Prevalence of metabolic syndrome among a sample of women using hormonal contraceptive pills in Erbil city-Iraq

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Abstract

Background and objectives: Women's Health Initiative demonstrated cardiovascular risk linked to the use of oral contraceptive pills therefore the aim of this study is to find out the prevalence of metabolic syndrome and the effect of oral contraceptives pills on lipid profile, blood pressure and body mass index in a group of women of reproductive age in Erbil city.

Materials and methods: This comparative cross-sectional study was conducted on 246 women of child bearing age (14-49 years) from the May 2015 to the April 2016 in maternity teaching hospital and primary health care centers of Erbil. They were divided in two groups: the first group involved 123 women used oral contraceptive pills; the second group involved 123 women age matched not using oral contraceptive pills. Waist circumference, Body Mass Index and blood pressure were measured in all subjects. Fasting levels of serum glucose, triglycerides, total cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol were obtained. Metabolic syndrome was diagnosed according to criteria made by the United Nation National Cholesterol Education Program Adult Treatment Panel III. Various parameters were compared among oral and control groups by using SPSS version 19.

Results: The prevalence of metabolic syndrome among users was significantly higher than that among non-users (71.5% and 5.7%, respectively) ($p<0.001$) and the prevalence of hyperlipidemia was significantly higher among users compared with non-users ($p< 0.001$). The oral contraceptive pill users were at higher risk for cardiovascular disease than non-users according to the atherogenic index (48% was compared to 5.7% respectively) ($p< 0.001$). Users showed that they are at high or very high risk of developing diabetes in comparison to non users (45.5%and 4.9%) respectively. There was no awareness of the long term effect of oral contraceptives on cardiovascular disease among women.

Conclusion: Using oral contraceptive pills by women in their reproductive age group increase significantly the risk of metabolic syndrome.

Key words: **Oral contraceptive pills, metabolic syndrome, cardiovascular disease, diabetes risk.**

Introduction

One of the most cost-effective public health interventions is family planning, which can significantly improve the health of women and their families. Family planning enables women to determine the timing and spacing of their children and gives mothers and newborns an opportunity to stay healthy. (1) There are several safe and highly effective methods of birth control available to prevent unintended pregnancy. The hormonal contraception in its different formulations is highly effective when taken on the prescribed schedule, by the perfect use of steroid hormone methods pregnancy rates drops to less than 1% per year. (2) All available contraception methods have both advantages and disadvantages and it is up to the health provider to make a rational choice. The metabolic syndrome (also known as the cardiometabolic syndrome) refers to the clustering of various metabolic risk factors that include abdominal obesity, dyslipidemia, hypertension, and hyperglycemia. It is now well known that it is associated with an increased risk of cardiovascular disease (CVD) and type 2 diabetes. (3) Metabolic syndrome is attributed to increasing obesity and sedentary lifestyles, and now is both a public health and clinical problem. (4) The use of certain medications like diuretics, beta-blockers, antipsychotics and glucocorticoid hormones may increase the risk of the metabolic syndrome by either promoting weight gain or altering lipid or glucose metabolism and insulin resistance. Many previous studies showed that hormonal contraceptives have deleterious effects on blood pressure, lipid profile, body weight and serum glucose concentrations.(5-7) These effects result from increase in serum cholesterol, triglyceride, low density lipoprotein (LDL), decrease in high density lipoprotein (HDL), impairment of glucose tolerance and elevated insulin level. These disturbances indirectly put women at high risk of cardiovascular disease (coronary artery disease, cerebrovascular disease and peripheral vascular disease). The overall estimated risk associated with low-dose oral contraceptive use increased by 2-fold. Since its introduction, efforts have been directed to balance its risks and advantage. Although contribution of these changes

to increase risk of coronary artery disease among users of oral contraceptive pills is uncertain, it would seem prudent to minimize these disturbances. (8) Centers of disease controls Division of Reproductive Health have a long history of conducting important epidemiologic studies on the safety and effectiveness of hormonal contraceptive methods. The results from these studies have had lasting effects on contraceptive practice. However still there is a lack of studies in the literature in many developing countries including Kurdistan province at northern of Iraq to address growing risk of metabolic syndrome. One quarter of the world's adult population have metabolic syndrome and the condition increases in frequency with age. Turkey reported a prevalence of 33.9% for metabolic syndrome, with a higher prevalence in women (39.6%) than in men (28%). (10) According to the International Diabetes Fredration (IDF), metabolic syndrome was prevalent in 16.1% of the Saudi Arabian population. (10) In Tunisia, metabolic syndrome incidence was 45.5% based on the IDF criteria and 37.4% of Iranians aging from 25-64, living in both urban and rural areas of all 30 provinces in Iran, had metabolic syndrome. (10) This study was carried out to estimate the prevalence of metabolic syndrome among women using hormonal contraceptive pills compared to the non users in addition to its cardiovascular risks by the effect of pills on lipid profile and blood glucose and finally to find out the risk of developing diabetes within 10 years in both groups.

Material and Methods

A cross-sectional study was conducted in Erbil city at north of Iraq starting from first of May 2015 when the approval of this research protocol by scientific and ethics committee at Hawler medical college to the April 2016. Sample size calculation was based on the estimate of the prevalence of metabolic syndrome in Iraq 20% (10,11) and the formula $n = Z^2P(1-P)/d^2$ (Daniel, 1999) (12), this gave a calculated sample size of 246 women. A total of 246 married fertile healthy women of child bearing age (14-49 years) attended outpatient clinics in maternity teaching hospital and two primary health care centers (Brayati and Nazdar Bamerney family medicine health centers) were invited to participate in this study. They were divided in two groups: Group 1 (125 women of

different formulation of oral contraceptive pills users at least for three months) and age matched controls non-users. Pregnant, and women on more than one type of contraception in addition those who were taking drugs that affect the results such as lipid lowering drugs, beta blockers or diuretics were excluded from the study. After they completed direct interviewed questionnaire, a fasting levels of serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and blood sugar was analyzed using chemistry analyzer. Body mass index (BMI), blood pressure (BP) and Waist circumference (WC) were directly measured.

Questionnaire and data collection:

All relevant data were collected through direct interview by the researcher with all participants that eligible and accepted to participate in this study using a questionnaire. The first part of the questionnaire showed information about general characteristic of the subjects including age, educational status, income, marital status, parity, residency and occupation. The second part of the questionnaire included questions regarding menarche age, marriage age, duration of hormonal contraceptive use, type of pills, history of lactation, family history of diabetes, dyslipidemia, hypertension or cardiovascular disease. The knowledge and awareness aspects were focused on the side effects and long term risk of OCP. In this part the response options include “yes,” “no,” “true,” “false,” or “don’t/not sure. The last part of the questionnaire address the 10 years risk of diabetes by a set of questions and parameters that include age, physical activity, waist circumference, eating habits and personal or family history of diabetes and hypertension. The participants were asked to answer either by “yes,” or “no,”. Waist circumferences in cm and blood pressure were measured in standard fashion. Serum glucose concentration estimated using glucose--oxidase-peroxidase colorimetric method (Randox, UK). Serum triglycerides, total-cholesterol and HDL-C measured by using special kits (Biolabo, France). LDL-C determined by Friedewald equation. (13) The risk of developing type 2 diabetes was calculated according to Finnish Diabetes Association scoring that range from 0-

20. Scoring lower than 7 is low risk, 7–11 is slightly elevated, 12–14 moderate, 15–20 high; and >20 is considered very high. Metabolic syndrome diagnosed according to the criteria made by the US National Heart, lung Blood institutes and American Heart Association, which require at least three of the following: WC >= 88 cm, TG ≥150 mg/dl (≥ 1.7 mmol/l), HDL-C <40 mg/ dl (<1.29 mmol/l), BP ≥130/≥ 85 mmHg and FSG ≥100mg/dl (≥6.1 mmol/l). (14)

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 19). Chi square test of association was used to compare between proportions. When the expected count of more than 20% of the cells of the table was less than 5, Fisher's exact test was used. Student's t test was used to compare between means of two independent samples. A p value of ≤ 0.05 was considered statistically significant.

Results

The total number of women who participated in the study was 246 women, 123 women were on oral contraceptive pills, and the other 123 women were non-users of these pills. The mean age ± SD of the users was 35.2 ± 6.9 years, while that of non-users was 31.1 ± 7.8 years ($p < 0.001$). Table 1 shows that more than half (56.9%) of the users aged ≥ 35 years compared with 33.3% of non-users ($p<0.001$). More than two thirds of the OCP users were residing in urban areas compared with 36.6% of the non-users ($p<0.001$). Table 2 shows that there are significantly higher rates of family history of diabetes and dyslipidemia among users compared with non-users. Table 3 shows that the prevalence of metabolic syndrome among users (71.5%) was significantly higher than the prevalence (5.7%) among non-users ($p<0.001$). Table 4 shows that the prevalence of hyperlipidemia was significantly higher among users compared with non-users ($p< 0.001$). Table 5 shows that 45.5% of the OCP users were at high or very high risk of developing diabetes compared with 4.9% among non-users ($p< 0.001$). Table 6 shows that 17.1% of the users and 16.3% of the non-users think that the long use of the OCPs leads to high risk of cardiovascular diseases (0.002). The same table shows that around half of the users had 3 or 4 abnormal lipid values compared with 0% among the

non-users (p< 0.001). The OCP users were at higher risk than non-users according to the atherogenic index. Table 4 shows that 48% of the users were at high risk compared with 5.7% among non-users (p< 0.001). The same table shows that the users were significantly more obese (as indicated by BMI and waist circumference) than the non-users (p<0.001).

Discussion

The combined OCP is a highly effective form of contraception and used to control fertility by almost 20% of women in child bearing age especially in developing countries including our society. Starting the OCP is an important and complex consultation in contrast to that in our country where most of the women used to take pills usually without doctor's prescription. On the other hand the metabolic syndrome has been linked with the risk of cardiovascular disease. This is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose deposition and function. Therefore the objectives of this study is to understand the best way to find and prevent the cardiovascular risks in women and the extent to which the metabolic syndrome are common in women taking OCP. Finally to find out the risk of developing diabetes among OCP users according to the finnish diabetes score.

The worldwide prevalence of metabolic syndrome is considered to be 10 to 84% , whereas the IDF estimates that one-quarter of the world's population has metabolic syndrome and 20% of adults in the Western world [15,10], Soon metabolic syndrome will overtake cigarette smoking as the number one risk factor for heart disease among the UA population. [16] The overall prevalence of metabolic syndrome among participants is 77.2 % and the present study showed that a statistical significant difference in the prevalence of metabolic syndrome among OCP users (71%) when compared to non users (38.6%) (p<0.001). In fact there is lack of studies on the effect of OCP on metabolic syndrome, however there are studies on the effect of OCP on lipid profile, BP and BMI which are determinants of metabolic syndrome and they were recorded a significant elevation in the levels of lipid profile, BP and BMI in women using COCPs. [17,18] Similarly in a study conducted in

Mosul city at northern of Iraq, among 51 OCP users revealed that the prevalence of metabolic syndrome was 17% compared to 13% among non users. [19] Conversely in other systematic review and meta-analysis studies they concluded that the use of OCP is not associated with clinically significant adverse metabolic consequences, because of limitations of the underlying observational studies. [20,21] The high level of lipids parameter, BMI and BP pose an increased risk to cardiovascular diseases (CVD). Our study revealed that the OCP users were at high risk to have cardiovascular disease according to the atherogenic index (48%) in comparison with only (5.7%) among non users. Several studies and reviews have assessed the risk of stroke and MI with the use of OCPs [22] and Multicenter observational studies found an approximate 2-fold increased risk of ischemic stroke among current users of OCs. [23,24] However Further prospective research is needed to further explain the findings with different hormonal contents of OCPs.

Dyslipidemia which is the gold determinant of both metabolic syndrome and aetherogenic index is found significantly higher among OCP users as compared to non users and these effects is higher with the presence of family history of other risk factors and with the age. So far the current study achieved one of the goals that designed to examine these biochemical changes between both groups and is corresponding to the results of the previous studies. In our study the levels of TC, LDL-C, and TGs were observed to be elevated in hormonal contraceptives users with significant p-value of <0.001. Our HDL-C level reduced with OCP users, the explanation of this may be due to fact that of poor regular exercise and sedentary life style among women in Erbil due to cultural reasons. Our results are consistent with those observed in previous studies on OCP users.[25,26] Inconsistent with our results, the findings of other two studies concluded that serum TC levels were not affected by combination oral contraceptives, whereas only serum TG level were increased by 13 to 75 % and HDL-C level is raised. The same results have been obtained in another two different communities. In a study among Sudanese women, results showed a significant increase in the mean serum levels of TC, TG and decrease in HDL in the test group

compared with the control group ($p < 0.05$). [27] In another study among Ghanian community there was a significant increase in TC, LDL-C (3.35±0.62 mmol/L and 1.74±0.57 mmol/L respectively) among OCP users. [28]

The prevalence of diabetes mellitus is increasing dramatically worldwide, resulting in more women of reproductive age having DM as mentioned recently management of contraception is a major issue due to the specific risks associated with pregnancy. There is no consistent evidence that OCP significantly influence the risk of developing diabetes. The current study emphasized that 45.5% of oral OCP users are at high or very high risk to develop type 2 diabetes according to the finnish diabetes score. Although data from specific studies remain sparse, no worsening effect has been reported in diabetic women, either in glycemic control or on the course of microvascular complications. Thus, the use of estroprogestive pills is now recognized as a safe and effective option for preconception care of women with uncomplicated diabetes. [29] However other studies found that there is deterioration in glucose tolerance combined with insulin resistance and the combined OCP drug increased incremental areas for glucose by 43 to 61 percent. [14]

WHO has developed a risk classification system to help physicians' advice patients about the safety of the OCP and the choice of pill formulation is influenced by clinical considerations. By choosing appropriately from the available pill formulations, family physicians can minimize negative side effects and maximize noncontraceptive benefits for their patients. Additional monitoring and follow-up are necessary in special populations, such as women over 35 years of age, smokers, premenopausal women and adolescents, accordingly evidence based guidelines should be available nationally for proper prescription of oral contraceptives and educating programs as far as most of women in the studied sample (78%) not aware about the effect of long term use of pills on cardiovascular disease.

Conclusion

The oral contraceptives has increasing effects on lipids, BP, glucose and BMI which in turn significantly induce metabolic syndrome and increase both cardiovascular disease and future

diabetes risks. The women should be screened and followed regularly for dyslipidemia, obesity and hypertension before and during COCs uses and increase awareness to the likelihood of these illnesses.

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Table 1. Baseline characteristics of the studied samples

		OCP Users		OCP Non-users		Total		p
	Categories	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Age (years)	< 25	8	6.5	31	25.2	39	15.9	< 0.001
	25-34	45	36.6	51	41.5	96	39	
	≥ 35	70	56.9	41	33.3	111	45.1	
Residency	Rural	37	30.1	78	63.4	115	46.7	< 0.001
	Urban	86	69.9	45	36.6	131	53.3	
Physical activity	Yes	34	27.6	65	52.8	99	40.2	< 0.001
	No	89	72.4	58	47.2	147	59.8	
Daily vegetables eating	Yes	35	28.5	63	51.2	98	39.8	< 0.001
	No	88	71.5	60	48.8	148	60.2	
BMI	< 25	17	13.8	56	45.9	73	29.8	< 0.001
	25-29	59	48	54	44.3	113	46.1	
	≥ 30	47	38.2	12	9.8	59	24.1	
Waist circumference	≤ 88	22	17.9	96	78	118	48	< 0.001
	>88	101	82.1	27	22	128	52	
Total		123	100	123	100	246	100	

Table 2. Prevalence of family history of risk factors among the two study groups.

		OCP users		OCP non-users		Total		
Family history	**Categories**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**p**
Diabetes	Yes	56	45.5	29	23.6	85	34.6	< 0.001
	No	67	54.5	94	76.4	161	65.4	
Hypertension	Yes	63	51.2	64	52	127	51.6	0.34*
	No	57	46.3	59	48	116	47.2	
	Not sure	3	2.4	0	0	3	1.2	
Dyslipidemia	Yes	39	31.7	15	12.2	54	22	0.001
	No	76	61.8	102	82.9	178	72.4	
	Not sure	8	6.5	6	4.9	14	5.7	

Cardiovascular disease	Yes	46	37.4	45	36.6	91	37	0.89
	No	77	62.6	78	63.4	155	63	
Total		123	100	123	100	246	100	

*By Fisher's exact test

Table 3. Prevalence of metabolic syndrome among the two study groups.

		Users		Non-users		Total		p
	Categories	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Metabolic syndrome	No	35	28.5	116	94.3	151	61.4	< 0.001
	Yes	88	71.5	7	5.7	95	38.6	
	Total	123	100	123	100	246	100	

Table 4. Lipid profile of the two study groups

		Users		Non-users		Total		p
	Categories	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Chol	< 200	77	62.6	119	96.7	196	79.7	< 0.001
	≥ 200	46	37.4	4	3.3	50	20.3	
TG	< 150	30	24.4	105	85.4	135	54.9	< 0.001
	≥ 150	93	75.6	18	14.6	111	45.1	
HDL	≥ 40	65	52.8	113	91.9	178	72.4	< 0.001
	< 40	58	47.2	10	8.1	68	27.6	
LDL	< 130	36	29.3	78	63.4	114	46.3	< 0.001
	≥ 130	87	70.7	45	36.6	132	53.7	
Abnormal lipids number	0	10	8.1	60	48.8	70	28.5	< 0.001
	1	20	16.3	49	39.8	69	28	
	2	34	27.6	14	11.4	48	19.5	
	3	40	32.5	0	0	40	16.3	
	4	19	15.4	0	0	19	7.7	
Atherogenic index	No risk	64	52	116	94.3	180	73.2	< 0.001
	Risk	59	48	7	5.7	66	26.8	
Hypertension	No	62	50.4	116	94.3	178	72.4	< 0.001
	Yes	61	49.6	7	5.7	68	27.6	
Total		123	100	123	100	246	100	

Table 5. Risk of developing type 2 diabetes within 10 years among women of both groups according to the Finnish Diabetes Association scoring

		Users		Non-users		Total		p
	Categories	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Risk of DM	Low	19	15.4	72	59	91	37.1	< 0.001
	Slightly elevated	33	26.8	34	27.9	67	27.3	
	Moderate	15	12.2	10	8.2	25	10.2	
	High	45	36.6	6	4.9	51	20.8	
	Very high	11	8.9	0	0	11	4.5	
Total		123	100	122	100	245	100	

Table 6. Opinion of the study groups regarding the cardiovascular risk of long term use of oral contraceptive pills.

		Users		Non-users		Total		p
	Categories	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Increased risk	Yes	21	17.1	20	16.3	41	16.7	0.002
	No	90	73.2	103	83.7	193	78.5	
	Not sure	12	9.8	0	0	12	4.9	
Total		123	100	123	100	246	100	