Early-Pregnancy Changes in Maternal Lipid Profile in Women with Recurrent Preeclampsia and Women with Normal Pregnancy

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Abstract

Background: According to the current knowledge, changes in lipid profile in pregnancy is a major contributor in the pathogenesis of preeclampsia. The present study was designed to compare the changes in lipid profile in normal pregnancy and in patients with history of recurrent pre-eclampsia (PE).

Objective: Assessment the relationship between lipid profiles changes in women with history of recurrent preeclampsia in comparison to normal pregnancy in early pregnancy.

Patients and Methods: Measurement of lipid profile changes in women with history of recurrent preeclampsia (more than two preeclampsia in previous pregnancies) at 12 to 16 weeks of pregnancy and compared to normal pregnancy as a control group who does not have history of preeclampsia also early in pregnancy

Results: The patients with history of recurrent Preeclampsia had significantly higher mean total cholesterol level compared to controls (216.1 ± 25.5 mg/dl) and (195.6 ± 23.2 mg/dl), respectively, ($P<0.05$).The mean HDL cholesterol (HDL-C) level was significantly lower in PE group (49.3 ± 9.2 mg/dl) than controls (52.2 ± 8.4 mg/dl), ($P<0.05$). The mean level of LDL cholesterol was (122.3 ± 28.7) mg/dl in PE group and it was significantly higher than the (108.6 ± 26.8 mg/dl) of controls, ($P<0.05$). Similarly, the mean VLDL cholesterol was also higher in women with history of recurrent preeclampsia than control group, (44.8 ± 12.6) vs. (34.8 ± 7.3) mg/dl, respectively, ($P<0.05$). The Triglycerides (TG) was also elevated in women with history of recurrent preeclampsia where the mean TG level was (224.2 ± 63.1 mg/dl) compared to (174.6 ± 36.3mg/dl) in controls, ($P<0.05$).

Conclusion: This study showed that the women who have history of recurrent preeclampsia had disturbed lipid profile (increased levels of total TC, TG, VLDL-C and LDL-C concentration) in addition to decrease the high density lipoprotein cholesterol (HDL-C) level in subsequent pregnancy compared to normal pregnancy.

Keywords: Preeclampsia, Changes in lipid profile during pregnancy

Introduction:

As pregnancy progresses, a well-integrated metabolic shift occurs to ensure an adequate supply of nutrients to a constantly feeding fetus from an intermittently fasting and feeding mother. During early pregnancy, maternal metabolic environment is modified by a rise in serum levels of estrogen and progesterone, pancreatic beta-cell hyperplasia occurs and there is an increase in secretion of insulin (1).

Hyperinsulinemia leads to an increase in peripheral glucose utilization, a decline in fasting plasma glucose levels, increased tissue storage of glycogen, increased storage of fats and decreased lipolysis (2).

It is known that high concentrations of many of the steroids occur as normal pregnancy advances. Since cholesterol is the source of most of the steroids found in increased amounts in the circulation of normal pregnant patients, the part played by lipid metabolism in pregnancy, becomes all the more intriguing – as cholesterol is a major factor for the development of atherosclerosis (2). Chauffard in 1911 undertook the first chemical study of blood lipids during pregnancy and suggested that an increase occurs in the cholesterol level (3).

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With the development of more techniques various studies observed an increase in various lipid fractions, though the increase was neither consistent in time of appearance nor proportion of changes in various fractions. Most authors believe that the increase in blood lipids is related to the requirements of the fetus and to development of the mammary apparatus (4). Preeclampsia is a pregnancy specific disorder, characterized by pregnancy induced hypertension (BP $\geq$140/90 mm Hg) on two occasion, at least 6 hours apart and proteinuria of $\geq$ 300 mg/24 hours or $\geq$1+dipstick after 20 weeks of gestation in previous normotensive women. It is the most common medical complication of pregnancy, whose incidence has continued to increase worldwide (5). It results in an increased risk for intrauterine growth restriction, prematurity, and death and it is also recognized as a major risk factor for cardiovascular disease later in life for both the woman and her child(6). There is no effective therapy for the management of preeclampsia, and the only cure is to deliver the infant (7). Preeclampsia is distinguished from the other hypertensive disorders of pregnancy by *new* onset hypertension and *new* onset proteinuria without seizure activity after 20 weeks of gestation. (8, 9, 10). During normal pregnancies (without accompanying morbidities such as gestational

diabetes or preeclampsia), total cholesterol levels increase by 50%, and triglyceride levels rise markedly by 2 to 4 fold. Moreover, high-density lipoprotein cholesterol (HDL-C) levels increase by 30%, while low-density lipoprotein-cholesterol (LDL-C) levels increase by 50%. These changes in lipid metabolism during pregnancy promote the accumulation of maternal fat stores in the first two-thirds of gestation in order to serve as a source of calories for the mother and fetus in late pregnancy and during lactation. Cholesterol is also necessary for placental steroid synthesis, and triglycerides are used for placental oxidation and membrane formation (11, 12) Reversal of the hyperlipidemia of pregnancy begins within hours of delivery and is essentially complete by 6-10 weeks postpartum (13).

Patients and Methods:
The patients attended Tikrit teaching hospital at outpatient department from Feb. 2014 to Jun.2014.Then those taken from Medical city hospital from Aug.2014 to Oct 2014 and those patient taken from Samarra city hospital from Oct.2014 to Dec.2014. The participant divided in to 2 groups, eighty three women with history of recurrent preeclampsia(cases – PE group) and eighty nine normal pregnant women. The inclusion criteria was singleton pregnancy and women with history of recurrent preeclampsia .Those who are excluded were hypertensive women or use of anti-hypertensive treatment, twin or higher multiple pregnancy, and those with history of gestational hypertension. At arrival, full history was taken from each patient, general and obstetrical examination is carried out, maternal vital signs (blood pressure, pulse rate, respiratory rate, and temperature) are taken, and approved previous history of recurrent preeclampsia by patient doctor card and previous investigations Venous blood was drawn from pregnant women with history of recurrent preeclampsia at 12-16 weeks and from normal pregnant women after overnight fasting. Each serum sample was evaluated for total cholesterol (mg/dl), triglyceride (mg/dl), and HDL-cholesterol (mg/dl) using diagnostic kit: Additional

parameters were LDL-cholesterol (mg/dl) and VLDL- cholesterol (mg/dl) using Friedewald formula Glucose also calculated.

Statistical analysis:
Descriptive statistics were presented as mean, standard deviation (SD), frequencies (No.) and proportions (%). Chi square and Fishers exact test were used alternatively to compare frequencies, when applicable to estimate the relationship between variables. Multiple logistic regression analysis (binary model) was used for further analysis of the correlation between variables. Odds ratio (as an estimator for the risk) was calculated, the significant Odds ratio and more than 1, indicated that the factor present in study group is a risk factor might associated with the occurrence of the outcome the larger odds ratio of a factor, indicated the higher risk level due to the presence of that factor. Level of significance (p. value) was set at ≤ 0.05 to be significant

Results:
A total of 100 pregnant women at the gestational age of 12 – 16 weeks with history of recurrent pre-eclampsia (PE group) in addition to 100 women with normal pregnancy (control group) were enrolled in this case control study, 17 women in cases group and 11 in control group were missed to follow up resulted in a net sample of 83 women in (PE group) and 89 in control group. The baseline clinical and demographic characteristics of the studied groups are shown in (table 1). The mean age of women in PE and control groups was (30.5 ± 6.1) and (29.8 ± 5.4) years, respectively. The Mean body mass index was 27.8 ± 3.5 kg/m2 in PE group and 26.9 ± 4.1 kg/m2 in controls. Hyperglycemia was found in only 7 women; 4 (4.8%) PE women and 3 (3.4%) controls. History of gestational DM was found in 5 (6%) PE women and 3 (3.4%) controls. However, no statistically significant differences between both studied groups had been found in the baseline clinical and demographic parameters, in all comparison P>0.05, (Table 1).

Table 1: Demorphic and clinical characteristics of studied group

Variable			PE group (n=83)	Control (n=89)	P.value
Age (year)		n (%)	22 (26.5)	33 (37.1)	
	30	n (%)	26 (31.3)	28 (31.5)	0.18
	40	n (%)	28 (33.8)	26 (29.2)	
		n (%)	7 (8.4)	2 (2.2)	
	Mean ± SD*		30.5 ± 6.1	29.8 ± 5.4	0.42
Mean body mass index kg/m2 *(mean ± SD)*			27.8 ± 3.5	26.9 ± 4.1	0.11
Mean systolic blood pressure mmHg *(mean ± SD)*			118.8 ± 9.9	120.7 ± 12.9	0.28
Mean diastolic blood pressure mmHg *(mean ± SD)*			80.4 ± 5.6	79.6 ± 7.2	0.38
Gravidity	1 - 2	n (%)	37 (44.6)	51(57.3)	
	3 - 4	n (%)	36 (43.4)	31 (34.8)	0.23
	> 4	n (%)	10 (12.0)	7 (7.9)	
Parity	Nulliparous	n (%)	19 (22.9)	18 (20.2)	0.82
	Multiparous	n (%)	64 (77.1)	71 (79.8)	
Hyperglycemia		n (%)	4 (4.8)	3 (3.4)	0.71
History of gestational DM		n (%)	5 (6.0)	3 (3.4)	0.48
*SD: standard deviation , n : number					

As it shown in table2, patients with history of recurrent preeclampsia (PE group) had significantly higher mean total cholesterol level compared to controls (216.1 ± 25.5 mg/dl) and (195.6 ± 23.2 mg/dl), respectively, (P<0.05).The mean HDL cholesterol (HDL-C) level was significantly lower in PE group (49.3 ± 9.2 mg/dl) than controls (52.2 ± 8.4 mg/dl), (P<0.05). The mean level of LDL cholesterol was (122.3 ± 28.7) mg/dl in PE group and it was significantly higher than the (108.6 ± 26.8 mg/dl) of controls, (P<0.05). Similarly, the mean VLDL cholesterol was also higher in PE than control group, (44.8 ± 12.6) vs. (34.8 ± 7.3) mg/dl, respectively, (P<0.05). The Triglycerides (TG) was also elevated in PE group where the mean TG level was (224.2 ± 63.1 mg/dl) compared to (174.6 ± 36.3mg/dl) in controls, (P<0.05). (Table2)

Table2. Comparison of mean levels of lipid profile of the studied groups.

Serum lipid		PE group (n=83)	Control (n=89)	*P.value**
Total cholesterol mg/dl	*mean ± SD*	216.1 ± 25.5	195.6 ± 23.2	0.001
	Range	163 – 272	154 – 261	
HDL cholesterol mg/dl	*mean ± SD*	49.3 ± 9.2	52.2 ± 8.4	0.026
	Range	34 – 64	38 – 62	
LDL cholesterol mg/dl	*mean ± SD*	122.3 ± 28.7	108.6 ± 26.8	0.002
	Range	73 – 197	73 – 182	
VLDL cholesterol mg/dl	*mean ± SD*	44.8 ± 12.6	34.8 ± 7.3	0.001
	Range	28 – 64	24 – 53	
Triglycerides mg/dl	*mean ± SD*	224.2 ± 63.1	174.6 ± 36.3	0.001
	Range	139 - 320	120 – 269	

*P< 0.05 significant

Further analysis was performed to assess the changes in lipid profile in both groups; the multiple logistic regression (binary) test was conducted for adjustment of any possible confounders, the results of this analysis are shown in table 3, where only three variables appeared to be associated with serum lipid levels, the more effect was found to the previous pre-eclampsia, (OR = 2.60, P=0.02) followed by fasting blood glucose (OR 1.19, P=0.04) and systolic blood pressure (SBP), (OR = 1.04, P=0.05). Nonetheless, these findings indicated that previous preeclampsia status was an independent risk factor for dyslipidemia and early undesirable changes in lipid profile which might be a risk factor to develop preeclampsia

Table 3. Results of multiple logistic regressions for the risk factors

Risk factors associated with serum variability	ß	Odds ratio (OR)	95% C.I.for OR	P.value*
Preeclampsia	0.96`	2.60	1.15 – 5.87	0.02
FBS	0.09	1.19	1.00 – 1.18	0.04
SBP	0.04	1.04	1.00 – 1.08	0.05
DBP	0.04	0.96	0.90 – 1.03	0.28
Age	0.03	0.97	0.89 – 1.06	0.47
History of Gestational HT	0.79	0.45	0.05 – 3.82	0.47
History of Gestational DM	0.20	1.22	0.66 – 2.31	1.00
Parity	0.14	1.14	0.44 – 2.98	0.78
Gravidity	0.10	0.91	0.42 – 1.95	0.80
Hyperglycemia	0.17	1.18	0.47 – 3.12	1.00

*P< 0.05 significant

Discussion

Most studies evaluating the HDL-C levels in pregnant women have determined the levels to be similar or lower in preeclampsia women, though a few did detect higher levels in women with preeclampsia (14). Conversely, most studies have observed LDL-C levels to be similar or higher in preeclamptic women; however, several have reported lower levels of LDL. The lipid group most consistently and positively associated with preeclampsia are triglycerides a finding reported by over 80% of the studies that evaluated it (15). To the best of our knowledge, no study has shown triglycerides to be significantly lower in preeclamptic women. Pregnant women who have history of recurrent preeclampsia had increased levels of total TC, TG, VLDL-C and LDL-C concentration as compared with pregnant women who remained normotensive, while women with history of recurrent preeclampsia showed significant fall in high density lipoprotein cholesterol (HDL-C) level as compared to normal pregnant women. This is consistent with that registered by Sep Semon *et al* (16) and Enquobahrie, Daniel A., et al (17). Reduced circulating levels of HDL-C in (recurrent) preeclampsia have been reported by Sep, Simone JS, et al (18) and Williams, Michelle A., et al (19). Many studies showed significant elevation in serum triglyceride; normal pregnancy is associated with hyper-oestrogenaemia, however, hypertriglyceridemia in pre-eclampsia is probably not due to hyper-oestrogenaemia as the level of oestrogen usually decreases in pre-

clampsia(20,21,22). Some studies have concluded that hypertriglyceridemia may be due to hyperinsulinism found in pregnancy complicated by hypertension as there appears to be an exaggeration of insulin resistance and associated metabolic changes (23, 24, and 24).

Conclusions:
This study showed that the women who have history of recurrent preeclampsia had disturbed lipid profile (increased levels of total TC, TG, VLDL-C and LDL-C concentration) in addition to decrease the high density lipoprotein cholesterol (HDL-C) level in subsequent pregnancy compared to normal pregnancy.

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