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Original Article

Impact of Demographic Characteristics on the Use of Combined Oral Contraceptives and their Effect on Biochemical Parameters in Females of Reproductive Age

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ABSTRACT

Use of combined oral contraceptives pills by women in Pakistan has recently been increased like other developing countries due to various governments and other private organizations campaigning for its use in order to space the pregnancies

Objectives: To determine the impact of demographic characteristics on use of combined oral contraceptive pills (COCs) and their effect on the biochemical parameters in females of reproductive age.

Materials & Methods: This cross sectional analytical study included 200 women of child bearing age (14-49 years) divided into three age groups (group A; 14-25years, group B; 26-36years, group C;37-49years), 100 of them using COCs were further divided into (6 months users, 1 year users and > 1 year users). Control group comprises of the remaining 100 participants. These groups were compared for the demographic characteristics like maternal age, age at menarche , menstrual cycle length ,age at marriage, age at first delivery, , gravida, time of combined oral contraceptive use and total duration of use and biochemical parameters like fasting blood glucose and lipid profile.

Results: In urban areas, the prevalence was twice more (9.8% vs. 3.9%) than that of rural. Lowest age group of women taking contraceptives was 22.93±0.62 years in A group and the highest age was 41.27±0.432 years in C group. The lowest age and highest age of marriage was seen in A and Control (12.46±0.16 and 20.07±0.87 years).The highest parity was seen in group C: 6.917±0.49 and the parity were decreasing in B and A respectively. A significant increase was seen in cholesterol ($p<0.0001$), triglycerides ($p<0.0001$), LDL ($p<0.002602$), VLDL ($p<0.0001$) and fasting blood sugar (p-<0.0002) haemoglobin ($p<0.04711$) & also in BMI, systolic and diastolic BP were significantly increased in the women treated with combined contraceptive pills by ($p<0.00041$), ($p< 0.00071$), ($p<0.00922$) respectively in the females treated with oral contraceptives

Conclusion: Demographic characteristics do play a role in the use of combined oral contraceptives and thus affect the biochemical parameters in females of reproductive age.

Keywords: Combined oral contraceptives (COC), Cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL), body mass index (BMI)

Introduction

To combat the population growth in Pakistan and its unfavorable effect on the successful running of development strategies, govt of Pakistan started a programme of family planning to control the fertility rate in the early sixties.

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Prevalence rate of contraception increased from 5% in 1974-75 to 17.8% in 1994-95 and after introduction of the family planning program in the private sector, the prevalence rate of contraception increased from 17.8% to 23% during the time period of 1995-1997.Use of combined oral contraceptives (COC) increased by 29%, contraceptives injections by 40% and intrauterine device by 60% during 1995-1997 [1].

Prevalence of COC use in Pakistan for 2000-2001 was about 27.6% of child bearing age women and among them 1.9% takes oral contraceptives.

The use of contraceptives in urban as well rural areas is affected by.

1. The husband and wife relation.
2. The religious beliefs.
3. Son Preference.
4. Female autonomy.
5. The family planning service and supply variables [2,3].

Use of combined oral contraceptives pills by women in Pakistan has recently been increased like other developing countries due to various governments and other private organizations campaigning for its use in order to space the pregnancies. The contraceptive prevalence in the urban Pakistan is 5.5% more than twice (9.8% vs. 3.9%) that of rural prevalence [4].

COCs are classified on the basis of its doses of estrogen and type of progestin content and according to the sequence of their introduction into the market of the United Kingdom into three generations. [4] COC preparations (50 µg ethinyl estradiol with androgenic progestins) are associated with adverse effects like strokes and thrombo embolism. [5]The COC pills were also found to be associated with cardiovascular risk factors that endorse myocardial infarctions in older women. [6] Attempts have been done to minimize these adverse effects and combined oral contraceptives were developed with lower doses of estrogen (50 µg ethinyl estradiol) and less androgenic type of progestin. The low-dose combined oral contraceptives used in United States have estrogens in the range of 20–35 µg. The low-dose oral contraceptives pills have improved metabolic profile than higher doses but the thrombo embolic and cardiovascular risks have not been eliminated. [7,8]

The effect of COCs on the level of serum lipid depend upon the concentration of estrogen and the concentration and type of progestogens (9) The ethinyl estradiol increase the level of HDL and triglycerides , and the progesterone increase total cholesterol and decrease HDL [9].

Weight gain with COCs containing nor-testosterone derivatives is also reported, the prevalence of overweight and obesity is strongly related to age and it is reported in earlier studies that BMI rise in COC user after the age of 30 years. [10,11] Inject able contraceptive user gained weight more than oral contraceptive users [12].

Progesterone can affect blood pressure also; this mechanism is complicated and involves both hormone cascades and direct effect on small blood vessels. The blood pressure can increases from very mild to potentially serious, and sometimes warrant discontinuing the COC [13,14].

Materials & Methods

This cross sectional/analytical study was undertaken on 200 women, 100 using Oral Contraceptives in their reproductive age groups coming to Family Planning Department of tertiary referral health care facilities. Participants were randomly selected without a personal and family history of hypertension, diabetes mellitus, renal/cardiovascular diseases, stroke, familial tendency of obesity and smoking and screened for changes in lipid and carbohydrate metabolism by taking fasting blood samples. From the same health facilities 100 healthy women with same inclusion criteria as cases were randomly selected as an age/body mass index, and socio-economic matched control group for comparison. After explaining aims and objectives, informed consent was taken from each subject for participation. Ethical approval was obtained from the Institutional Ethical Research Board (IERB) of Post graduate medical institute, Hayatabad Medical Complex Peshawar.

History of patient was recorded on a well-designed questionnaire, information regarding socio demographic characters, maternal age, age at marriage, age at menarche, age at first delivery, history of breast feeding, menstrual cycle length, gravida, Para, obesity, , time and total duration of combined oral contraceptive use, the use status (never, former and current use within the previous year) . 5 ml of blood was obtained through routine method applying aseptic technique. Each blood sample was centrifuged at 3000 rpm for 10 minutes to get a clear and cell free serum. Samples were isolated with proper labeling. Biochemical analysis of lipoprotein included total cholesterol, high density lipoprotein, low density lipoprotein, very low density lipoprotein, triglycerides, and fasting blood sugar. These investigations were performed in Institute of basic Medical Sciences and PMRC Research Centre, Khyber Medical College, Peshawar.

Serum triglycerides and total cholesterol were measured by using enzymatic method of Elitech Diagnostic kits of France. Serum HDL-C was measured by using kits of Merck Diagnostics. Serum LDL-C was calculated by Frederickson-Friedwald's formula (LDL-C = TC - HDL cholesterol – VLDL cholesterol). VLDL cholesterol was calculated as 1/5 of triglycerides. Data was processed on computer software package SPSS version 16.

Results

Demographic characteristics of the study groups are shown in Table 1; lowest age group is Group oral A with mean age of 22.93±0.62. Highest age group taking oral contraceptive, age of marriage and parity was seen in oral C group with mean age 41.27±0.43 and 6.917±0. Lowest age of marriage was seen in oral A as 12.46±0.16 and the parity was decreasing in oral B and oral A respectively. Highest mean BMI was seen in oral C 29.077±0.58. Systolic B.P among the three age groups of oral contraceptive users was high as compared to the respective age groups of control.

Table 1: Demographic characteristic of the study groups

Variables	Combined Oral contraceptive users			Control group		
	A	B	C	A	B	C
Age Years	22.93 ±0.62	31.55 ±0.47	41.27 ±0.43	21.69 ±0.60	31.75 ±0.47	41.61 ±0.47
Menarche age(years)	12.46 ±0.16	12.40 ±0.13	12.77 ±0.17	12.53 ±0.18	12.59 ±0.13	12.30 ±0.09
Marriage age(years)	12.46 ±0.16	17.60 ±0.40	16.13 ±0.44	18.64 ±0.18	18.10 ±0.47	20.07 ±0.87
Age at 1st delivery (yrs)	18.13 ±0.62	19.06 ±0.39	17.85 ±0.38	19.30 ±0.72	19.59 ±0.42	21.76 ±0.80
Parity (n)	3.00 ±0.41	5.00 ±0.33	7.00 ±0.49	2.00 ±0.43	5.00 ±0.28	5.00 ±0.91
Male babies(n)	1.00 ±0.30	2.00 ±0.23	4.00 ±0.28	1.00 ±0.21	2.00 ±0.18	3.00 ±0.23
Female babies(n)	1.00 ±0.19	2.00 ±0.22	4.00 ±0.30	1.00 ±0.22	2.00 ±0.18	2.00 ±0.68
BMI kg/m²	25.56 ±0.88	26.96 ±0.51	29.07 ± 0.57	24.43 ±0.73	24.60 ±0.46	25.22 ±0.64
Systolic B.P mmHg	135.00 ±4.05	130.20 ±2.01	136.80 ±3.43	117.69 ±3.02	123.91 ±1.77	123.46 ±2.52
Diastolic B.P mmHg	85.33 ±2.20	83.77 ±1.65	86.00 ±2.13	78.46 ±2.22	81.35 ±1.28	81.15 ±1.50
Platelets thousands/u L	260000 ±20597	267571 ± 12405	256666 ±15860	231923 ±15978	260432 ±12983	246538 ±17243
Hb% g/d L	12.53 ±0.30	12.81 ±0.25	13.30 ±0.25	12.30 ±0.44	12.78 ±0.23	12.11 ±0.29

Values are used as mean± SEM.

BMI of groups was compared in table 2 .Women in oral group were found almost three time more obese with BMI >27(kg/m2) 53% in oral vs.16% of control group with OR 2.90, CI (0.91-9.80), $\chi 2$ 3.18, P-value 0.07.

Table 2: Comparison of BMI among Oral contraceptive users and Control groups

BMI(kg/m²)	Oral group (n)	Control group (n)	Crude odd ratio		
			OR	$\chi 2$	P value
<22.99	10	25	Referent		
23 – 24.99	19	41	1.57(0.53-4.69)	0.49	0.5080
25 – 26.99	18	23	1.90(0.62-5.90)	1.01	0.3154
≥27	53	21	2.90(0.91-9.80)	3.18	0.0747

Significant difference (*P<0.05)

Different biochemical parameters of the study groups were compared in **Table 3**.The student t- test was applied and P value was determined. The highest significant value (0.0001) was seen in cholesterol, VLDL and triglycerides. The fasting blood sugar when compared showed high significance of P value 0.0002. Haemoglobin was significant at a level of 0.04 while platelet count was found non-significant as compared to the control group.

Table 3: Comparison of different Biochemical Parameters among Oral and Control groups

Parameters	Oral group Mean ± SEM	Control group Mean ± SEM	t-Test P value
Total- Cholesterol mg/dL	185.00 ±3.26	158.26 ±2.80	0.0001***
HDL-Cholesterol mg/dL	46.18 ±0.82	45.92 ± 0.90	0.8337
LDL-Cholesterol mg/dL	98.20 ±3.11	85.19 ± 2.65	0.0026**
VLDL-Cholesterol mg/dL	41.50 ±0.98	27.40 ± 0.86	0.0001***
Triglycerides mg/dL	207.33 ± 4.92	135.63 ± 4.48	0.0001***
FBS mg/dL	118.31 ± 4.50	91.51 ± 2.06	0.0002***

Significant difference (*P<0.05, **P<0.01, ***P<0.001)

Comparison between the effect of duration of use of COCs on different biochemical parameters t-test applied and P value found. VLDL, Triglycerides and platelet showed significance with value of 0.012, 0.010 and 0.0067 respectively.

Table 4: Comparison of different parameters with duration of use of combined oral contraceptives

Parameters	6 months COCs Users (n= 23) Mean ± SEM	1 year COCs users (n=36) Mean ± SEM	t-test p value
Total cholesterol mg/dL	170.73 ± 6.08	174.27 ± 4.85	0.6511
HDL-C mg/dL	43.95 ± 1.63	44.50 ± 1.28	0.7938
LDL-C mg/dL	90.69 ± 5.88	90.63 ± 4.63	0.9939
VLDL-C mg/dL	36.08 ± 1.32	39.13 ±0.43	0.0127
Triglycerides mg/dL	180.00 ± 6.58	195.63 ± 2.14	0.0102*
FBS mg/dL	114.00 ± 2.48	115.97 ± 9.19	0.8668

Significant difference (*P<0.05)

Discussion

The combined oral contraceptives have been in use for more than 50 years in Pakistan and the contraceptive prevalence in the urban Pakistan is 5.5% more than twice that of rural prevalence (9.8% vs. 3.9%)[4]. It is proved that it is highly effective but their components steroidal hormones the estrogens and progestogen have various metabolic effects, which include impairment of lipid and carbohydrate metabolism and increase BMI and systolic and diastolic blood pressure also. Epidemiologically an increased risk of CVD remains a cause for concern in the COCs users. Several factors associated with CVD risk in women taking COCs, including the EE dose and type of progestogen used [15].

The high level of lipid and sugar raised systolic and diastolic blood pressure and BMI has an increased risk of cardiovascular diseases [16] . Our study revealed these risk factors in COCs users and also the association between these risk factors with age of COCs users and duration of COCs and compares them with control.

Age of patients taking COCs is important. According to recently available data on the mortality from cardiovascular diseases in women aged 35 and 44 years, cardiovascular diseases increased as compared to all other age groups because in same age groups there was coincident of increased use of contraceptives during the same decades from 4% to 17% [17]. Other studies conducted on women of child bearing age using COCs, their result showed that age is the most relevant risk factors. Risk increases four-fold in women between the ages of 15 and 40 years [8].

In our study we divided the participants in different child bearing age groups; the lowest age group of women taking contraceptive is oral A group (14-25yrs) with mean age of 22.93±0.621yrs. The middle age group oral B (26-37yrs) with the mean age of 31.55 ± 0.47 yrs and the highest age group taking oral contraceptive is oral C (37-49) with mean age 41.27±0.43. Similar study was conducted by [9] and their results showed the mean age of the subjects 27.4±4.2 years (range, 19–35 years). Another study conducted by [18]and their results showed the mean age 24.1±5 years.

Analysis of the studies literature reports that there was an increase in weight, BMI of women using COCs with age[10,19]. A study conducted on third generation COCs using women in their child bearing age. The results of the study do not indicate a long-term influence of COCs on weight gain but it was the age of the COCs users reported a weight increase in excess of10 kg during period from 19 to 44 years of age [20] . The study reported that there was no evidence of weight gain in combined contraceptives users. In a study conducted by M Nobuko proportion of obese (BMI> 25) subjects was high in the age groups 30–39, 40–49 and 50–59, 39•4%, 51•1% and 48•5% respectively.[21]

In our study the mean BMI in the three age groups using OCPs was significantly high (p<0.0004) when compared with control of their respective age groups. The highest mean BMI was seen in oral C (37-49 years) 29.077±0.579, similar study conducted showed the proportion BMI > or = 25 women was high in the age groups 30-39years, 40-49 years by 39.4%, 51.1% respectively.[5]. Analysis of the literature reports either minimal weight increase or little evidence for a causal relationship with oral contraceptive pills. [12].

In our study it was noted that the mean serum cholesterol level of women using COCs was increased with a p- value of high significance (0.0001). In a study conducted on the Nigerian women using COCs showed increased level of cholesterol with p<0.001[7].The high level of lipids parameters, raised BMI and systolic and diastolic blood pressure has an increased risk of cardiovascular diseases (CVD). Our study revealed these risk factors in COCs users. HDL-cholesterol levels increase with COCs use because estrogen inhibits hepatic lipase activity, the enzyme responsible for clearing HDL-cholesterol from the circulation [7].

In our study the HDL-C was not changed significantly (p> 0.83), while the mean LDL and VLDL was increased with significant p-value of 0.002 and 0.0001

respectively. The levels of HDL, LDL, VLDL and TGs were experienced elevated in hormonal contraceptives users. In a study conducted on the women receiving monophasic oral contraceptives reported reduction in HDL-C and an elevation in LDL-C and total triglycerides[22].Our results are consistent with those observed in previous studies on combine oral contraceptives users [22].

In our study the triglycerides was significantly increased in COCs users with the p- value of 0.0001 which is highly significant. Therefore, by causing an increase in TG levels, COCs use may be worsening cardiovascular risk. The increased level of triglycerides was experienced in the COCs using group as reported by others [18].

In our study the mean fasting blood sugar of these secondgeneration monophasic combined oral contraceptives users was118.310± 4.502 mg/dl and the mean fasting blood sugar of control group was 91.513± 2.063 mg/dl with the P- value of high significance of 0.0002. Same results was reported in a comparative study on two different monophasic second generation COCs, where significant increase in the glucose was found in women taking COCs[23].

Conclusion

Use of combined oral contraceptives is affected by demographic features like maternal age, age at marriage, age at menarche, age at first delivery, menstrual cycle length, gravida, time and total duration of combined oral contraceptive use .Time and duration of use of COCs can have an effect on the biochemical parameters of the users.

Conflict of Interest: Authors declare no conflict of interest.

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