



## Evaluation of Different Biochemical and Hematological Parameters in Different Body Mass Index of Age Groups of Combined Oral Contraceptive Users

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### ABSTRACT

**OBJECTIVE:** To determine the effect of combined oral contraceptive pills (COC) on lipid profile, blood pressure and body mass index in the childbearing age women

**METHODOLOGY:** This analytical cross-sectional study was carried out in the Family Planning Department of Peshawar's tertiary hospital from January to December 2011 on 204 women of reproductive age group. Of which group I consisted of 102 subjects using COC, and group II was a control group of 102 subjects. They were further subdivided into 3 groups (A: 14-25 years, B: 26-36 years, C: 37-49 years), The goal of the current study was to find out the effect of COC on serum lipid profiles, BMI, and blood pressure. Computer software SPSS version 21 was used to analyse the data.

**RESULTS:** Significantly higher levels of total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL), high density lipoprotein (HDL) were measured in oral contraceptive users to confirm the impact of age on these various parameters, including VLDL, triglycerides, and systolic BP were noted in all three age groups of treated groups. When compared to the control group, all parameters were higher in the group C of COC users, TC by ( $p < 0.0027$ ), HDL by ( $p < 0.031$ ), LDL by ( $p < 0.051$ ), VLDL by ( $p < 0.0001$ ), triglyceride by ( $p < 0.0001$ ), fasting blood sugar (FBS) by ( $p < 0.00043$ ), BMI by ( $p < 0.0004$ ) and systolic BP by ( $p < 0.01$ ).

**Conclusion:** This study showed that combined oral contraceptives use causes changes in lipid profile, body mass index, and blood pressure. The metabolic risk factors associated with these increased values may result in cardiovascular disease.

**KEY WORDS:** Combined Oral Contraceptive Pills, BMI, Cardio metabolic risk factors.

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### INTRODUCTION

Contraceptive pills are used to prevent the ovum from fertilizing.<sup>1</sup> The daily drug taken orally to prevent conception, known as combined oral contraceptives (COC), contains a combination of the hormones estrogen and progestin.<sup>2</sup>

Worldwide, 100 million women of childbearing age utilize contraceptive tablets. About 18% of people using contraceptives worldwide use oral contraceptives as a reliable way of contraception.<sup>3</sup> In the United States, oral contraceptives are commonly used by around 11.6 million women, and 80% of American women who are childbearing age have taken oral contraceptives at some time during their lives. Urban Pakistan has a contraceptive prevalence that is 5.5% higher than rural Pakistan (9.8% vs. 3.9%) About 5% of women who used early, high-dosage formulation COC suffered hypertension, and some women who use formulations with the 30-35-g Ethinyl estradiol

(EE2) dose still experience a notable increase in blood pressure.<sup>4</sup>

The adrenal gland and gonads are the primary sites for steroid hormone synthesis. They regulate salt balance (mineralocorticoids), sexual function, energy metabolism, and energy metabolism as well as stress reactions (androgens and estrogens).<sup>5</sup> All steroids are synthesized from cholesterol. The initial steps of cholesterol mobilization and transport into the mitochondrial matrix for conversion to pregnenolone are regulated in steroid hormone synthesis. Pregnenolone's fate in the body is tissue-specific: it is converted to cortisol in the adrenal cortex's zona fasciculata, aldosterone in the zona glomerulosa, and estrone and estradiol in the gonads. Excessive blood cholesterol can assemble in the surrounding arterial walls, forming plaques. Bulk amounts of plaque add to the possibility of having a stroke or heart attack.<sup>5</sup> Kalwaska et al. in 2020 conducted a study, and they came to the conclusion that oral contraceptive users had noticeable effects on the enzymes, carbohydrates, lipids, and other hematological parameters. The

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high level of lipids exposes these COC users to the danger of heart disease due to excessive cholesterol levels in long-term COC users.<sup>6</sup>

George A Asare et al. 2014 conducted a study, and concluded that oral contraceptive users had noticeable effects on the enzymes, carbohydrates, lipids, and other hematological parameters. The high level of lipids exposes these COC users to the danger of heart disease due to excessive cholesterol levels in long-term COC users.<sup>7</sup>

This study was conducted to find out the effect of use of combined oral contraceptive pills in reproductive women of different age groups, on biochemical and hematological parameters, blood pressure, and body mass index in our setup.

## METHODOLOGY

This cross-sectional/analytical study was conducted in the Family Planning Departments of Peshawar's tertiary care facilities (Khyber Teaching Hospital, PGMI Lady Reading Hospital, and Hayatabad Medical Complex). We obtained institutional research ethics board (IREB) approval for the project.

A total of 204 women of reproductive age (15–50 years) were selected and enrolled in the study. The study's purpose was described, and written informed consent was obtained. There were two groups of these women: 102 women between the ages of 15 and 50 years taking combined oral contraceptives were included in group I. The same number of age-matched controls who weren't taking COC was included in group II.

All the women had no previous history of hypertension, diabetes mellitus, stroke, or renal or cardiac disease.

Fasting blood samples were sent to the laboratories for analysis immediately after venipuncture.

According to their reproductive years, the combined oral contraceptive user and control groups were divided into three subgroups.

Group-1A: COC-using women between the ages of 14 and 25 in early reproductive life.

Group-1B: COC-using women between the ages of 26-37 in mid-reproductive life.

Group-1C: COC-using women between the ages of 38-50 in late reproductive life.

Group-1C: COC-using women between the ages of 38-50 in late reproductive life.

Group- II A: Women between the ages of 15 and 25 who do not use combined oral contraceptives.

Group- II B: Women between the ages of 26-37 years who do not use combined oral contraceptives.

Group Control- II C: Women between the ages of 38-49 years who do not use combined oral contraceptives.

The Institute of Basic Medical Sciences at Khyber Medical University and the Pakistan Medical Research Council (PMRC) research centre analysed the specimen. Haematological measures comprised of hemoglobin and platelet count, whereas total serum cholesterol, high-density lipoprotein, low-density lipoprotein, and very low-density lipoprotein were included in the biochemical study of lipoprotein.

Chemistry Auto Analyzer was used to do an enzymatic analysis of the serum lipids, and 'the three-dimensional, fully automated Hematology Analyzer Huma count plus 'was used to evaluate the hematological parameters. Using Elitech Diagnostic kits' enzymatic technique, serum triglycerides and total cholesterol were measured (France).

Serum HDL was analyzed (using a kit from Merck Diagnostics). Serum LDL-C was determined using Friedwald's formula.<sup>8</sup> ( $LDL-C = TC - HDL \text{ cholesterol} - VLDL \text{ cholesterol}$ ),. One-fifth of triglycerides were used to calculate VLDL cholesterol. Using the following formula, the BMI was determined using weight and height measurements: BMI is calculated as  $\text{Weight in Kg}/\text{Height in (meter)}^2$ <sup>9</sup> SPSS version 21 was used to analyse the data.

## RESULTS

According to the socio demographic characteristics of the study groups, the lowest age group of women using combined oral contraceptives is group-1 A, with a mean age of  $21.81 \pm 0.51$  years. Group-1 C, whose mean age is  $40.16 \pm 0.32$  years, is the eldest age group using oral contraceptives. When compared to the control of their respective age groups, the mean BMIs were high in COC user groups. In group 1C  $28.07 \pm 0.46$ , the mean BMI was highest.

Moreover, in comparison to the corresponding age groups of controls, the systolic blood pressure was higher in the three age groups of combined oral contraceptive users.

Various biochemical and hematological parameters among combined oral contraceptive users group-1A and controls group-IIA are shown in Table 1

When compared to control groups, the cholesterol, VLDL, Triglycerides, diastolic, and systolic blood pressure were all significantly higher with p-value of (0.02, 0.0007, 0.0007, 0.03, and 0.002) respectively in the combined oral contraceptive users. (Figure 1)

In table 2 the biochemical and hematological parameters of group-1B of COC users and same age group control group-II B

Parameters	Group-1A	GROUP- IIA	p -value
Cholesterol (mg/dL)	184.53 ± 9.45	158.00 ± 6.37	0.028*
HDL-C (mg/Dl)	46.46 ± 2.36	42.69 ±2.01	0.234
LDL-C (mg/dL)	96.13 ± 9.19	91.30 ± 4.95	0.648
VLDL-C (mg/dL)	41.93 ± 3.07	24.00 ± 2.18	0.0007***
Triglycerides (mg/dL)	209.46 ±15.34	120.07 ±10.9	0.0007***
FBS (mg/dL)	121.46 ± 15.01	110.00 ± 4.50	0.477
BMI (Kg/m2)	25.56 ± 0.88	24.43 ± 0.73	0.334
Systolic B.P(mmHg)	135.00 ± 4.05	117.69 ± 3.02	0.002**
Diastolic B.P (mmHg)	85.33 ± 2.20	78.46 ±2.22	0.037
Platelets (1000/u L)	260000 ±2059	231923±1598	0.291
Hb% (g/dL)	12.533 ± 0.307	12.308 ±0.44	0.672

Table 1. Comparison of biochemical and hematological parameters among group1A of COC users and group 2-A of the control group. Significant difference (\*P<0.05, \*\*P<0.01, \*\*\*P<0.001)(n = 17 eachgroup)

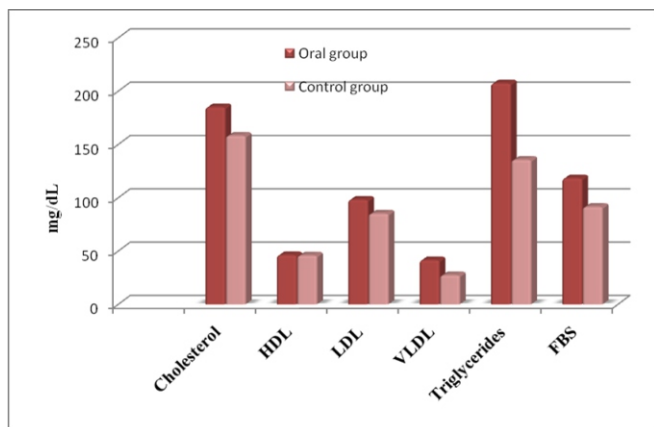


Figure 1:Comparison of different biochemical parameters are shown. When compared to control groups, the TC LDL-C, VLDL-C, TGs, FBS, BMI, and Systolic B.P were all significantly higher with a p-value of (0.0001, 0.010, 0.0001, 0.0001, 0.0004, 0.00102, 0.0006) respectively in combined oral contraceptive users.

In table-3 the COC user group-1C parameters compared with the control group- IIC When compared to control groups, the TC, HDL, LDL, VLDL, TGs, FBS, BMI, Systolic B.P, Hb., P-value were all significantly higher with values of (0.002, 0.031, 0.051, 0.0001, 0.0001, 0.0004, 0.0004, 0.011, 0.003) respectively in combined oral contraceptive users.

In age group-1A (14-25 years), there was a significant association between different parameters like TC, VLDL, TG diastolic and systolic blood pressure. In the age group 1B, there was a significant association between TC LDL, VLDL, TG, FBS, BMI, and Systolic B.P. In age group 1C (38-49 years), there was a significant association between TC, HDL, LDL, VLDL, TG, FBS, BMI, Systolic B.P, and Hb. A significant association in group 1C

Parameters	Group-B	Group- II B	p -value
Cholesterol (mg/dL)	186.81 ±4.36	156.73 ±3.78	0.0001***
HDL-C (mg/Dl)	47.34±1.25	45.29±1.3	0.259
LDL-C (mg/dL)	98.08±4.03	83.11±4.03	0.010****
VLDL-C (mg/dL)	41.38±1.509	28.32±1.24	0.0001***
Triglycerides (mg/dL)	206.77±7.55	141.43±6.21	0.0001***
FBS (mg/dL)	111.46±1.64	95.73±2.30	0.0004***
BMI (Kg/m2)	26.96±0.51	24.60±0.46	0.001**
Systolic B.P(mmHg)	135.20±2.01	123.91±1.77	0.0006***
Diastolic B.P (mmHg)	83.77±1.65	81.35±1.28	0.249
Platelets (1000/u L)	267571± 1240	260432±1298	0.692
Hb% (g/d L)	12.81±0.25	12.78±0.23	0.93

Table 2. Comparison of biochemical and haematological parameters among group-1B of COCs users and group-II B of the control group. Significant difference (\*P<0.05, \*\*P<0.01, \*\*\*P<0.001)(n = 49 eachgroup)

with the age group of (38-50years) more than in the control group was noted.

Parameters	Group-1C	Group- II C	P -value
Cholesterol (mg/dL)	186.16±5.76	160.57±5.43	0.002**
HDL-C (mg/Dl)	44.47±1.14	48.42±1.41	0.031
LDL-C (mg/dL)	99.22±5.41	85.11±4.62	0.051
VLDL-C (mg/dL)	41.47±1.33	27.80±1.39	0.0001***
Triglycerides (mg/dL)	207.19±6.67	135.15±7.87	0.0001***
FBS (mg/dL)	126.94±10.54	88.73±4.29	0.0004***
BMI (Kg/m2)	29.07± 0.57	25.22±0.64	0.0004***
Systolic B.P(mmHg)	136.80 ±3.43	123.46 ±2.52	0.011*
Diastolic B.P (mmHg)	86.00±2.13	81.15±1.50	0.068
Platelets (1000/u L)	256666±1586	246538±1724	0.66
Hb% (g/d L)	13.30±0.25	12.11±0.29	0.003**

Table 3. Comparison of biochemical and hematological parameters among the group-1C of COCs users and the group-2 C of the control group. Significant difference (\*P<0.05, \*\*P<0.01, \*\*\*P<0.001)(n = 36 eachgroup)

## DISCUSSION

COC is used by about 100 million women globally, with 11.6 million women, or 19% of the adult female population in the United States, demonstrating their efficacy and safety since their introduction.<sup>10</sup> High cholesterol and sugar levels, elevated systolic and diastolic blood pressure, and BMI all increases the risk of cardiovascular disease (CVD).<sup>11</sup> Our study discovered these risk variables in COCs users, as well as the relationship between these risk factors and the age of COCs users, and compared these to control group.

According to statistics on the mortality from cardiovascular

diseases in women between the ages of 35 and 44, cardiovascular diseases increased relative to all other age groups because, for the same age groups, there was a coincident rise in the use of contraceptives from 4% to 17% during the same decades.<sup>11</sup> Other research evaluating COCs on women of childbearing age revealed that age is the most important risk factor. Women between the ages of 15 and 40 have a fourfold increased risk.<sup>12</sup>

The participants in our study were classified into several childbearing age groups; the lowest age group of women using oral contraceptives (15-25 years) the highest age group using oral contraceptives is group C (37-50 years), and intermediate age group using oral contraceptives is group B (26-37 years). Thindwa et al., 2019 carried out a study that was similar, and their findings revealed that the subjects' average age was  $27.4 \pm 4.2$  years using contraceptive (range, 19–35 years). Another study finding also revealed that the mean age of COC users was 24.15 years.<sup>13</sup>

According to a review of the studies' literature, the weight and BMI of women who use COC rise with age.<sup>14</sup> In this study, the three age groups utilizing COC had a high mean BMIs when compared to controls in the same age groups. The group-1C (37-49 years) had the highest mean BMI at  $29.07 \pm 0.57$ . A comparable study was carried out by Ferreira-Filho et al. 2020, in which the proportion of women with a BMI > 25 was high in the age ranges of 30-39 years and 40-49 years, respectively, by 39.4% and 51.1%.<sup>15</sup>

Systolic and diastolic blood pressure was also a significant factor for women using combine oral contraceptives (COC), as it is gradually raised with increasing age in COC users. In a survey of Royal College of General Practitioners, COC users had a 2.6 times greater incidence of hypertension than non-users.<sup>16</sup> The COC estradiol component induces the hepatic production of angiotensinogen, which is known as a key element in raising blood pressure. It was previously reported that four different monophasic combinations of oral contraceptives were linked to slight elevations in systolic and diastolic blood pressure in women using them while they were of childbearing age.<sup>17</sup>

In current study, we found that the mean systolic blood pressure and the mean diastolic blood pressure increased with the age of the contraceptive users when we compared the systolic and diastolic blood pressure of COC users with controls. The mean systolic blood pressure was  $135.00 \pm 4.05$  mmHg and the mean diastolic blood pressure was  $85.33 \pm 2.20$  mmHg for the oral group-1 A age group ( $22.93 \pm 0.62$  years), oral group-1B group systolic BP was  $135.20 \pm 2.01$  for the oral group-1B age group ( $31.55 \pm 0.47$  years), and diastolic BP was  $83.77 \pm 1.65$  and for the oral group-1 C age group ( $41.27 \pm 0.43$  years), and mean systolic and diastolic was  $136.80 \pm 3.43$  mmHg and  $86.00$  mmHg.

## CONCLUSION

Our findings revealed that COC can cause alterations in lipid, carbohydrate metabolism, BMI, and blood pressure in women of childbearing age. As metabolic risk factors, these increased values may contribute to CVD.

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#### CONFLICT OF INTEREST

Author declare no conflict of interest.

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#### AUTHORS CONTRIBUTIONS

**NS:** Conception, Design of the work, Data collection, and Drafting, Reviewed, Final approval, Agreement to be accountable.

**HZ:** Conception, Design of the work, Acquisition, Data Analysis, and Drafting, Reviewed, Final approval, Agreement to be accountable.

**KT:** Conception, Design of the work, Interpretation of data for the work, and Drafting, Reviewed, Final approval, Agreement to be accountable.



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