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Hormonal Disturbance in Women Who Suffer from Delayed Pregnancy After Stopping the Oral Contraceptive Pills in Kut City

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Abstract:
Objective*:* To assess our local status of concentrations hormonal and biochemical in response to combined oral contraceptive pill between women who suffer from delays in the case of pregnancy after stopping use of the oral contraceptive pill and control group women's and its relationship to age.**Methods*:*** study was included (80) married women in Kut city the ranged age between (20-40) years. who have given birth to at least one child , they do not suffer from any medical condition , since the beginning of January until end of August has divided : (40) the case of women who suffer from delays in the case of pregnancy after stopping use of the oral contraceptive pill .control group women's who did not take their no way to prevent pregnancy included 40 married divided by age to twenty women each age group.**Results:** There was a significant (P <0.05) in hormonal testes : decrease in the rate of follicles stimulating hormone (FSH) in the women have left the oral contraceptive pill and suffer from late pregnancy , a rise in the rate of the hormone progesterone in the women have left the oral contraceptive pill and suffer from late pregnancy compared to control women . Significant increase (P <0.05) in the concentration of total cholesterol (T.ch) in women's who suffer from late pregnancy after stopping use oral contraceptive pill compared control group women's. non Significant decrease (P >0.05) in the mean values of High density lipoproteins (HDL). exist the effect of age in the study of all parameters hormonal and biochemical in this study. Prevalence the case of late pregnancy in the women have left the oral contraceptive pill in Kut city.
Keyword: oral contraceptive pill, FSH, Progesterone ,cholesterol ,HDL, Age.

Introduction

Most women currently use oral contraceptives pill to prevent pregnancy. The pill is the most widely used method of birth control (**Mosher and Jones, 2010)**. Many women not only use birth control pills for family planning, but also because the pills can alleviate some symptoms associated with their menstruation cycle such as acne, anemia due to heavy menstrual bleeding, and premenstrual dysphoric disorder (**José *et al*., 2013)**.Contraceptive pills is Synthetic hormones derivatives manufactured chemically, and their influence and physiological impact of natural hormones secreted by the ovary help prevent pregnancy in spite of continuing sexual relationship (**Noe *et al*., 2011 ; Novikova *et al*., 2007) .**

The basic mechanism by which they operate to prevent the development of the vesicle and thus inhibiting ovulation (**David *et al*., 2004**) it affects the hypothalamus gland through the suppression of secretion Gonadotrophine Releasing Hormones (GnRH) (**Trussell and James, 2007**) and follicle stimulating hormone (FSH) and is responsible for the evolution and maturity of Graffinn Follicle and Leutinizing hormone (LH) responsible for the explosion of the vesicle and then the start of the egg (**Ferro and Jamie, 2005**). the presence of progesterone receptors are less than the estrogen receptors on various tissues of the body ; including brain tissue cells leads to two types of nutritional regulation, and potentially the estrogen change neurons secreting Neurosecretory cells properties that produce and secrete hormones of the hypothalamus, progesterone hormone, synthetic steroids that mimic the actions of endogenous progesterone. The new progesterone definition progestins (**Su and Lian**, 2012) .One of the main actions of progestin is the secretory transformation of an estrogen-primed endometrium. Both hormones prevent the over-proliferation of the endometrial tissue. The effects of progestins are related to interactions not only with progesterone receptors, but also with other steroid hormone receptors: androgen receptors, estrogen receptors, glucocorticoid receptors, or mineral corticoid receptors (**Frempong *et al.*, 2008**). These interactions may either induce trans activation of a steroid receptor or prevent activation. In the target organ, the balance between the receptor coactivators and corepressors recruited by a progestin determines whether the overall effect of the molecule will be agonistic or antagonistic (**Endrikat *et al*., 2011**). All progestins bind to the progesterone receptor and have the expected effect on the uterine endometrium, progesterone has several biological actions. It transforms the endometrium into a secretary tissue to permit implantation of a fertilized ovum, In addition, progesterone has an antiandrogenic effect (**Skouby *et al*., 2005**) .Progesterone competitively inhibits the action of androgen, as it is a preferred substrate to the enzyme 5a-reductase, preventing the conversion of testosterone into its active metabolite dihydrotestosterone . Progesterone also interacts with the mineral ocorticoid receptor; competitive binding to this receptor by progesterone prevents

its trans activation and inhibits the mineralocorticoid effect (**Mohammad *et al*., 2013**).

Experimental design:
The study included follow-up (80) cases married women, and revisions to the hospital after the confirmation of their health and that they do not suffer from any medical condition in Obstetrics , Zahra teaching Hospital and Kut Hospital for Women and prerace of Kut, since the beginning of January 2016 until the end of the month of August have been divided into two groups :

Group I: Included follow-up (40) the case of women who suffer from delays in the case of pregnancy after dropping the use of the pill (given birth to at least one child before use of oral contraceptive pill). The type of oral contraceptive pills used Microgynon German origin type, ((0.03) mg Ethinyl-Estradiol,(0.15) Levonorgestrel). were divided according to their age into sub groups: The first group ranged between (20-30) years,The second group ranged between (31-40) years.

Group II: A control group included 40 married women who did not use oral contraceptive pills or any objection earlier and be of those who have given birth to at least one child too, ages ranged between (20-40) years, were divided by age as in the first set by twenty women each age group, has also been making sure their fertility through a hormonal and biochemical tests.

Data and blood sample collection
5 mL venous blood had been taken for each women's conducted the study , the samples were transferred to a private pipe free of any anti-clotting substance and left degree lab temperature for a period of 10-15 minutes, then renounced mediated Centrifuge speeds of 3000 r / min for the purpose of separating the serum from the rest of its components. Serum was separated and put in two tub, the first biochemical tests: Tch, HDL, were conducted using Biosystem kits auto analyzer . the second hormonal tests preserved at a temperature of (20) - ° C:FSH, Progesterone hormones

FSH: It has been drawing blood in the Follicular phase, particularly in the second day of the Menstrual cycle.

Progesterone hormones : It has been drawing blood in the luteal phase specifically in the days (17-21) of the menstrual cycle

Statistical analysis:
Statistical analysis was performed with SPSS software. Data were analyzed using analysis of paired-samples T-test for comparison between different group. Results were reported as mean ± S.E. and differences were considered as significant when $P<0.05$.

Results:
Table (1) shows Hormonal and biochemical of the study population. Results of the Hormonal testes is The mean values of FSH in the follicular phase were reduced significantly Among the women's users group of the oral contraceptive pill and left users who suffer from late pregnancy than control women's group not users of the oral contraceptive pill never ($P<0.05$) respectively (2.063 ± 0.134), (7.570 ± 0.521) while progesterone hormone in the luteal phase were show high significantly ($P<0.05$) respectively mean (36.186 ± 1.007) , (17.152 ± 2.065) in women's users group of the oral contraceptive pill and left users who suffer from late pregnancy than control group not users of the oral contraceptive pill never.

We found a high significant in Total cholesterol (T.Ch) between women's users group of the oral contraceptive pill and left users who suffer from late pregnancy and control women's group not users of the oral contraceptive pill never in this study in average (176.192 ± 0.925) , (163.776 ± 1.225) respectively ($P<0.05$). while was reduces no significant in mean High density lipoproteins (HDL) (39.158 ± 0.314) , (39.670 ± 0.602) ($P>0.05$).between women's users group of the oral contraceptive pill and left users who suffer from late pregnancy than control women's group not users of the oral contraceptive pill never.

oral contraceptive pill In this study has shown when compared to the effect of age on the concentrations of parameters : showed in table (2).

Results indicated the presence of a significant decrease ($P< 0.05$) in the concentration of follicle stimulating hormone FSH in the follicular phase of the group of women who have left the use of oral contraceptive pill who suffer from late pregnancy and two age groups (20-30) and (31-40) rates (2.678 ± 0.169) , (1.449 ± 0.076) when compared with the women control group who did not take their no way to prevent pregnancy rates (9.020 ± 0.263) , (6.120 ± 0.324) respectively, whereas when comparing totals for age groups themselves in concentration FSH has emerged a significant decrease ($P <0.05$) was above the second age class (31-40) of both groups set women who have left the oral contraceptive pill who suffer from late pregnancy at a rate of (1.449 ± 0.076) when compared with the first age class (20-30) at the rate of (2.678 ± 0.169) . in the control group of women who did not take their no way to prevent pregnancy rate of decline was more a rate

(6.120 ± 0.324) in the second age class (31-40) when compared with the first age group (20-30) at the rate (9.020 ± 0.263).

As for the progesterone hormone, the results shown in the study significant increases (P< 0.05) of the concentration in the luteal phase of the women group who have stop the use of oral contraceptive pill who suffer from late pregnancy and two age groups (20-30) and (31-40) rates (30.179 ± 0.415) , (42.193 ± 0.443) when compared with the women control group who did not take their no way to prevent pregnancy rates (11.062 ± 0.340) , (23.242 ± 0.733) respectively, whereas when comparing totals for age groups themselves in concentration progesterone hormone has show a significant increases (P <0.05) was above the second age class (31-40) of both groups set women who have left the oral contraceptive pill who suffer from late pregnancy at a rate of (42.193 ± 0.443) when compared with the first age class (20-30) at the rate of (30.179 ± 0.415) . in the women control group who did not take their no way to prevent pregnancy mean of height was more a rate (23.242 ± 0.733) in the second age class (31-40) when compared with the first age group (20-30) at the rate (11.062 ± 0.340).

in the study shown (table 2) high significant (P< 0.05) of the concentration in the total cholesterol (T.Ch) of the group of women who have left the use of oral contraceptive pill who suffer from late pregnancy in two age groups (20-30) and (31-40) rates (170.582 ± 0.356) , (181.803 ± 0.273) compared with the women control group who did not take their no way to prevent pregnancy rates (160.780 ± 1.304) , (166.772 ± 0.750) respectively, when comparing totals for age groups themselves in concentration T.Ch has show a significant increases (P <0.05) in the second age class (31-40) of women groups who have left the oral contraceptive pill who suffer from late pregnancy at a rate of (181.803 ± 0.273) when compared with the first age class (20-30) at the rate of (170.582 ± 0.356) . in the women control group who did not take their no way to prevent pregnancy the concentration T.Ch height but non significant a rate (166.772 ± 0.750) in the second age class (31-40) when compared with the first age group (20-30) at the rate (160.780 ± 1.304) .

Results presence of a not significant decrease (P> 0.05) in the concentration HDL of the women group who have left the use of oral contraceptive pill who suffer from late pregnancy and two age groups (20-30) and (31-40) rates (40.614 ± 0.285) , (37.702 ± 0.320) when compared with the women control group who did not take their no way to prevent pregnancy rates (40.738 ± 0.698) , (38.602 ± 0.757) respectively, when comparing totals for age groups themselves in concentration HDL has present at (P <0.05) is significant decreases in the second age class (31-40) of women groups who have left the oral contraceptive pill who suffer from late pregnancy at a rate of (37.702 ± 0.320) when compared with the first age class (20-30) a rate (40.614 ± 0.285). in the control group of women who did not take their no way to prevent pregnancy rate of decline was more a rate (38.602 ± 0.757) in the second age class (31-40) but non significant when compared with the first age group (20-30) at the rate (40.738 ± 0.698).

Table (1): shows the laboratory characteristics of the study population Control Group and women's left using oral contraceptive pills who suffer from late pregnancy Group

Hormonal and biochemical parameters	Control Group (Mean ± S.E.) N=40	women's left using oral contraceptive pills who suffer late pregnancy Group (Mean ± S.E.) N=40
FSH	7.570 ± 0.521 *	2.063± 0.134 *
Progesterone hormone	17.152 ± 2.065 *	36.186± 1.007 *
T.Ch	± 1.225 * 163.776	176.192 ± 0.925 *
HDL	39.670 ± 0.602	39.158 ± 0.314

***: Means significant difference between the two groups when (P<0.05).**

Table (2): shows the effect of age on the laboratory characteristics of the study population Control Group and women's left using oral contraceptive pills who suffer from late pregnancy Group

Hormonal and biochemical parameters	Control Group (Mean ± S.E.) N=40		women's left using oral contraceptive pills who suffer late pregnancy group (Mean ± S.E.) N=40	
	year 20-30 N=20	Year--4031 N=20	year 20-30 N=20	Year--4031 N=20
FSH	9.020 ± 0.263 * a	6.120 ± 0.324 * b	2.678 ± 0.169 * a	1.449 ± 0.076 * B
Progesterone hormone	11.062 ± 0.340 * a	23.242 ± 0.733 * b	30.179 ± 0.415 * a	42.193 ± 0.443 * B
T.Ch	160.780 ± 1.304 * a	166.772 ± 0.750 * a	170.582 ± 0.356 * a	181.803 ± 0.273 * B
HDL	40.738 ± 0.698 a	38.602 ± 0.757 a	40.614 ± 0.285 a	37.702 ± 0.320 B

***: Means significant difference between the two groups when (P<0.05).**
a.b : Means with different superscript letters are significantly different (P<0.05).

Discussion

oral contraceptives pills (OCPs) afford not only excellent contraception but also a variety of non-contraceptive benefits, ranging from regulation and reduction of both menstrual bleeding and treatment of premenstrual syndrome, menstrual migraines, acne (**Shulman, 2011**) . Long-term benefits include reduced rates of endometrial, ovarian, and colorectal cancer **(Maguire and Westhoff, 2011**), Although it found that there are several risk factors associated with OCPs , in One study found the percentage of deaths among women ever using OCPs was 12% Compared to women who did not use (OCPs) (**Tsismenakis *et al.*, 2009)**. through this study we found a number of the women have left OCPs for reproduction ; have no pregnancy comparation with control group . there is significant difference in (FSH ,Progesterone hormone ,T.ch, HDL). The results indicated that significant reduction in the FSH and significant height in the progesterone hormone with positive relationship with age . artificial pills hormone works continuously to inhibit the secretion of this hormone GnRH (**Trussell and James, 2007**) , through a competitive link with the receptors and thus inhibits the secretion of FSH & LH, and this indicated that the current study show the existence of a significant decrease (P <0.05) in the concentration FSH in the follicular phase of women who have left OCPs compared with the control group, the results of this study, matching the results obtained (**Huirne and Loenen, 2006**) . came the results of the study show decreases the concentration of these hormone FSH with age and through the comparison between the age groups existence of a significant decrease (P <0.05) was above the second age group.

The present study showed a large rise significantly in the concentration of the progesterone hormone in the women who have OCPs when compared with the control group, this result consistent with the findings of the (**Zhang *et al.***, 2009) . the reason for the rise is due to the remnants of steroidal hormones of the pills are stored in the body and which interfere with the normal functioning of the menstrual hypothalamic pituitary-ovarian HPO- axis (**Lidegaard *et al.* 2012**), or because of differences in the concentration of hormones (progesterone and Estrogen) to the effect of activity of Steroid Hormones Binding Globulin (SHBG) (**Manzoli *et al.*, 2012**) , and that the OCPs contraception is working on the inhibition of ovulation and an increase in the ovarian hormones (progesterone and estrogen), by stimulate the gene in liver cells which increased formation SHBG and these in turn are associated with high level of hormone (**Shulman, 2011**) . Results of the study also showed that with age concentrations of progesterone increased in women who have OCPs compared with a control group, and the reason is due to physiological changes associated with offering woman's age .Current steroid contraceptive pills still achieve the goal of suppression of pituitary – ovarian activity but the margins for error are minimal (**Heusden and Fauser, 2002**) . Most studies show that effect on the endometrial, indicating prevent implantation (**Meng** *et al*., 2009 ; **Meng** *et al*., 2010 ; **Palomino *et al.*, 2010)** . Although clients chose good, effective OCP, their use was not always maintained occurrence of pregnancy . Further work is needed to understand the reasons for the change of method and plans to improve acceptability and accessibility to more effective contraception are being developed to assist women in having more control over their fertility (**Graham, 2013**) . Showed the results of the current study, the presence of the effect of age on the studied parameters. This is identical to what was in the study (**Ozalp *et al.*, 2013**) with lack of likelihood of conception pregnant T.Ch were significantly different in the women's Group stop using OCPs who suffer late pregnancy group compared to the control group of this study. A number of studies into the pill affect the metabolism of fat, so significantly changes in the concentrations of T.Ch, (**Yesmin *et al.*, 2013**) those studies have included conflicting results on

the impact of the pill on the concentration of total cholesterol in the blood, some of which have pointed to an increase in the concentration of T.Ch (**Santos *et al.*, 2008**), while others pointed to the existence of a significant decrease in the concentration of T.Ch (**Von-Rooijen *et al.*, 2002**) , as other studies have not affected total cholesterol using contraception pills explained (**Graff-Iversen** *et al*., 2006). The results indicated the presence of significant increase ($P < 0.05$) in the concentration of total cholesterol in the serum of women who have left the pill compared with the control group, has reason to metabolize hormones pills because contraception and stored, the residues can have a continuous effect on metabolism cholesterol even after leaving their use and that this effect remains constant even those hormones implemented once and for all, and these results are consistent with the findings of the researchers (**Emokpae** *et al*., 2010) . may be due the reason for increasing the concentration of total cholesterol to the inability of the bile salts dissolved, since progesterone hormone works to discourage the conversion of cholesterol into bile acids bile acids process so less than the level of bile salts (**Stanczyk, 2002**) . In both cases, higher results were obtained as a result of T.ch When the data were stratified to age , statistically significant increases were seen in the women groups who have stop the OCPs who suffer from late pregnancy and control groups for both in (31-40) age, T.ch is high when compared to the (20-30) age. Oral contraceptives pill alter the lipid profile through the genomic pathway, in which estrogen receptor alterations affect hepatic apolipoprotein upregulation. (**Nelms** *et al*., 2010) . these results similar to the study of (**Jones *et al.*, 2002**). also statistically significantly higher Tch in a study **(Okeke *et al.*, 2012)** . Furthermore, statistically significant change in TC and no statistically significant in HDL levels in women on OCP was observed in that study. The results of this study also showed a lack of moral differences in the concentration of high-density lipoprotein HDL in the serum of women who have left the level of use of the pill when compared with the control group. It was reported (**Berenson *et al.*, 2009 ; Druckmann, 2009**) that the use of birth control pills do not cause a significant increase in the concentration of HDL due to the lack of effect on HDL receptors, this result is matching the current results of the study concluded that the use of these pills or leave it does not affect the concentration of HDL . However, a significant increase was observed in the TC of the OCP group and a slight but statistically reduces non-significant of HDL in the OCP group of the present study compared control group. In the study **(Okeke *et al.*, 2012)**, HDL was significantly increased in the OCP group ,This is unlike the current study, in contrast Asare .etal. indicated the presence Significant changes in lipid profile were observed with HDL (**Asare *et al.*, 2014**) .

Conclusion:
use of oral contraceptive Pills linked to change the criteria levels (FSH ,Progesterone hormone ,T.ch, HDL) are linked to a strong relationship with age, especially in the group (31-40)

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