Comparative study of lipoprotein lipase enzyme, ApoE and ApoC2, in pregnant women with and without preeclampsia

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Abstract---Background: Preeclampsia (PE) is a multisystemic syndrome specific to pregnancy. Although PE is the most common cause of death from pregnancy-related problems, its underlying cause is still unknown. In PE, lipid metabolism is altered. When lipids are damaged, both the mother and the foetus may be at risk. Methods: Blood samples were taken from 45 normotensive and 45 preeclamptic pregnant women. These samples were analyzed for LPL, Apo E and C2. Results: Concentrations of LPL, Apo C2 and Apo E differ significantly between preeclamptic women and pregnant controls which were higher in preeclamptic than in pregnant controls. Conclusions: In preeclamptic women, the increase in LPL, ApoC2 and Apo E concentration may serve as a marker for preeclampsia complication that which leads to worse consequences and could be a relevant factor in the pathogenesis of preeclampsia.

Keyword---lipoprotein, enzyme, pregnant women, preeclampsia.

Introduction

Preeclampsia is disorder of pregnancy associated with new-onset hypertension, which occurs most often after 20 weeks of gestation and frequently near term. Although often accompanied by new-onset proteinuria, hypertension and other signs or symptoms of preeclampsia may present in some women in the absence of proteinuria[1]. Preeclampsia is diagnosed when Systolic blood pressure of ≥140 mm

Hg or diastolic blood pressure of ≥ 90 mm Hg on two occasions at least 4 hours apart after 20 weeks of gestation with proteinuria (300 mg/24 h or a urinary protein: creatinine ratio of 0.3 mg/dl in a spot urine random sample dipstick reading of 2+)[2,3]. Severe feature (such as thrombocytopenia, renal insufficiency, impaired liver function, or pulmonary edema) is present, hypertension alone is enough to make the diagnosis [4]. During a healthy pregnancy, the extravillous cytotrophoblast of fetal origin invades the spiral arteries in the decidua and myometrium. This spiral remodeling is disrupted in preeclamptic condition[5]. Due to impaired spiral artery remodeling, the placenta is deprived of oxygen, which leads to a condition called placental ischemia. This favors the production of antiangiogenic factors into maternal circulation that contributes to endothelial damage. Previous study have shown that increased concentrations of antiangiogenic substances including soluble endoglin (sEng) and tyrosine kinase-1 (sFlt-1)[6] produced by the placenta into the mother's bloodstream during preeclampsia promote endothelial dysfunction and proteinuria[7].

Lipoprotein lipase is a 55 kDa glycoprotein that expressed with high levels in cells and organs with a high oxidative metabolism, but it is also expressed in other tissue types, not related to intravascular lipolysis such as the spleen, testis, lung, kidneys, and brain as well as in macrophages[8,9].The triglycerides in the neutral cores of chylomicrons and VLDLs are hydrolyzed by LPL at the luminal face of the capillary endothelium producing chylomicron remnants and IDLs respectively [10].ApoC-I and ApoC-III serve as inhibitors of LPL while ApoC-II and ApoA-V positively regulate LPL during intravascular lipolysis[11]. Mature human apoC-II has a molecular mass of 8916 Da and includes 79 amino acid residues after losing its signal peptide and being secreted into plasma[12]. Apolipoprotein C-II is primarily expressed in the liver and secreted into plasma, but it is also produced by other tissues, including the intestine, macrophages, adipose tissue, brain, skin, lungs, retina, and retinal pigment epithelium[13]. ApoC-II may regulate LPL activity in a pressure-dependent model. In this concept, triacylglycerol hydrolysis is mediated by LPL, while ApoC-II stays affixed to the VLDL and chylomicron surfaces. The surface pressure on triglyceride rich lipoproteins (TRLs) rises as LPL consumes the neutral core TGs. When this surface pressure exceeds a specific ApoC-II retention pressure, ApoC-II is forced out of the TRL[14]. All lipoproteins, with the exception of low-density lipoprotein (LDL), contain the 34 kDa glycoprotein apolipoprotein E, which is mostly produced by the liver and plays a crucial role as a cholesterol transporter[15] .Through its attachment to the LDL receptor, ApoE controls the removal of lipoproteins from plasma and makes it easier for fat and cholesterol to enter cells[16]. It is a polymorphic protein with three isoforms including: ApoE2, ApoE3, and ApoE4[17].

Materials and Methods

This Case - control study was carried out in Babylon Teaching Hospital for Maternity and Pediatrics , Babylon Province . The studied patients attended the outpatient clinic, Labour room. All samples were collected from October 2021 till February 2022. They were diagnosed by specialist Gynecology physicians depending on the clinical features and laboratory finding . The biochemical tests under study were performed at the laboratory of the Department of Clinical Biochemistry, College of Medicine, University of Babylon. The study groups of the

present study include (90) pregnant women , (45) of them were with preeclampsia and (45) healthy pregnant women taken as control group. In patient group (9) women with sever preeclampsia and (36) woman without sever feature .All participant was with no preexisting hypertension ,renal disease , diabetes mellitus and liver disease. Verbal and written consent was obtained from each subject. Complete obstetrical and family history was recorded on a proforma designed for the study. By using the ELISA technique, the levels of serum lipoprotein lipase, apolipoprotein C2, and apolipoprotein E were determined for all patients and controls . The data were analysed using SPSS-10 and Standard Deviation were calculated. The mean values were compared between cases and controls using t-test at 5% level of significance.

Results

The general characteristics for two groups of pregnant women are shown in Table 1. Age , Body mass index and Gestational age did not differ between the two groups. Preeclamptic women divided as primigrivida (75.5%), multigravida (24.5%) and control group divided as primigravida (46.6%), multigrivida (53.4%). The results were calculated and showed highly significant variances at (p. value <0.001) between the matched groups. Preeclampsia patients had a significantly higher LPL than the controls, 200.10ng/dl vs. 134.80 ng/dl respectively. Therefore, the mean of LPL was highly significant, as (P< 0.001) and there is no significance difference in means of LPL concentrations between subgroups. The means of serum levels of apolipoprotein C2 in preeclampsia patients and controls was (186.08 ng/ml) (121.7 ng/ml) respectively .The means of apolipoprotein C2 was highly significance as (P<0.001) and there is no statistical difference in means of apolipoiprotein C2 concentrations between subgroups. Preeclampsia patients had a significantly higher apolipoprotein E than the controls, 793.2ng/ml vs. 512.4ng/ml, respectively. Therefore, the mean of apolipoprotein E was highly significant, as (P< 0.001). There is statistical significance difference in means of Apo E concentrations between subgroups, As shown in Table 2.

Table 1
General characteristics of studied groups

Variable	Preeclampsia Mean ± SD*		Normal pregnant Mean ± SD	p. value
Age (years)	29.1 ± 8.3		26.8 ± 4.02	> 0.05
BMI (kg/m^2)	25.12 ± 2.97		23.9 ± 3.1	> 0.05
Gestational age (Weeks)	31.2 ± 4.2		28.9 ± 4.4	> 0.05
Parity N (%)	Primigravida	34 (75.5%)	21 (46.6%)	<0.001
	Multigravida	11 (24.5%)	24 (53.4%)	

Table 2
LPL, Apo C2 and Apo E from Normal and Preeclamptic Pregnant Women

Variable	Preeclampsia Mean ± SD	Normal pregnant Mean ± SD	p. value
LPL	200.10 ± 27.15	134.80 ± 11.88	<0.001
Apo C2	± 18.8 186.08	121.7 ± 39.3	<0.001
Apo E	793.2±201.8	512.4 ± 198.3	<0.001

Discussion

Risk of preeclampsia is increased in association with abnormal maternal lipid concentrations[18]. Previous study was revealed significantly higher concentrations of serum total cholesterol, triacylglycerol were found in the preeclamptic cases compared to pregnant controls[19] . Our study revealed the mean of LPL was highly significant, as (P<0.001) with mean 200.10ng\dl. The study on LPL gene polymorphisms that conducted by Procopciuc and his colleague disagreement with our study , was revealed reduce LPL serum activity, increasing hypertriglyceridemia and decreasing HDL levels[20] .Lipoprotein lipase anchored in the luminal surface of the vascular endothelium normally hydrolyzes triglycerides to glycerol and fatty acids available for extrahepatic tissues. However, the amount of LPL and whether it increases or decreases may differ in various tissues at late gestation: LPL activity decreases in adipose tissue but increases in placenta and mammary gland[21].

The study that conducted by Tesfa and his colleague was revealed highly statistical significant association between the serum levels of VLDL-c and pre-eclampsia as compared to normotensive pregnant women and low HDL-c level in patient group [22]. Increased levels of Apo C2 in preeclampsia may be due to ApoC2 found in VLDL so increase in VLDL concentration may lead to increase in ApoC2 . High density lipoprotein act as reservoir for apolipoprotein C2 after activation of lipoprotein lipase so decrease in HDL concentration may cause increase in apolipoprotein C2. High levels of Apo E may be related to the oxidative stress and inflammatory state reported in preeclampsia[23]. Apolipoprotein E isoforms and gene variants have been postulated and highlighted as potential predictors of preeclampsia development[24].The high levels of serum TG in preeclamptic women are believed to be due to high circulating levels of apolipoprotein E that interfere with TG clearance by interfering with lipoprotein lipase activator, apolipoprotein C-II[25.] We conclude that in preeclamptic women high concentrations of LPL , Apo E and Apo C2 may serve as a marker for preeclampsia complication that which leads to worse consequences .Apolipopotien E and Apo C2 modulates LPL activity and could be a relevant factor in the pathogenesis of preeclampsia .

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