USE OF LIPID PROFILE AS MARKER OF SEVERITY IN PRE-ECLAMPSIA

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ABSTRACT

Background

Pre-eclampsia is the major cause of maternal morbidity and mortality, preterm birth, perinatal death, and intrauterine growth restriction. The incidence of pre-eclampsia globally varies widely from 5-15 percentages. Studies results find correlation of essential hypertension with alteration of serum cholesterol, triglycerides and HDL-C. Various studies claim that abnormal lipid synthesis leading to increase of thromboxane level and the decrease of prostaglandin levels.

Objectives

To assess changes in lipid profile in pre-eclampsia and if these changes can be used as a marker of severity of the condition.

Patients and Methods

Case-control Study at Sulaimani Maternity Teaching Hospital from 01. Feb. 2017 to 01. Aug. 2017, it includes 100 pregnant women divided into three groups. Control group who remained normotensive during study period and case group who subdivided to two groups including those cases who developed mild and sever pre-eclampsia during the study period.

Results

There was significant rise in the serum TC, TG, LDL and VLDL and decrease in HDL in pre-eclamptic groups compared to normal healthy pregnant women. When we compare patient with sever pre-eclampsia with patient with mild pre-eclampsia, we found that women with sever pre-eclampsia has significantly higher level of TG (334.9 ± 97.8vs 250.2 ± 31.5) and VLDL (66.4 ± 19.8vs45.4 ± 12.7 only.

Conclusion

Maternal dyslipidemia early in second trimester may be an indicator for development of future pre-eclampsia.

Keywords: *Pre-eclampsia serum cholesterol, Triglyceride, Low-density lipoprotein, High-density lipoprotein, Very low-density lipoprotein.*

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INTRODUCTION

Hypertension is an important cause of morbidity and mortality for mother and fetus during pregnancy [1]. Hypertension in pregnancy occurred when diastolic blood pressure is > 110 mmHg on anyone occasion or > 90 mmHg on Two or more consecutive occasions more than 4 hours apart after 20 weeks gestation in previously normotensive woman [2]. The hypertensive disorders of pregnancy cover a wide spectrum of conditions, which pre-eclampsia poses the greatest potential risk and remains one of the most common causes of maternal death. Pre-eclampsia is a multi-system disorder of pregnancy [3]. Studies result's find correlation of essential hypertension with alteration of serum cholesterol, triglycerides and HDL-C, various studies claim that abnormal lipid synthesis leading to increase of thromboxane level and decrease of prostaglandin levels, as well as the imbalance of lipid peroxidase and anti-oxidants is responsible for pre-eclampsia [3,4]. Relative to normal pregnancies women destined to develop pre- eclampsia have marked increases in serum triglyceride and free fatty acid concentration with a shift to smaller , denser low density lipoprotein (LDL). These changes are evident as early as 16-18 weeks gestation [4]. From 10 weeks to 35 weeks of pregnancy mean serum estradiol concentration increased steadily and there is a strong relationship between the rise in estradiol and the increment in plasma triglyceride and plasma cholesterol [5].

The objective of this study was to assess if there are changes in lipid profile in pre-eclampsia and if these changes can be used as markers of severity of the condition.

PATIENTS AND METHODS

Case control study conducted on 100 pregnant women admitted to department of Obstetrics& Gynaecology Maternity Teaching Hospital in Sulaimani from 1st February 2017 to 31 August 2017. Normotensive pregnant women between the age 14-40 years old, gestation from 27-32 week and singleton pregnancy were included. Cases excluded if had multiple pregnancies, history of essential hypertension, diabetes mellitus, renal disease and hepatic disease, blood disease, epilepsy and had history of medical disease and history of chronic drug intake. After taking informed consent from all patients, detailed history taken with proper obstetric examination. Apart from routine investigations, a serum lipid profile including total cholesterol (TC), Triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and very low-density lipoprotein (VLDL), was performed for all cases, and all cases were followed up during the study period for development of pre-eclampsia depending on measuring systolic and diastolic blood pressure and measuring urine for albumin by dipstick method. Ten patients lost follow-up and 90 patients remained at the end and distributed into three groups:-

Control group: Those that remained normal through out study period (n=33).

Study group: Those women who developed pre-eclampsia (PE). In whom (n=30) developed mild PE BP ≥140/90 mmHg and urine albumin +1 (By dipstick method) and (n=27) developed _severe PE: BP≥160/110mmHg and urine albumin ≥ +2 (By dipstick method).

Blood pressure recorded by mercury sphygmo-manometer in sitting position with suitable cuff for large and small arms. Korrotkoff phase 5 (k5) used to detect diastolic pressure which is now recommended for diagnosing diastolic hypertension (6). From all subjects five millilitres (5 ml) blood samples collected for biochemical analysis, after (8-10) hours of fasting, blood collected through the antecubital vein using 5 ml disposable syringe, after putting it into labelled plain container allow it to clot at room temperature. To obtain serum blood samples centrifuged for 10 minutes, serum put into new-labelled sample containers and stored by frozen mode -40C until analysis time. Serum lipid tests include total cholesterol (TC), Triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and very low-density lipoprotein (VLDL). Data entered and analysed using SPSS software 21-version, results expressed as mean, standard deviation and or as a percentage, t-test or chi-square tests used to find correlation between variables with consideration of p-value < 0.005 as the lower limit of statistical significance.

RESULTS

Regarding the demographic characteristic of studied group, there is no statistically significant result in all parameters as shown in Table 1.

Total cholesterol were at proportional relation with pre-eclampsia, pre-eclampsia groups had higher total cholesterol level 250.2 ± 31.5 and 236.7 ± 23.2 for sever preeclampsia and mild preeclampsia respectively than control group 206.9 ± 24.4, especially in severe

pre-eclampsia group were pregnant women at highest risk compared to other groups, Table 2.

Mean Very Low-Density Lipoproteins (VLDL) were found to be higher among study group66.4 ± 19.8 and 45.4 ± 12.7 for severe preeclampsia and mild preeclampsia respectively with statistically significant difference ($p<0.001$) with control group 33.3 ± 7.6, Table 2.

As compared to control group, serum triglyceride level was higher in study group 334.9 ± 97.8 and 224.9 ± 63.4for severe preeclampsia and mild preeclampsia respectively with statistically significant difference ($p<0.001$) with control group166.5 ± 38.0, Table 3.

While comparing the serum lipid profile between the mild and severe pre-eclampsia, there was statistically significant difference between mean and standard deviation for level of TG and VLDL, while there were no significant relation in the level of CH, HDL and LDL, Table 3.

Generally the mean of all serum lipid profile (except in HDL) were higher in pre-eclampsia group than in control group, Table 3.

Table 1. The characteristic of women enrolled in this study.

Variable	Control	PET / Mild	PET/ Sever	P value
Age (year) Mean ± SD	30 ± 6.0	29.6 ± 6.6	28.8 ± 6.5	0.75 NS
Gestational age (week) Mean ± SD	29.5 ± 3.6	32.5 ± 2.8	29.7 ± 3.5	0.001 S
Parity N (%)				
Nulliparous	9 (30%)	5 (16.7%)	6 (20%)	0.7 NS
Para (1 - 2)	13 (43.3%)	17 (56.7%)	14 (46.7%)	
parity > 2	8 (26.7%)	8 (26.7%)	10 (33.3%)	
Gravida N (%)				
1- 2 pregnancies	13 (43.3%)	9 (30 %)	14 (46.7%)	0.7 NS
3- 4 pregnancies	11 (36.7%)	13 (43.3%)	9 (30%)	
≥ 5 pregnancies	6 (20%)	8 (26.7%)	7 (23.3%)	

Table 2. The changes in the mean level of lipid profile among study groups.

Variable	Control	Mean ± SD		P value
		PET / Mild	PET/ Sever	
TC	206.9 ± 24.4	236.7 ± 23.2	250.2 ± 31.5	0.001
TG	166.5 ± 38.0	224.9 ± 63.4	334.9 ± 97.8	0.001
HDL	52.4 ± 12.5	46.4 ± 13.2	50.7 ± 8.5	0.13
LDL	121.7 ± 26.3	148.8 ± 34.2	133.1 ± 31.9	0.004
VLDL	33.3 ± 7.6	45.4 ± 12.7	66.4 ± 19.8	0.001

Table 3. Compared mean levels and significance relation of lipid profile tests between sever and mild pre-eclampsia groups.

Variable	No.	TC	TG	HDL	LDL	VLDL
PET / Mild BP ≥ 140/90	30	236.7 ± 23.2	224.9 ± 63.4	46.4 ± 13.2	148.8 ± 34.2	45.4 ± 12.7
PET/ Sever BP ≥ 160/110	27	250.2 ± 31.5	334.9 ± 97.8	50.7 ± 8.5	133.1 ± 31.9	66.4 ± 19.8
P value		0.06 NS	< 0.001 S	0.14 NS	0.07 NS	< 0.001 S

DISCUSSION

Pre-eclampsia is a vascular disorder of pregnancy associated with increased maternal mortality as well as perinatal morbidity and mortality [7]. Normal pregnancy is characterised by a state of hyperlipidaemia, the process that is principally modulated by hyperestrogenemia, characteristic of pregnancy [8, 9]. This is in turn modulated by relative insulin resistance and hyperinsulinemia found in pregnancy [10, 11].

Many studies has been done by different authors trying to asses the serum lipid during pregnancy and find out its relation to the severity of preeclampsia [12]. Vidyabati RK et al described that serum lipid profile early in second trimester can be used as a marker to predict development of preeclampsia [13].

Baker AM et al in their study, concluded that maternal serum lipid derangement occurs early in pregnancy I women with mild preeclampsia [14].

In current study the mean level of cholesterol in studied groups mild/sever preeclampsia was (236.7 ± 23.2 mg/dl and 250.2 ± 31.5 mg/dl) significantly higher as compared to control group (206.9 ± 24.4 mg/dl) with (p=0.001).

The mean levels of cholesterol in mild preeclampsia group was 236.7 ± 23.2 mg/dl and in severe preeclampsia was 250.2 ± 31.5 mg/dl respectively, that was significantly higher as compared to the control group, however there was no statistically significant difference seen between two studied groups i.e. mild and severe preeclampsia and severity of preeclampsia was not directly proportional to levels of cholesterol. This result is consistence to that of Vidyabati RK et al as in their study the level of cholesterol in those subject who developed preeclampsia was 237.19 ± 33.95mg/dl and that was significantly higher than cholesterol level of the control group 204.15± 23.47 mg/dl (p=0.001) [13].

Also Danial Enquabahrie et al. concluded that the risk of developing preeclampsia increase with increasing level of cholesterol (cholesterol > 205 mg/dl is associated with 3.60 fold increased risk) [15].

Baker AM et al stated that mean level of cholesterol in control group was 207 ± 35.8 mg/dl and was lower when compared to mild preeclampsia group 219 ± 36.0 mg/dl, this was not statistically significant (p=0.14) but the level in severe preeclampsia group was 191 ± 21.6 and was lower than both control and mild preeclampsia group [14].

In current study mean level of triglyceride was 166.5 ±38.0 mg/dl in control group and 224.9 ±63.5 mg/dl and 334.9 ±97.8 mg/dl in mild and severe preeclampsia groups respectively and this deference was statistically significant (p<0.001).

In mild preeclampsia the mean value of triglyceride was 224.9 ±63.5 mg/dl and 334.9 ±97.8 mg/dl in severe preeclampsia group and it was seen that both group had significantly higher levels as compared to control group and also statistically significant difference was found between mild and severe preeclampsia group (p<0.001).

This shows that if triglyceride level is higher in second trimester, there is increased risk of developing preeclampsia and the higher the level of triglyceride the more severe is degree the of preeclampsia.

According to current study mean levels of VLDL were lower (33.3± 7.6 mg/dl) in control group as compared to study groups (45.4± 12.7 mg/dl and 66.4 ±19.8 mg/dl)

in mild and severe preeclampsia respectively and the difference was statistically significant (p=0.001).

VLDL value was found to be higher in severe preeclampsia group (66.4 ±19.8 mg/dl) as compared to mild preeclampsia group (45.4± 12.7 mg/dl) and the difference was statistically significant (p< 0.001).

This is agree with Cong-K.J study who also concluded that the triglyceride and VLDL levels were significantly higher in preeclampsia group and also he concluded that the deranged lipid profile can be used as marker for severity of preeclampsia and can be related to vascular pathology characteristic of the syndrome[16].

In conclusion, abnormal lipid profile early in pregnancy may be is associated with increased risk of developing pre-eclampsia. The higher the level of lipid profile, the more severe is the degree of pre-eclampsia, so dyslipidemia can be used as marker for severity of this condition.

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