the following for concerned bodies:

- Routine evaluation of lipid profiles and FBS is advisable before initiating hormonal contraceptives.
- Hormonal contraceptive users are recommended to undergo regular evaluation of their lipid profile and FBS at each visit to the family planning unit.
- Women who had cardiovascular problems (myocardial infarction, congestive heart failure, increased blood pressure, pulmonary embolism, tachycardia, and thromboembolic disorders) should be counselled to use best options of contraceptives (nonhormonal contraception). If the use of hormonal contraceptive is mandatory, implants would be preferable to DMPA and OCP with regular follow-up.
- Counselling should continue on how to use them and which option is safest than and for which client (DMPA produces more changes in mean value of serum lipid profile and FBS level than the other methods are and implants have a minimal effect on the level of all lipid profiles).
- Effort should continue to improve the formulation of DMPA in order to bring the dose necessary for effective contraception to the lowest dose possible and thereby decrease its effect on lipid metabolism.
- This study is cross-sectional in design; further large-scale longitudinal studies are needed to determine the effect of hormonal contraceptives on serum lipid and blood glucose levels. Thus, this study can be used as baseline information for further studies related to the effect of hormonal contraceptives on serum lipid levels and blood glucose levels.

10. Strengths and Limitations

Starting from the strengths of the study, data on the general condition of the respondents were obtained from direct interviews with the participants, and body weight, body height, blood glucose level, and lipid profile measurements were conducted directly instead of via self-reported and secondary data. Therefore, it was possible to represent real conditions.

The limitations of the study include the following: This study is facility-based with a relatively small sample size, but it would have been better if it were community-based with a large sample size, which makes generalization to a wider population better.

Confounding factors such as sedentary lifestyle, type of food regularly consumed, degree of exercise, and family history were not considered.

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12. Annexes

Annex-I: Participant information sheet

Project title: Assessment of blood glucose level and lipid profiles among hormonal contraceptive users at ACSH, Tigray, Northern Ethiopia

Investigator: Seare Teklay

Email: Seareteklay555@gmail.com

Phone: 0937019181

Supervisor: Gidey Gebremeskel (Asst. Prof. of Medical Biochemistry)

Sponsor: Mekelle University

Introduction

Hello, I am Seare Teklay from Mekelle University, College of Health Sciences. I am here today to collect data on "assessment of blood glucose level and lipid profiles among hormonal contraceptive users in ACSH, Tigray, Northern Ethiopia. The objective of this study was to assess blood glucose levels and lipid profiles among hormonal contraceptive users at ACSH, Tigray, Northern Ethiopia, from October to January 2023. I kindly request that you take part in this study. Your cooperation and willingness are greatly helpful in identifying information related to blood glucose levels and lipid profiles. Approximately 20 minutes are needed for interviews and blood collection. There is no direct benefit or possible risk associated with participating in this study except for the time spent responding to the questionnaire and collecting blood. The information you provide will be kept strictly confidential. Your participation is voluntary, and you are not obliged to answer any question that you do not want to answer. If you feel uncomfortable with the question or the blood collection producers, it is your right to drop it at any time you want.

Purpose

The overall purpose of this study was to assess blood glucose levels and lipid profiles among hormonal contraceptive users at ACSH, Tigray, Northern Ethiopia, from October to January 2023. I want to determine the derangement of blood glucose and lipid profiles of hormonal contraceptive users at ACSH, Tigray, Northern Ethiopia. With this information, I will be able to provide information to health care providers and policymakers and share it with the rest of the world to raise awareness about the effects of hormonal contraceptives on blood glucose and lipid profiles at ACSH, Tigray, Northern Ethiopia.

Procedure and participation

You will receive the Tigrigna version of this information sheet and consent form to read until you completely understand it. If you cannot read, that will not be a problem because I will also provide you with an oral briefing so that maximum understanding and clarity will be created. Then, subjects with an interest in participating in my study will be asked to sign the consent form, and the investigator will record their personal information. After providing your consent, I will ask you for demographic information and other relevant clinical data, and 5 mL of blood samples will be collected from you.

Confidentiality

We strongly assure you that your name and other identifiers will not be disclosed to anyone outside of the study.

Rights, risk and benefits of the study

Your participation in the study will not have any adverse effects and will have minimum invasive procedures. One may experience minor discomfort and pain during blood collection, and there may also be mild redness or swelling at the site from which the blood is drawn. However, this will be minimized, as the procedure will be carried out by experienced health professionals in the hospital under standard aseptic conditions. You will not receive a direct benefit from participating in this research. However, public health professionals should be assisted to gain an improved understanding of the adverse effects of hormonal contraceptives. At the same time, you will see some biochemical parameters and a clinical assessment of your health condition for free. The information you provide is confidential and will only be used for the objective mentioned above. Information about your health collected from the study will be stored in code numbers. No personal identification will be mentioned in the results of the study, which may be published for scientific purposes. Therefore, I want to assure you that your participation in this study will not involve any risks to you.

Inducement, incentives and compensation

There will not be any monetary payment linked with your participation in this study. The benefits you will gain are mentioned above under the section ‘‘Benefit’’, Freedom to withdraw

Your participation in this study is completely voluntary. No penalty or loss of benefit is involved if you change your idea that you do not want to participate.

Person to contact

In case you have any questions, unclear ideas or doubts about the study, please feel free to contact the following individuals through their addresses:

Principal investigator: Seare Teklay (BSc. in Health Officer)

Email: Seareteklay555@gmail.com

Cell phone: 0937019181

Principal supervisor: Gidey Gebremeskel (Asst. prof. of medical biochemistry)

Email: ghidena12@gmail.com

Cell phone: 0913469746

Annex-II: Informed consent

I understand that the purpose of the study is to collect information regarding the assessment of blood glucose level and lipid profiles among hormonal contraceptive users at ACSH, Tigray, Northern Ethiopia. I have read the above information, or it has been read to me. I have had the opportunity to ask questions, and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate in this study and understand that I have the right to withdraw at any time without, in any way, affecting my social life or medical care.

1. Yes, of course, ☐
2. No. ☐

Data collection tool (English version)

Questionnaire on assessment of blood glucose level and lipid profiles among hormonal contraceptive users at ACSH, Tigray, Northern Ethiopia

To be answered by both hormonal contraceptive users and control group individuals:		
Participants ID/MRN		…………………..
S. No	I. Questions on Sociodemographic Characteristics	
001	Age in years	…………..
002	Marital status	A) Married B) Divorced C) Widowed D) Others………
003	Educational status	A) Illiterate B) Able to read and write C) Grade 1-8 D) Grade 9-12 E) College and above
004	Occupational status	A) House wife B) Governmental employee C) Farmer D) Merchant Other specify………

005	Religion	Specify…………
II. Questions on maternal health and contraceptive status		
006	Do you practice regular exercise?	A) Yes B) No
007	Do you Suspect pregnancy?	A) Yes B) No
008	Do you have any of the following health problems?	A) Cardiovascular disease B) Liver disease C) Kidney disease D) Other chronic illness…
009	If your answer is yes for question number 009, would you list the drug(s) you are taking for managing the disease?	……………………………………………………
010	Do you breast-feed?	A) Yes B) No
011	Do you use other substances?	A) Alcohol B) Khat C) Cigarette D) Others………
012	Do you use contraceptive?	A) Yes B) No
If yes for question No 012 proceed to next question number 013 and 014 will be answered only by hormonal contraceptive users.		
013	What types of hormonal contraceptive method you are using?	A) Oral contraceptive pills B) Depo Provera C) Implanon D) Norplant
014	If you are hormonal contraceptive users, for how long you were using	A). For Oral Contraceptive users in month: … B). For depo users in month: …….

	without discontinuation?	B). For Implanon users in month …. D) For Norplant users in month………..
Anthropometric measurement		
015	Height…………. Weight…………	Calculated BMI: Weight in kg/ Height in m^2……….
IV. Biochemical Parameters /Laboratory results		
	Parameter / laboratory request	Results
016	HDL-C	.... (mg/dl)
017	LDL-C	.... (mg/dl)
018	TC	.... (mg/dl)
019	TG	.... (mg/dl)
020	FBS	.... (mg/dl)

<u>ልጋብ</u>-1: ንተሳተፍቲ ብዛዕባ ዘካይዶ መጽናዕቲ ሓበሬታ ወሃቢ ጽሑፍ

<u>ርእሲ እዚ መጽናዕቲ</u>: - ኣብ ኮምፕሬሄንሲቭ ስፔሻላይዝድ ሆስፒታል ዓይደር ዘለዋ ሆርሞናል መከላከሊ ጥንሲ ተጠቀምቲ ኣብ ደምን ዉሽጢ ዘለዉ ዓቀን ሽኮርን መጠን ስብሕን ብምልካዕ ዝፍጠር ናይ ሽኮርን ስብሕን ምዝባዕ ዳህሳስ”

<u>*ተመራማሪ*</u>: <u>ሰዓረ ተክላይ</u>

ስፖንሰር: ባዮሜዲካል ዲፓርትመንት ኮሌጅ ጥዕና ሳይንስ ፣ ኣክሱም ዩኒቨርሲቲ

መማከርቲ:ግደይ ገ/መስቀል (ኤም.ኤስ.ሲ ሐጋዚ ፕሮፌሰር)፣ ሙላታ ሃይለ (ኤምኤስ.ሲ ሓጋዚ ፕሮፌሰር) ፣ ረዘነ ኣብራሃ (ኤም.ኤስ.ሲ)

<u>*መእተዊ*</u>

እዚ ሓበሬታ ወሃቢ ጽሑፍ ሓፈሻዊ ዕላምኡ ኣብዚ ዘካይዶ መጽናዕቲ ተሳተፍቲ ንኽትኮኑ ፍቓድኩም ንምሕታት ኮይኑ ብዛዕባ እዚ ዘካይዶ መጽናዕቲ ሙሉእ ሓበሬታ ክዋህበኩም እዩ። ብተወሳኺ እውን ካብ ተሳተፍቲ እንደልዮ ሓገዝ ብዝርዝር ዝተገለጸ ኮይኑ ኣብዚ ከይዲ ድሕንነት፣ ክብርን መሰልን ተሳተፍቲ ብዘረጋገጸ መንገዲ ንኽኸውን እንወስዶም ጥንቃቐታት እውን ኣቐሚጥና ኣለና። ስለዝኾነ ኣብዚ መጽናዕቲ ተሳታፊ ንምኳን ንኽውስኑ/ና እዚ ሓበሬታ ብዕምቆት ምርዳእ ጠቓሚ ይኸውን። ዝኾነ ዓይነት ሕቶ ወይ ከዓ ግልጺ ዘይኮነ ነገር እንተጋጢምዎም/ወን ብዘይዝኾነ ስኽፍታ ክንዲዝደለይዎ/አ ግዜ ንኽሓታ/ቱና ይላቦ። ኣብዚ መጽናዕቲ ተሳታፊ ንምኳን እንተወሲኖም/ነን እሞ እዚ ውሳኔኦም/አን እቲ መጽናዕቲ ይኹን ንሶም/ንሰን ዝገብሩልና/ራልና ሓገዝን ካልኦት ዝተጠቐሱ ዛዕባታት ሙሉእ ብምሉእ ተረዲእዎም/ወን ብሰናይ ድሌቶም/ተን ፈቂዶም/ደን ምኻኖም/ነን ኣብቲ ዝተዳለወ ናይ ስምምዕ ቕጥዒ ብምፍራም ከረጋግጹልና/ከራጋግፃልና እዮም/እየን። ንዝገብሩልና/ዝገብራልና ምትሕብባርን ሓገዝን ብቕድምያ ምስጋናይ የቕርብ።

<u>*ዓላማ ናይዚ መጽናዕትን ናቶም/ናተን ተሳትፎን*</u>

ሓፈሻዊ ዕላማ እዚ መፅናዕቲ ኣብ ኮምፕሬሄንሲቭ ስፔሻላይዝድ ሆስፒታል ዓይደር ዘለዋ ሆርሞናል መከላከሊ ጥንሲ ተጠቀምቲ ኣብ ደመን ዉሽጢ ዘለዉ ዓቀን ሽኮርን መጠን ስብሕን ብምልካዕ ዝፍጠር ናይ ሽኮርን ስብሕን ምዝባዕ ዳህሳስ”ብዝብል ርእሲ ንምፅናዕ እዩ፡፡ ማለት እውን ኣብ ተጠቀምቲ ሆርሞናል መከላከሊ ጥንሲ ዘሎ ናይ ደም ዓቀን ሽኮርን መጠን ስብሕን

ምዝባዕ ንምፅናዕን ካብዚ መፅናዕቲ እዚ ብዝርከብ መረዳእታ ድማ ብቐንዱ ንነደፍቲ ፖሊሲን ንባዓል ሞያ ጥዕና ሓበሬታ ብምሃብ ዝክኣል ግንዛበ ንኽፍጠር ክግበር እዩ፡፡

<u>ተሳተፍቲ እዚ መጽናዕቲ ብኸመይ ይሕረዩ?</u>

ዒላማዊ መረፃ ተሳተፍቲ ምስኣካየድና እቲ ሓበሬታ ወሃቢ ወረቐት ክተንብብዎ/ኦ ክወሃበኩም/ን እዩ። ድሕሪ እዚ ተወሳኺ መብራህርሂ ክዋሃበክኩም/ን እዩ። ዝተወሰነ ሕቶታት ብምሕታት ሕድሕድ ነጥቢ ከምዝተረደኣኩም/ክን ምስ ኣረጋገጽኩ ኣብዚ መጽናዕቲ ንምስታፍ ድሌት ዘለዎን ሆርሞናል መከላከሊ ጥንሲ ተጠቀምቲን ዘይተጠቀምቲን ብድሌተንን ፈቃደንን ኣብቲ ናይ ስምምዕ ቕጥዒ ብምፍራም የረጋግፃ። ብድሌተን ምስገለፅክናልና ነዚ መፅናዕቲ እዚ ዝተዳለዉ ሕቶታት ብቐደም ሰዓብ ብምሕታትን ነቲ ዕንዓት ዘድሊ 5 ሚ/ሊ ናይ ደም ናሙና ካብ ደመ ሰራዉር ኢድክን ብምዉሳድ ዝከኣል መልሲ ክንረክብ ኢና፡፡

<u>ኣብዚ መጽናዕቲ ብምስታፍክን እንታይ ጥቕሚ ይረኽባ?</u>

ምስ እዚ መጽናዕቲ ዝተተሓሓዘ ንተሳተፍቲ ዝኽፈል ቀጥታ ክፍሊት ከምዘይህሉ ክንገልጽ ንፈቱ። ኮይኑ ግና ካብዚ መፅናዕቲ እዚ ብዝርከብ ሓበሬታ መሰረት ሆርሞናል መከላከሊ ጥንሲ ኣብ ናይ ደም ዓቀን ሹክርን መጠን ስብሕን ዘምፅኦ ለዉጥን ተፅዕኖን ኣብ ግንዛበን ኣብ ምምራፅ ዝሓሸ መከላከሊ ጥንሲን ከም ውልቀ ሰብ ኮነ ከም ዓዲ ተረባሒት እየን ኢለ የኣምን፡፡

<u>ኣብዚ መጽናዕቲ ብምስታፊይ እንታይ ጉድኣት ክበጽሐኒ ይኽእል?</u>

እዚ መጽናዕቲ ናይ ተሳተፍቲ ድሕንነት፣ ክብርን መሰልን ብዝለዓለ ደረጃ ብዘረጋገፀ ክይዲ ንኽፍፀም ዓብዪ ጥንቃቐ ክገብር ኢየ። እቲ ዝእከብ ናሙና ብበዓል ሞያታት ስለ ዝኮነ ምስዚ ተተሓሒዙ ዝመፅእ ምንም ዓይነት ሳዕቤን የለን፡፡ ኮይኑ ግና ናሙና ኣብ ዝዉሰደሉ ከባቢ ዝተወሰነ ናይ ሕማም ስምዒት ክህሉ ይክእል እዩ፡፡ብስሩ እውን ግን ኣብዚ መጽናዕቲ ንተሳተፍቲ ጉድኣት ዘብጽሕ ወይ ከዓ ናብ ሓደጋ ዘጋልጽ ተግባር የለን። ነዚ ቃለ መሕትት 20 ደቒቃ ግዜኦም/ኣን ክህቡ/ባና እዮም።

<u>እቲ መጽናዕቲ ከቋርፆ ይኽእል ‘ዶ?</u>

ቅድም ኢሉ ከምዝተገለፀ ኣብዚ መፅናዕቲ ምስታፍ ሙሉእ ንሙሉእ ኣብ ሰናይ ድሌት ተሳተፍቲ ዝተመርኮሰ እዩ። ኣብ ከይዲ ካብቲ መጽናዕቲ ምቁራጽ ይከኣል እዩ። ስለዘቋረፃ ዝበጽሖን ዝኾነ ዓይነት ክፍሊት ይኹን ቅጽዓት ኣይህሉን፡፡

ካብ ተሳተፍቲ እንወስዶ ሓበሬታ ምስጢራውነት ብዝምልከት

ካብ ተሳተፍቲ እንወስዶ ሓበረታ ናይመን ምኻኑ ብዘየፍልጥ መንገዲ ብኮድ እዩ ክፍፀም። ስለዚ ነዚ ፅነዓት ኢሎን ዝሃቦኦ ሓበሬታ ምስጢሩ ዝተሓለወ እዩ፡፡

ምዝርጋሕ ውፅኢት ናይዚ መፅናዕቲ ዝምልከት

ውፅኢት ናይዚ መፅናዕቲ ብመልክዕ ሕታም ወይ ከዓ ኣብ ኮንፈረንስታት ብምቕራብ ክሰራጮ/ክዝርጋሕ እዩ። ከከም ኣድላይነቱ ካልኦት ሜላታት እናተጠቀምካ እውን እቲ ውፅኢት ናይ ምዝርጋሕ ስራሕቲ ክስራሕ ይኽእል እዩ።

ንመን ክረኽቡ/ባ ይደልዩ/ያ?

ኣብቲ ፅንዓት ዝልዓል ሕቶ እንተሃልይዎም/ን ዋና ተመራማሪ በዚ ዝስዕብ አድራሻ ምርካብ ይክእሉ/ላ፡

ሰዓረ ተክላይ

ስልኪቁፅሪ:0937019181

ኢሜይል:Seareteklay555@gmail.com

ልቃብ 1.1: <u>ኣብ ኣፍልጦ ዝተመስረተ ናይ ተሳታፉይነት ስምምዕነት</u>

ዓላማ ናይዚ መፅናዕቲ ብዛዕባ ኣብ ኮምፕሬሄንሲቭ ስፔሻላይዝድ ሆስፒታል ዓይደር ዘለዋ ሆርሞናል መከላከሊ ጥንሲ ተጠቀምቲ ኣብ ደመን ዉሸጢ ዘለዉ ዓቀን ሹከርን መጠን ስብሕን ብምልካዕ ዝፍጠር ናይ ሹከርን ስብሕን ምዝባዕ ጸህሳስ"ብዝብል ርእሲ መረዳእታ ንምእካብ ም'ኳኑ ብዝግባእ ተረዲአ ኣለኹ፡፡ ዝርዝር ብዛዕባ ንተሳተፍቲ ዝዋሃብ ሓበሬታ ወሃቢ ጽሑፍ እውን ኣንበበን ተነቢቡለይን ኣሎ፡፡ ዘይበረሀለይ ሕቶ ናይምሕታት እ'ኹል ዕድል ዝረኸብኩ እንት'ኽውን ዝግባእ እ'ኹል መልሲ እውን ተዋሂቡኒ እዩ፡፡ ብተወሳኺ ብሰናይ ድለየተይ ኣብዚ መፅናዕቲ እዚ እናተሳተፍኩ እንት'ኾን ኣብ ዝደለኽዎ ግዜ ብዘይዝኾነ ምቅዋስ/ሃሰያ ማሕበራዊ ሂወት ወይካዓ ጥዕናዊ ኣገልግሎት ካብዚ መፅናዕቲ ምስታፍ ዓርሰይ ከግልል ዝኽእል ም'ኳነይ ተረዲአ ኣለኹ፡፡

1. እወ፣ ብዝግባእ ☐
2. ኣይፋል ☐

ልቃብ 1.3. መሕትት (ስርሒት ትግርኛ)

ብሆርሞናል መከላከሊ ጥንሲ ተጠቀምቲን ዘይተጠቀምቲን ዝምለሱ ሕቶታት		
ናይ ተሳታፊ ካርድ ቁፅሪ/መ.ቁ		…………………..
ታ. ቁ	1.ማሕበራዉን ስነ-ህዝባውን ኩነታት	
001	ዕድመ ብዓመት	…………..
002	ኩነታት ሓዳር	ሀ) ዝተመርዐወት ለ) ዝተፋተሐት ሐ) ሓዳር ዘይብላ (ሰብኣያ ዝሞታ) መ) ካሊእ………
003	ናይ ትምህርቲ ደረጃ	ሀ) ምንባብን ምፅሓፍን ዘይትክእል

		ለ) ምንባብን ምፅሓፍን ትክእል ሐ) 1ይ ብርኪ (1-8) መ) 2ይ ብርኪ (9-12) ረ) ኮለጅን ካብኡ ንላዕልን
004	ኩነታት ስራሕ	ሀ) ስራህ ዘየብላ (ናይ ገዛ ስራሕ) ለ) ተቆፃሪ (ኣብ መንግስቲ) ሐ) ሓረስታይ መ) ነጋዲት ካሊእ………
005	እምነት	ይገለፅ………….
	2. ኩነታት ጥዕናን መካላከሊ ጥንስን ኣዶ	
006	ሱሩዕ ምንቅስቃስ ትገብሪ ዶ?	ሀ) ኣወ ለ) ኣይፋሉን
007	ጥንሲ ትጥርጥሪ ዲኺ?	ሀ) ኣወ ለ) ኣይፋሉን
008	እዞም ዝተገለፁ ወይ ዉን ካሊእ ሕዱር ናይ ጥዕና ፀገም ኣለዉኺ ድዮም?	ሀ) ሕማም ልቢ ለ) ሕማም ፀላም ከብዲ ሐ) ሕማም ኮላሊት መ) ካሊእ እንተሃልዩ ይገለፅ…
009	እንድሕር ን ቁፅሪ 009 መልሰን እወ ኮይኑ ነቲ ሕማም ንምቁፅፃር ዝወስዶኦ መድሓኒት እንተሃልዩ ምዘርዘራልና ዶ ወይ መርኣያና ዶ?	……………………………………………………
010	መጥቦቢት ዲኺን?	ሀ) ኣወ ለ) ኣይፋሉን

011	ትጥቀሞኦም ወልፊታት ኣለዉ ድዮም?	ሀ) ኣልኮል ለ) ጫት ሐ) ሺጋራ መ) ካሊእ………
012	መከላከሊ ጥንሲ ትጥቀሚ ዶ?	ሀ) ኣወ ለ) ኣይፋሉን
እንድሕር ን ቁፅሪ 012 መልሰን እወ ኮይኑ ናብ ዝቅፅል ተራ ቁፅሪ 013 ን 014 ብ ብሆርሞናል መከላከሊ ጥንሲ ተጠቀምቲ ጥራሕ ዝምለስ ይሕለፉ		
013	እንታይ ዓይነት ሆርሞናል መከላከሊ ጥንሲ ትጥቀሚ?	ሀ) ብኣፍ ዝወሓጥ ናይ 30 ማዓልቲ ከኒን(ከኒና) ለ) ኣብ ቅልፅም ኢድ ዝዉጋእ ናይ 3 ወርሒ መርፌእ ሐ) ኣብ ቅልፅም ኢድ ዝቅበር ናይ 3 ዓመት ኢምፕላኖን መ) ኣብ ቅልፅም ኢድ ዝቅበር ናይ 5 ዓመት ኢምፕላኖን
014	እቲ ትጥቀሞኦ ሆርሞናል መከላከሊ ጥንሲ ጠቅላላ ብዘይ ምቁራፅ ንክንደይ ወርሒ ወሲድክን?	ሀ) ብኣፍ ዝወሓጥ ናይ 30 ማዓልቲ ከኒን(ከኒና) ብ ወርሒ………… ለ) ኣብ ቅልፅም ኢድ ዝዉጋእ ናይ 3 ወርሒ መርፌእ ብ ወርሒ……. ሐ) ኣብ ቅልፅም ኢድ ዝቅበር ናይ 3 ዓመት ኢምፕላኖን ብ ወርሒ........... መ) ኣብ ቅልፅም ኢድ ዝቅበር ናይ 5 ዓመት ኢምፕላኖን ብወርሒ…………….
3. ኣንትሮፖሜትሪክ መዐቀኒ		
015	ቁመት…………. ክብደት…………	ተሰለሐ (ክብደት/ቁመት^2) ……….

4. ባዮ ኬሚካል መለክዕታት/ላቦራቶሪ ወጺኢት		
	መለክዒ	ወጺኢት
016	HDL-C	.... (mg/dl)
017	LDL-C	.... (mg/dl)
018	TC	.... (mg/dl)
019	TG	.... (mg/dl)
020	FBS	.... (mg/dl)

Figures

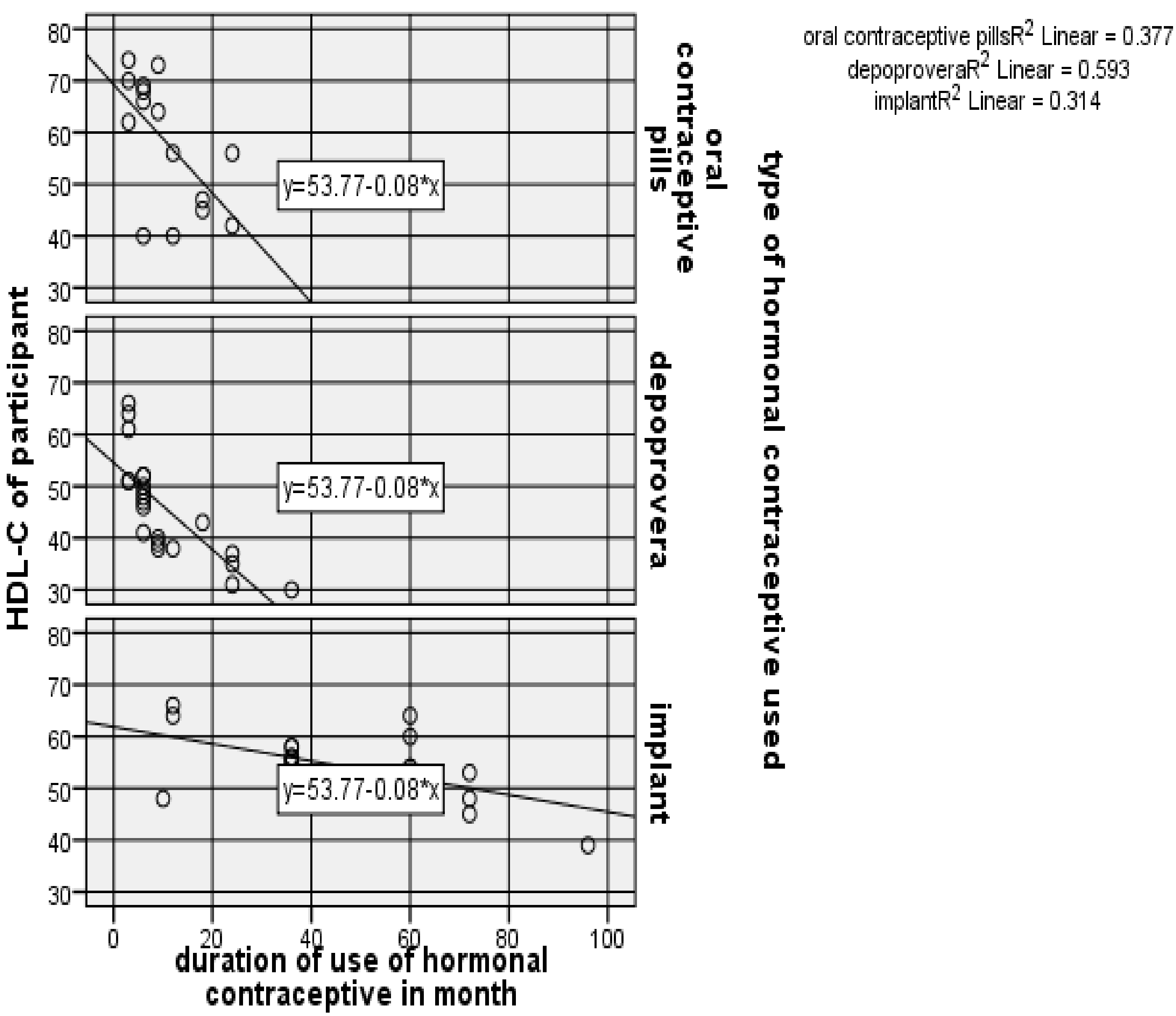

Figure - 1 : The correlation between HDL-c and duration of use of hormonal contraceptive in month in Ayder Comprehensive and Specialized Hospital, Tigray, North Ethiopia, 2024

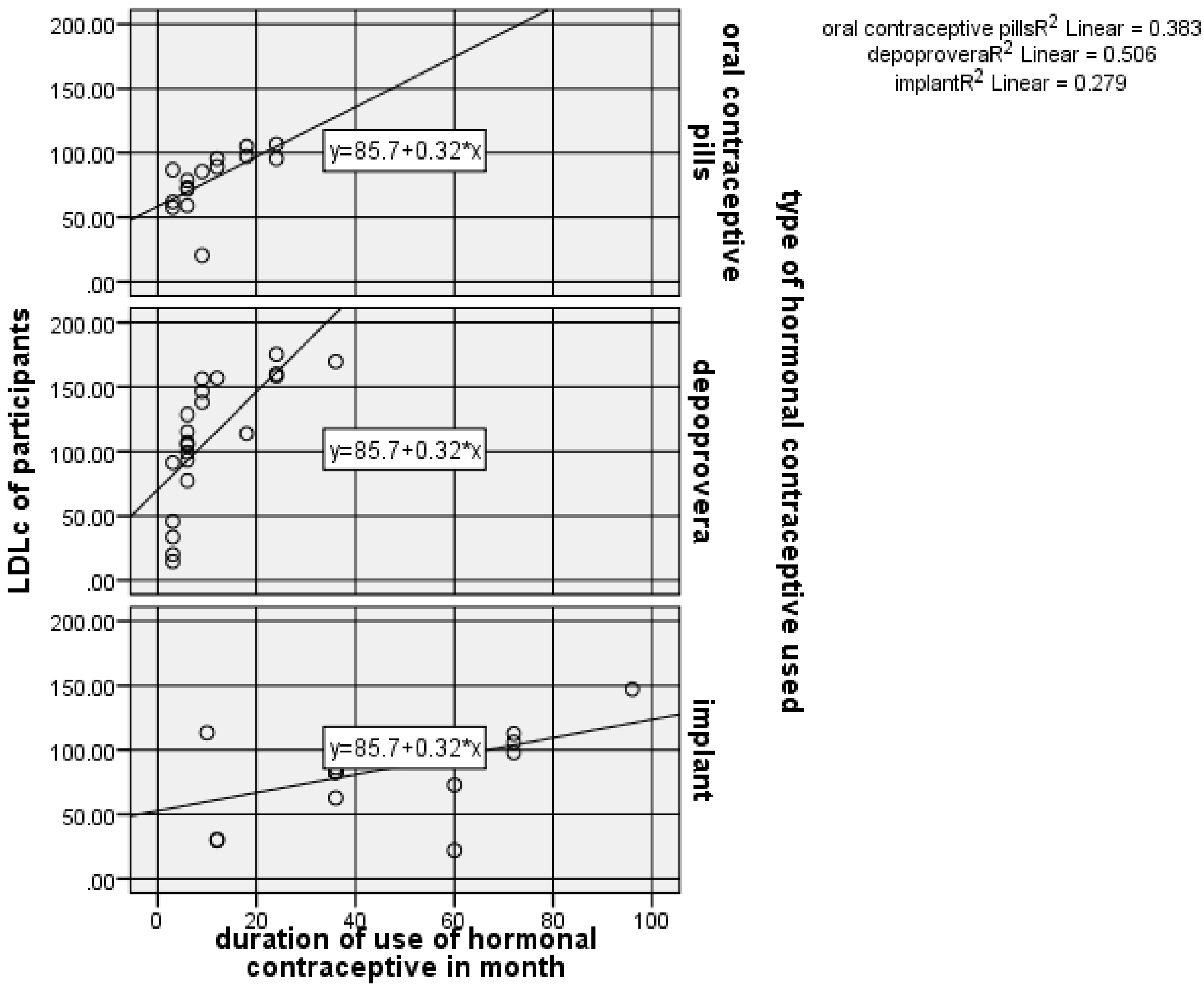

Figure -2: The correlation between LDL-c and duration of use of hormonal contraceptive in month in Ayder Comprehensive and Specialized Hospital, Tigray, North Ethiopia, 2024

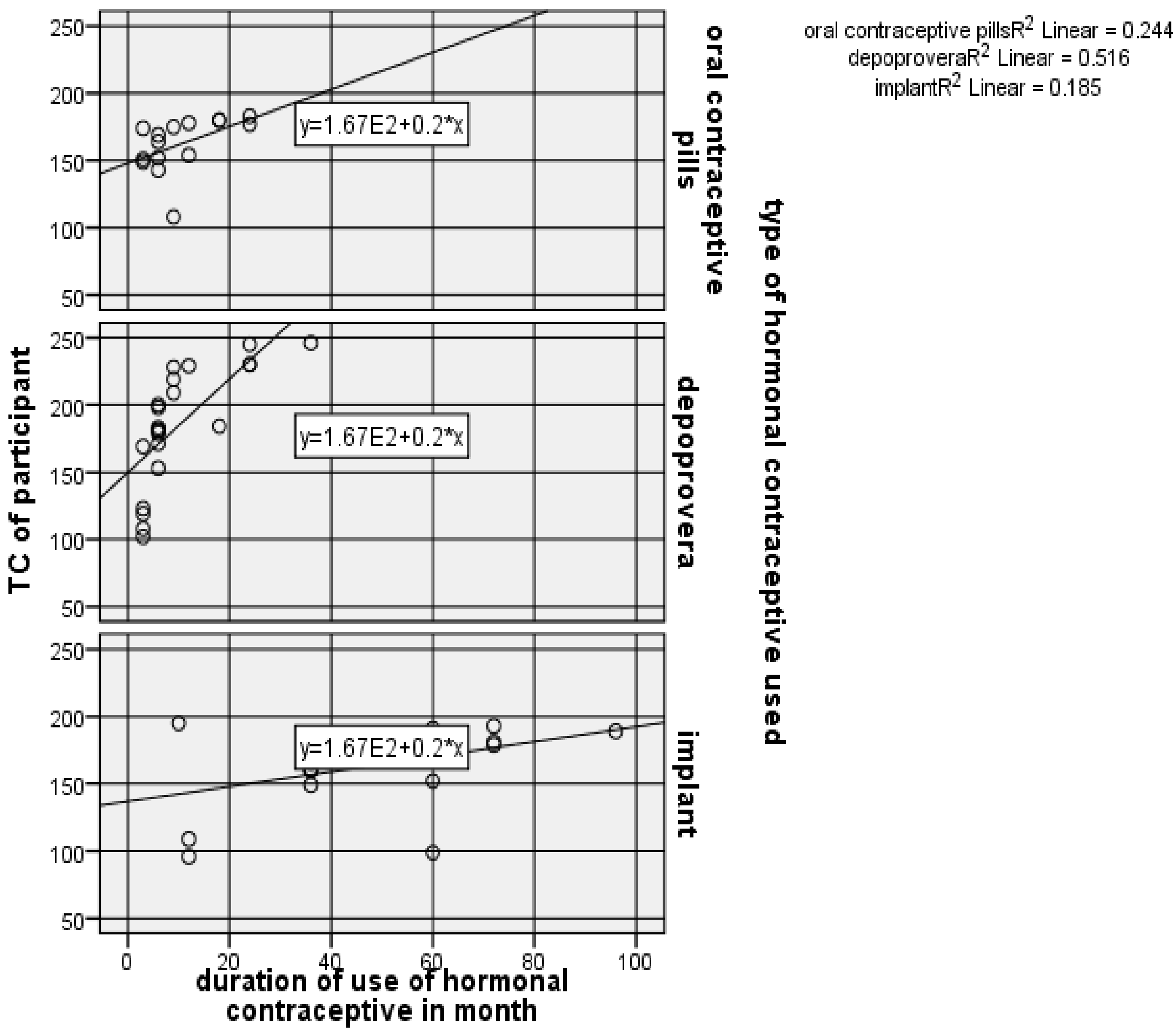

Figure _3: The correlation between TC and duration of use of hormonal contraceptive in month in Ayder Comprehensive and Specialized Hospital, Tigray, North Ethiopia, 2024

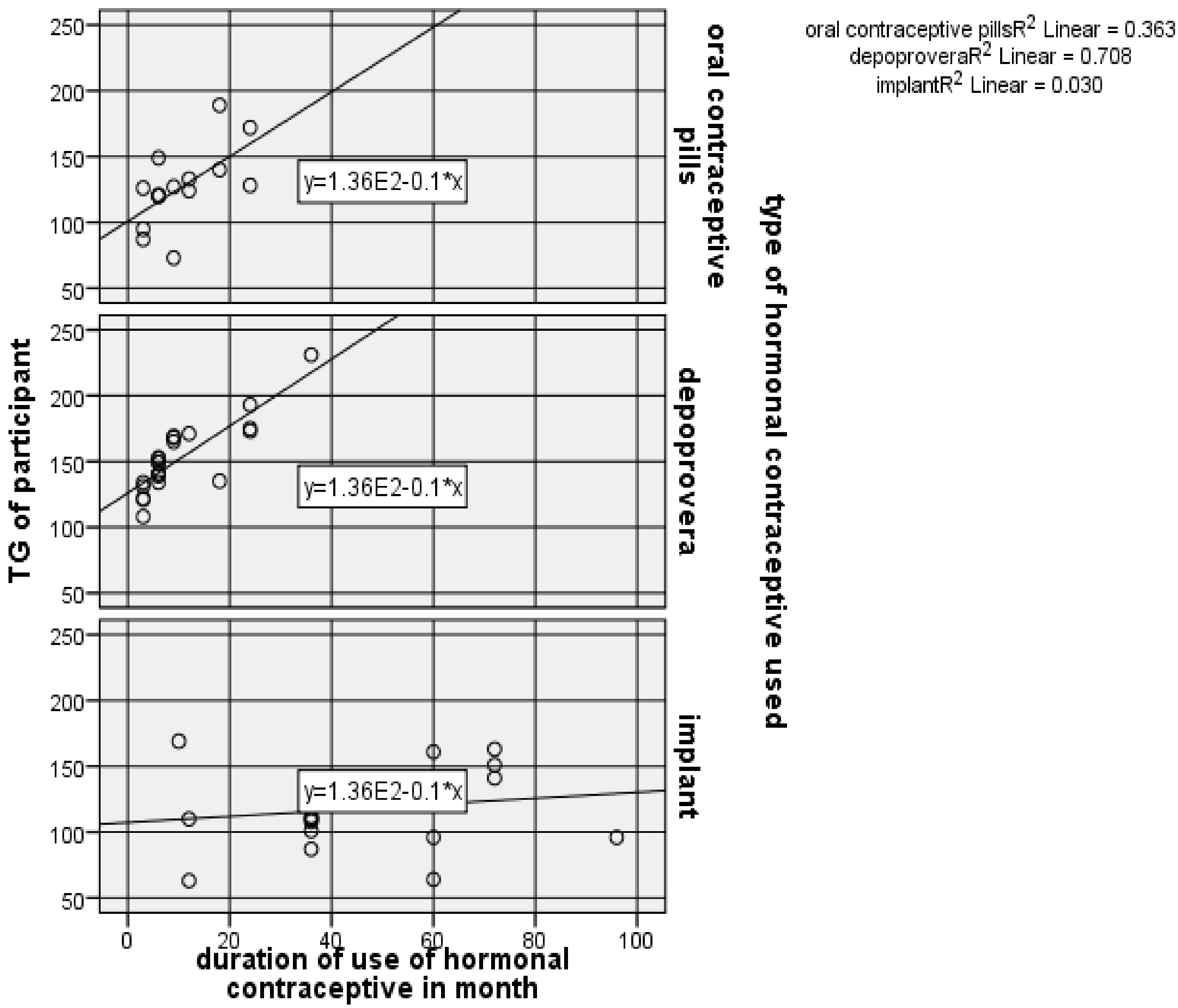

Figure _4: The correlation between TG and duration of use of hormonal contraceptive in month in Ayder Comprehensive and Specialized Hospital, Tigray, North Ethiopia, 2024

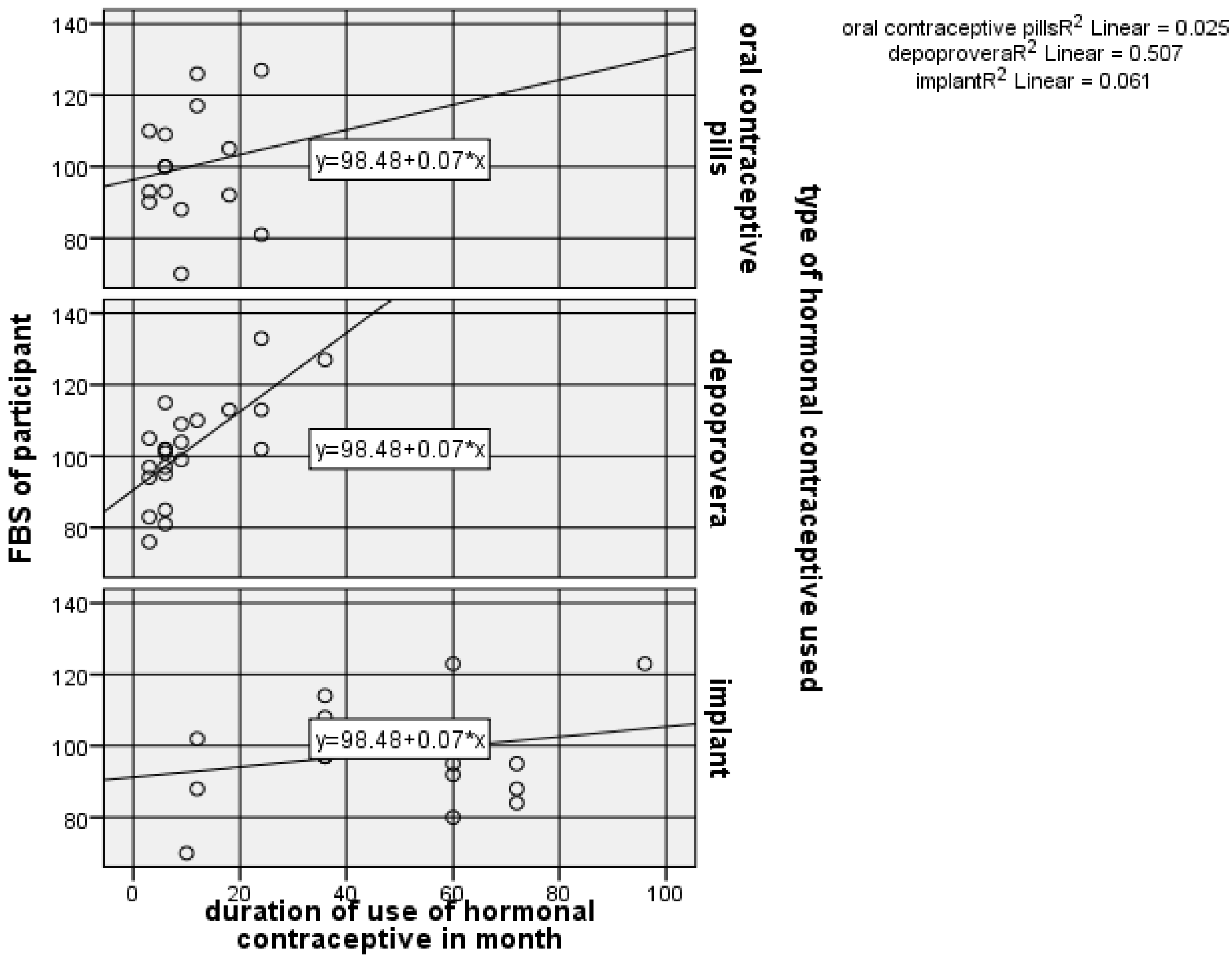

Figure -5: The correlation between HDL-c and duration of use of hormonal contraceptive in month in Ayder Comprehensive and Specialized Hospital, Tigray, North Ethiopia, 2024

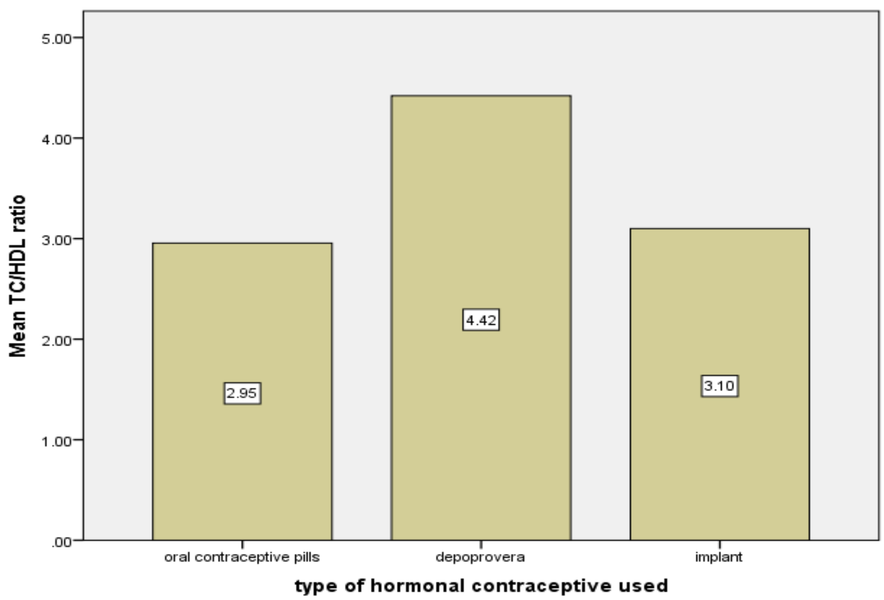

Figure -6: Castelli Indices I (Total cholesterol- HDL ratio) of hormonal contraceptive users in Ayder Comprehensive and Specialized Hospital, Tigray, North Ethiopia, 2024

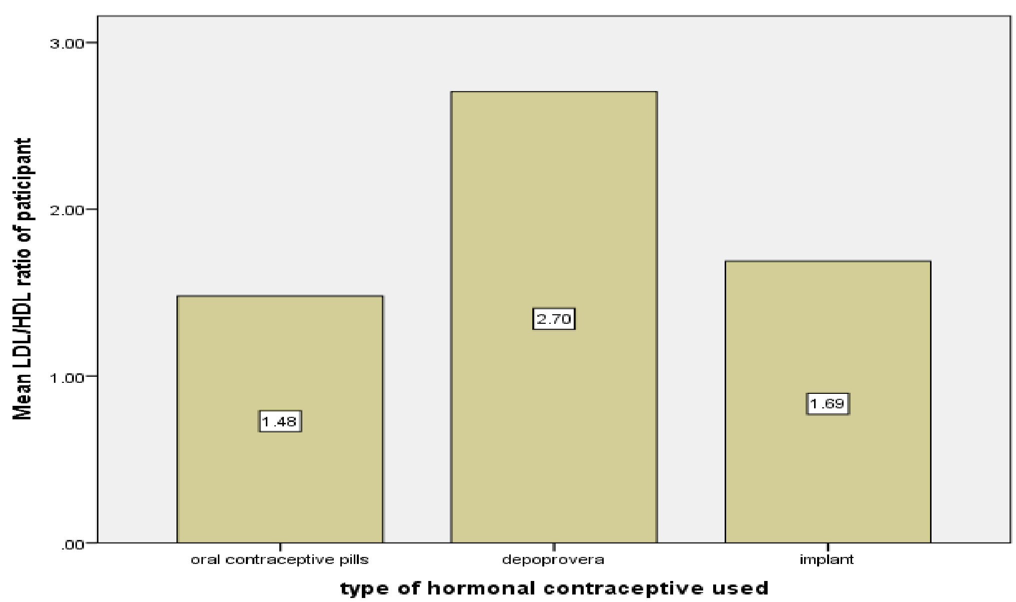

Figure- 7: Castelli Indices II (LDL- HDL ratio) of hormonal contraceptive users in Ayder Comprehensive and Specialized Hospital, Tigray, North Ethiopia, 2024

13. Operational definition

Contraceptives - birth control methods that include pills, Depo-Provera, IUCD, implant, natural or surgical procedures to prevent conception.

Hormonal contraceptive users - women who have been using oral contraceptive pills, Depo-Provera, Implanon, or Norplant.

Apparently healthy volunteer women - An individual who has no sign, symptoms or history of any disease and who wanted to participate in the study for the purpose of health checkup at the time of data collection.

Chronic alcohol use is defined as a persistent pattern of alcohol use characterized by the consumption of a large amount of alcohol, unsuccessful efforts to reduce alcohol consumption, and a strong desire to use alcohol (64).

Lipid profile - a panel of blood tests of TC, TG, HDL-c, and LDL-c.

Blood glucose level - a panel of blood test of fasting blood sugar.

Castelli risk index - lipid ratios are estimated as TC/HDL-c and LDL-c/HDL-c to predict cardiovascular disease risk.

Castelli risk index I - lipid ratios estimated as TC/HDL-c.

Castelli risk index II - lipid ratios estimated as LDL-c/HDL-c.

Castelli risk index classification -A ratio of < 3 indicates a below average, but not absent risk. A ratio of 3–5 indicates average risk. Ratios > 9 clearly pose a marked elevation in risk according to Framingham study (65).