Pattern of Fasting Blood Sugar, Blood Pressure and Body Mass Index among Combined Oral Contraceptive (COC) Pills Users in Chencha, Southern Ethiopia: a cross-sectional study

Zelalem Kofole (kzelalem2008@gmail.com)
Arba Minch University

Diresbachew Haile
Addis Ababa University School of Medicine

Yerukneh Solomon
Debre Berhan University

Eyayu Girma
Arba Minch University

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Abstract

Background: The use of contraceptives has become prevalent among women in Ethiopia. Oral contraceptive use has been suggested to trigger changes in glucose metabolism, energy expenditure, blood pressure, and body weight, among the various populations and ethnic groups.

Objective: To elucidate the pattern of fasting blood sugar (FBS), blood pressure and body mass index (BMI) among combined oral contraceptive (COC) pills users, taking into account other confounding factors including socioeconomic conditions and physical activity status. Methods: An institution based cross-sectional study design was employed. A total of 110 healthy women using pills were recruited as cases. Another 110 healthy women not using any hormonal contraceptives were recruited as matched controls. A study was conducted between October 2018 and January 2019. Fasting Capillary blood sample was collected from the study participants for the estimation of the FBS level. Systolic and diastolic blood pressures were measured and means arterial blood pressure was calculated for each participant. Body weight and height were measured to compute body mass index. Data obtained was entered and analyzed using IBM SPSS version 23 software packages.

Results: FBS level in users was significantly increased compared to controls (88.55 ± 7.89 vs. 86.00 ± 9.85 in users and controls respectively, P = 0.025). There was a significant difference in mean arterial blood pressure of users compared to controls (88.2 ± 8.48 vs. 86.0 ± 6.74 respectively, P=0.04). The mean weight and body mass index of users were significantly increased (P = 0.03 and P = 0.003, respectively). Changes in mean fasting blood sugar level and mean weight of users were independent (P = 0.27 and P = 0.46) to the duration of use (3-12, 13-24 and ≥ 25 months). On the other hand, changes in mean body mass index and mean arterial blood pressure of users were dependent of the duration of use (P = 0.03 and P = 0.000 respectively).

Conclusions: Overall, oral contraceptive pills use appears to cause a 2.9% increase in fasting blood glucose level, a 2.5% increase in mean arterial blood pressure and a 3.9% increase in body mass index among the users.

Background

In the early 1960s, the oral contraceptive pill, ' the pill, ' was introduced [1]. Since its launch, there have been significant improvements in the formulation of COC pills in terms of the type and dosage of both estrogen and progestin in order to balance their risks and benefits [2]. Currently, there are two types of pills available in the market; combined pills containing both estrogen and progesterone and progestin-only pills. There are three formulations of pills, which are mono-phasic, biphasic and triphasic. Some pills contain estrogen called mestranol, which combined with various types of progestin that use the single-dose throughout the month (monophasic) or at increasing weekly dose (biphasic or triphasic) [3]. Pills are categorized in generations depending on the timing of their product release, the dose of estrogen and the type of progestin used. First-generation pills contain high doses of estrogen (150 µg) which is associated

with increased metabolic and thrombotic side effects. In the second-generation pills the dose of estrogen reduced by more than half from the first generation (50 µg). Currently available preparations contain lower estrogen doses (20–35 µg) Ethiniyl estradiol with lower metabolic and thrombotic side effects. The first and second generation progesterone (norethindrone and ethynodiol diacetate) and (levonorgestrel and norgestrel) respectively are associated with more androgenic side effects. The third generation (desogestrel, norgestimate, and gestodene) and the fourth generation (chlormadinone acetate and drospirenone) have less androgenic and metabolic side effects [4]. More recently, with a shift in the form of estrogen, COC products have been launched on the market. In order to overcome metabolic effects and reduce the thrombotic risk of formulations with Ethinyl estradiol, a naturally occurring human hormone, estradiol, and estradiol valerate are used. In homeostasis and metabolism trials, a recently approved four-phase pill containing estradiol valerate and dienogest has shown positive results [5]. Today, about 100 million women around the world are currently users of combined hormonal contraceptives, most widely used in the western world. In fact, about 80 percent of all women in the U.S. can be viewed as consumers of all time. This could make hormonal contraceptives one of the prescription drugs most widely used in the world [6]. The main contraceptive effect of COC pills is via negative feedback inhibition of the hypothalamus-pituitary-ovarian axis, which is designed to suppress the secretion of pituitary gonadotropins which, in turn, prevents follicular maturation, ovulation, and subsequently prevent pregnancy [7]. Progestin prevents ovulation, mediated by a negative feedback mechanism resulting in a decrease in luteinizing hormone. Progestin also reduces cervical mucus receptivity of the sperm. Estrogen contributes to the anti-ovulatory mechanism of COC pills by suppressing both follicle -stimulating hormones and luteinizing hormone [8]. The drug is contraindicated for those women with thromboembolic disorders, known or suspected malignancy of the breast and cervix, severe hypertension, cerebrovascular accident (stroke), acute myocardial infarction, being smoker and over 35 years old at the same time and severe liver dysfunction [9–11].

Methods

Study area and period

The study was conducted at three health centers, found in Chencha Woreda, between the months of October 2018 and January 2019. The Woreda is located at 484 km south of Addis Ababa, the capital of Ethiopia. The total population size of the district estimated to be 143,560. According to the information obtained from the Woreda health office; there are five health centers, which render family planning services for the community.

Study design and subjects

An institution-based cross-sectional study design was employed on 220 subjects in two groups. 110 healthy women who had been using COC pills were grouped as cases and 110 healthy matched controls that were not using any hormonal contraceptive. Both groups were comparable in age, income, baseline weight, physical condition, and nutritional status.

Inclusion Criteria

Aged between 18 to 45 years, clinically stable and COC pills use for more than 3 months included in the study as cases and healthy women who have the same inclusion criteria as users, but not using pills were included as controls.

Exclusion Criteria

Age less than 18 and over 45, chronic alcohol and/or tobacco use, pregnancy, breastfeeding, women who were using other hormonal contraceptives, chronic co-morbidities (thromboembolic disorders, cardiovascular disorders like hypertension, cerebrovascular accident like stroke, chronic renal disease, chronic liver disease, diabetes mellitus), and BMI ≥ 30 kg/m^2 were excluded from the study.

Sample Size Determination and Sampling

The two-sided population proportion formula was used for the determination of sample size. The prevalence for users was 35% and for controls was 18%, taken from previously published studies.

$$n = \frac{(P_1q_1 + P_2q_2)\,(z_{1-\alpha/2} + z_{1-\beta})^2}{(P_1 - P_2)^2}$$

The total sample size was 220; 110 for study subjects and 110 for the control group after adding 10% of the non-response rate. There are five health centers in Chencha woreda, from which three health centers were selected randomly. From two health centers, 37 cases were selected and 36 cases were selected from the third health center randomly. Similar numbers of controls subjects were selected from the aforementioned health centers by convenient sampling.

Data Collection Procedure

A structured questionnaire that is modified form of the world health organization was used for the purpose. A pretested questionnaire pertinent to the study objectives was developed and used. All women were screened for eligibility based on a medical interview, and those who volunteered to participate in the study were recruited. Study participants answered questions in the questionnaire, which were relevant to their socio-demographic and physical activity information. Afterward, blood pressure, height, and body weight of each participant was measured. The capillary blood sample was collected from each participant following overnight fasting, for estimation of fasting blood sugar.

Data processing and analysis

SPSS software version 23 was used for data management and statistical analysis. Standard statistical methods were used to determine the mean, standard deviation, and range. Independent samples t-test was used to compare the results of the FBS level, blood pressure and BMI of cases with the control group.

One way ANOVA was used to identify the variation of variables in relation to the duration of use of the drug. The P-value of < 0.05 at the 95% confidence level was considered to be statistically significant.

Results

Socio demographic characteristics

This institution based cross-sectional study was conducted to investigate the pattern of fasting blood sugar, mean arterial blood pressure, body weight and body mass index among pills users. A total of 220 study participants (110 cases, and 110 controls) were included in the study. All study participants in both groups were healthy, and no woman reported a history of any chronic diseases (hypertension, diabetes mellitus, liver disease, renal disease). Socio demographic characteristics of study participants were listed in (Table 1) blow.

Table 1
Participant Characteristics, Including Marital Status, Income/month, Age (in years), Educational Status, Occupation and Ethnicity in Chencha South Ethiopia.

Variables		**Cases (n =110)**	**%**	**Controls (n = 110)**	**%**
Marital status	Married	108	99	88	80.0
	Single	2	0.9	22	20.0
Monthly Income in Ethiopian Birr	≤ 1500	64	58.2	52	47.3
	1501–3000	30	27.3	40	36.4
	> 3000	16	14.5	18	16.4
Age (in Years)	< 20	0	0	1	0.9
	20–30	70	63.6	82	74.5
	> 30	40	36.4	27	24.5
Educational status	Illiterate	20	18.2	29	26.4
	Read and write	22	20.0	7	6.4
	Primary education	9	8.2	6	5.4
	Secondary education	33	30.0	24	21.8
	College and above	26	23.6	44	60.0
Occupation	Housewife	55	50.0	38	34.4
	Governmental	20	18.2	36	32.8
	Private	35	31.8	36	32.8
Ethnic group	Gamo	105	95.5	106	96.4
	Wolaita	1	0.9	1	0.9
	Gofa	4	3.6	3	2.7

Physical Activity Status of Participants

All participants in both groups were physically active (Fig. 1) below.

Use of Combined Oral Contraceptive Pills

Pills users received the contraceptive regularly for a mean duration of 16 months, ranging from 3–36 months. The mean age at the beginning of use is 28.3 ± 3.45 with range 18–38 years.

Physical and Biochemical Measurements

Fasting blood sugar level in cases was increased by 2.9% from controls. Mean FBS level of cases was 88.55 ± 7.89 mg/dL and 86.00 ± 9.85 mg/dL in controls. The difference was statistically significant (P = 0.025), the range is 67–111 mg/dL and 64–109 mg/dL in cases and controls, respectively. There were 4.5% of the cases with FBS value ≥ 110 mg/dL. Even though it was significantly different between cases and controls, the one-way ANOVA analysis didn't show a statistically significant difference between groups of pills users in relation to the duration of use.

Mean arterial blood pressure of cases (88.2 ± 8.48 mmHg) and the control group (86.0 ± 6.74 mmHg) was significantly different (P = 0.04). The mean SBP of cases and controls were (121.8 ± 8.03 and 111.0 ± 8.12 mm Hg) respectively. This difference was significant (P = 0.000). The one-way ANOVA (Table 3) showed significant (P ≤ 0.05) changes in mean SBP, DBP and MAP between groups of pills users in relation to the duration of use.

Table 2
The Mean Fasting Blood Sugar Level, Mean Arterial Blood Pressure, Height, Weight, and Body Mass Index of Participants; in Chencha South Ethiopia.

Variables	Cases (n = 110), M ± SD	Control Group (n = 110), M ± SD	Mean Difference	% of Change	P-value
FBS (mg/dL)	88.55 ± 7.89	86.00 ± 9.85	2.55 mg/dL	+ 2.9	0.025*
SBP (mm Hg)	121.8 ± 8.03	111.0 ± 8.12	10.8 mm Hg	+ 9.7	0.000**
DBP (mm Hg)	72.8 ± 8.58	74.0 ± 7.06	1.2 mm Hg	-1.6	0.29
MAP (mm Hg)	88.2 ± 8.48	86.0 ± 6.74	2.2 mm Hg	+ 2.5	0.04*
Height (m)	1.63 ± 5.79	1.64 ± 5.73	0.01 m	-0.6	0.39
Weight (kg)	56.5 ± 4.88	55.1 ± 5.40	1.4 kg	+ 2.5	0.03*
BMI (kg/m^2)	21.3 ± 2.29	20.5 ± 1.82	0.8 kg/m^2	+ 3.9	0.003*

Where: BMI = Body mass index, FBS = fasting blood sugar, MAP = mean arterial blood pressure, SBP = systolic blood pressure, DBP = diastolic blood pressure, % = percentage of change, (+) = Increased from baseline, (-) = Decreased from controls, *=statistically significant, **=highly significant (P < 0.001), variables statistically significant at P < 0.05 and P-values were obtained by independent - samples t-test

Discussion

Fasting Blood Glucose Level

The finding from the present study suggests that the FBS level of cases was higher when compared to the controls. However, it still remained in the normal range for almost all users. Similar findings have been published in England [12] on the effect of different formulations of COC agents on lipid and carbohydrate metabolism. The analysis showed that increased plasma glucose, which was (40–60%) higher in cases than controls. The percent of the increment is much higher than our findings. Another similar study in 1992 revealed the same result [13]. A study in Finland [14] found that consumers of COC pills had significantly higher mean serum glucose levels compared to their baseline values, with an increased risk of developing glucose metabolism abnormalities. In the present study, it is important to note that even though the FBS level has increased, only small number of COC pills user demonstrated abnormally high glucose level. We observed that only 4.5 percent of users of COC pills had FBS level of ≥ 110 mg/dL. This is significantly lower than the figure reported in Godsland et al cross-sectional study [12]. The mechanism through which hormonal contraception causes blood glucose levels to rise has yet to be elucidated. One possible mechanism as demonstrated in rats [15] investigated the influence of estradiol on the insulin receptor of ovariectomized rats treated with different hormonal doses. Results showed that high doses of estradiol decreased the sensitivity of insulin by the carbohydrate mechanism. Contrary to the findings of the present study, a cohort study conducted in Texas[16] reported changes in mean blood glucose level of users of COC pills were not significantly different from controls. This result was supported by a study [17] which recommended best practice in the prescription of hormonal contraceptives in women, especially those with diabetes mellitus.

This disparity may be due to the variation in the study protocol used in the previous and current research. Berenson's and co-workers ' study is a cohort study involving 703 participants, whereas the current cross-sectional study involved a comparatively small sample size of 220 people. The discrepancy may also be due to the age difference between the studies. Unlike the other study [16] whose age bracket is between 25 and 33 years, the participants in this study were aged between 18–45 years. Because the women in our sample also include subjects reaching menopause that are predicted to show high blood glucose level correlated with age. The disparity in gender, food habits and behaviors can also lead to the discrepancy.

Use of COC Pills and Blood Pressure

This study revealed that mean SBP and MAP values showed a statistically significant increment in cases as compared to their matched controls and among pill users in relation to the duration of use. Diastolic blood pressure was not different when compared to controls, but, it was significantly different among users in relation to the duration of use. Such results from this research were consistent with a study in Pakistan [18] that found significantly higher SBP and DBP among pill users than controls. A related follow-up analysis by Azima and Mousavi [19] found that one year after pills intake, SBP was significantly higher compared to the baseline level. Likewise, the study conducted in Korea [20] found similar results with current research that is prolonged use of oral contraceptive related to increased blood pressure than non-users. A cross-sectional study on blood pressure in women using COC pills in England [21] found that blood pressure among users was significantly higher than the controls. The Chronic use

of COCs, irrespective of estrogen concentration, can increase blood pressure in both normal and hypertensive women [22]. A similar study of hypertension among users of oral contraceptive pills conducted in Texas showed an increased blood pressure in both over the counter and clinic users of the pill [23]. Contrary to the present study, a follow-up study conducted in Minnesota, (24) reported that pill-users had a decrease in SBP and DBP after the 3rd, 6th, and12th month of follow-up. Earlier studies have shown the relationship between use of the contraceptive pill and raise of blood pressure [25]. Recent research also highlighted that, estrogen containing hormonal contraceptives always changes the blood pressure by increasing hepatic production of angiotensinogen, which in turn causes the renin-angiotensin-aldosterone system to elevate the blood pressure [26, 27].

COC use, Body weight and BMI

Results from this study showed that users of pills had significant weight gains and increased BMI compared to control groups. This is in line with a study carried out in Thailand [28] on the effect of the use of COC pills on BMI and blood pressure, according to which the use of pills containing estrogen and progestin tends to increase BMI and body weight. Another study of the effect of COC pills on lipid profile, blood pressure and BMI in Pakistan [18] also showed similar results with this report. While another study in Minnesota indicated that pills users pose increased body weight in comparison to their controls, however, changes were not statistically significant [24]. The disparity found between the studies could be attributed to the difference in race associated with a genetic weight gain predisposition, where black women had a higher mean weight gain compared to white [29]. However, the existing literature does not provide a clear picture of the mechanism of COC pills use related weight gain. Theoretically, the biological mechanism for contraceptive-induced weight gain could be attributed to fluid retention secondary to the activation of the mineralocorticoid and/or renin-angiotensin-aldosterone system and/or an increase in subcutaneous fat secondary to an increase in appetite and food intake caused by hormones [30,31].

Table 3
Mean Changes in Serum FBS Level, SBP, DBP, MAP, Weight, and BMI in COC Users with Relation to the Duration of Use, in Chencha South Ethiopia.

Parameters	Duration use (Month)	N = 110	M ± SD	P-value
Change in mean FBS (mg/dL)	3–12 13–24 ≥ 25	42 50 18	87.3 ± 6.40 89.9 ± 5.96 87.7 ± 13.73	0.27
Change in mean SBP (mm Hg)	3–12 13–24 ≥ 25	42 50 18	115.2 ± 5.52 125.6 ± 6.44 126.7 ± 6.86	0.000**
Change in mean DBP (mm Hg)	3–12 13–24 ≥ 25	42 50 18	70.0 ± 9.37 74.6 ± 7.62 74.4 ± 7.84	0.024*
Change in mean MAP(mm Hg)	3–12 13–24 ≥ 25	42 50 18	83.3 ± 9.45 91.1 ± 6.16 91.4 ± 6.47	0.000**
Change in mean Weight (kg)	3–12 13–24 ≥ 25	42 50 18	56.5 ± 4.98 56.1 ± 3.88 57.8 ± 6.87	0.46
Change in mean BMI (kg/m^2)	3–12 13–24 ≥ 25	42 50 18	21.3 ± 2.16 20.9 ± 1.93 22.6 ± 3.13	0.03*

Where: BMI = Body mass index, FBS = fasting blood sugar, DBP = diastolic blood pressure, MAP = mean arterial blood pressure, SBP = systolic blood pressure, *=statistically significant, **=highly significant ($P < 0.001$), variables statistically significant at $P < 0.05$ and P-values were obtained by one-way ANOVA.

Conclusions

The use of combined oral contraceptive pills induced changes in carbohydrate metabolism, manifested by a high fasting blood sugar level. This change in carbohydrate metabolism was independent of the duration of use. Women taking combined oral contraceptive pills showed a significant increment in mean arterial blood pressure compared to controls, which indicates its use did have unfavorable effects on blood pressure. Users had a significant increase in the body weight and body mass index when compared with the control groups, and this effect appeared to be dependent on the duration of use of the drug.

Abbreviations

BMI: Body Mass Index; COC pills: Combined Oral Contraceptive Pills; DBP: Diastolic Blood Pressure; MAP: Mean Arterial Blood Pressure; SBP: Systolic Blood Pressure

Declarations

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Authors' contributions

ZK and DH designed and implemented the study. ZK, DH, YS and EG contributed to the analysis and interpretation of the data. ZK and DH led the writing of the manuscript with significant contributions from YS and EG. All authors read and approved the final manuscript.

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This study was conducted by the research fund obtained from the Addis Ababa University. The funding body had no role in the design of the study, collection, analysis, and interpretation of data, or in writing the manuscript.

Availability of data and materials

The data that support the findings of this study are from different datasets (e.g. Google, Google Scholar), are included in the list of references.

Ethics approval and consent to participate

The study was carried out after ethical clearance and approval was obtained from the research committee of the Department of Physiology, Addis Ababa University. Additionally, permission to conduct the study in the area was also obtained from Chencha Woreda Health Office and the heads of health centers. Both verbal and written informed consents were obtained from each participant. The confidentiality was kept in place and code numbers were used to identify the subjects. The participants had a full right to refuse or discontinue the study without any precondition at any time of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

1, 4 Department of Biomedical Science, Arba Minch University, Arba Minch, Ethiopia. 2 Department of Physiology, Addis Ababa University, Addis Ababa, Ethiopia. 3 Department of Biomedical Science, Debre

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Figures

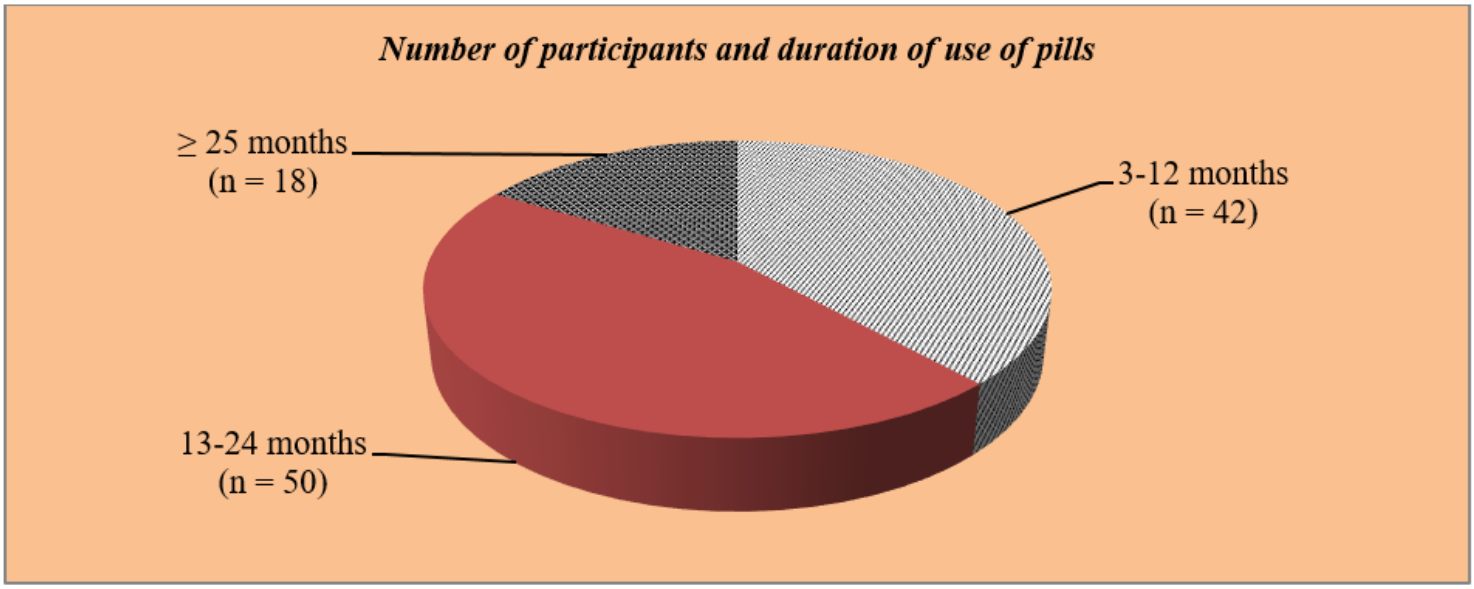

Figure 1

Bar Chart Indicating the Participant Physically Activity Status in Chinch, South Ethiopia.

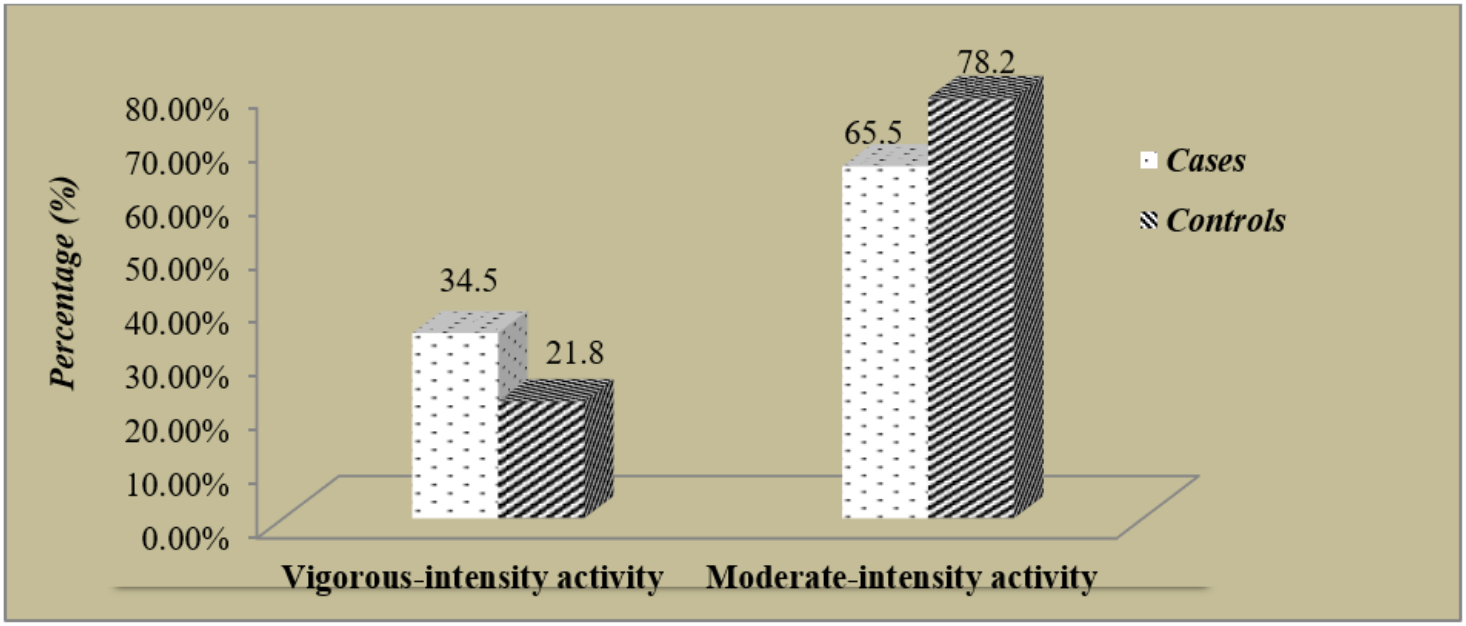

Figure 2

Duration of Use of oral contraceptive pills in Chencha, South Ethiopia