Lipid profile and pre – eclampsia

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الخلاصة

تهدف الدراسة الحالية لتقييم ما إذا كانت هناك تغييرات في نسبة الدهون المصاحبة لمقدمة الارتعاج وامكانية استخدام هذه التغيرات كعلامات لشدة المرض.شملت هذه الدراسة 100 امرأة حامل وقسمت الى ثلاث مجموعات ,المجموعة الأولى تضمنت 25 امرأة حامل لديها مقدمات ارتعاج حادة في الثلاثينيات من العمر والمجموعة الثانية 25 امرأة حامل لديها مقدمات ارتعاج معتدلة في الثلاثينيات أيضا وتم مقارنتها مع 50 امرأة بحالة صحية جيدة في سن مماثلة كمجموعة ضبط حيث شملت الدراسة الفحوصات المختبرية (قياس مستوى الكوليسترول في الدم,قياس مستوى الـ Triglyceride,قياس مستوى الـ LDL , قياس مستوى الـ VLDL وقياس مستوى الـ HDL) حيث بينت النتائج ان هنالك زيادة واضحة في مستوى VLDLو Triglyceride و LDL وانخفاض في مستوى HDL لدى النساء المصابات بمقدمة الارتعاج,كما ان النساء المصابات بمقدمة الارتعاج من النوع الشديد لديهن ارتفاع في مستوى TGوVLDL عند مقارنتهن بالنساء المصابات بمقدمة الارتعاج من النوع المعتدل.

Abstract

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

Study design: This study include 100 pregnant women divided into 3 groups.

1) 25 pregnant women with sever pre-eclampsia in the third trimester.
2) 25 pregnant women with mild-moderate pre-eclampsia in the third trimester .
3) 50 apparently healthy pregnant women of comparable age &parity in the third trimester.

All were investigated for serum lipid profile including
serum cholesterol(CH)
serum triglyceride(TG)
serum high density lipoprotein(HDL)
serum low density lipoprotein(LDL)
serum very low density lipoprotein(VLDL)

Result: There was significant increase in serum TG ,VLDL and LDL level in women with pre -eclampsia than the control group and no significant difference in the serum cholesterol, while patient with pre-eclampsia had lower HDL level.
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 and VLDL only.

Introduction

Pre-eclampsia (PE):

Is a pregnancy- specific multisystem disorder that characterized by the development of hypertension and proteinuria after 20 weeks of gestation .In an average UK population the incidence of pre-eclampsia occurs in less than 1 in 20 women .In the primigravida population in Ireland the incidence was as low as 2%[(1)] .

Definition of hypertension:

A- One measurement of diastolic blood pressure of 110 mmHg or more.
B- Two consecutive measurement of diastolic blood pressure of > 90 mmHg 4 hour or more apart. [(2)]

Definition of porteinuria :

Proteinuria is defined as
A- One 24-hour urine collection with a total protein excretion of 300 mg or more .
B- Two random clean catch or catheter urine specimens with 2+(1g albumin/L), or more on reagent strip or 1+(0.3 g albumin /L) if specific gravity less than 1030 and ph is <8. [(2)]

Risk factors for per- eclampsia:

Pregnancy associated factors:
Chromosomal abnormalities(triploidy)
Hydatiform mole
Hydrops fetalis
Multi fetal pregnancy
Structural congenital abnormalities. [(3)]
B. Maternal-specific factors:
Age greater than 35 years or less than 18 years
Black race Family history of pre-eclamsia

Nulliparity Pre- eclampsia in a previous pregnancy
Specific medical condition e.g. chronic hypertension ,gestational diabetes, renal disease and systemic lupus erythematosus.
obesity[3]
C. Paternal-specific factors:
First time father Previously fathered a pre - eclamptic pregnancy in another woman. [3]

Pathophysiology:

Although the exact cause of pre-eclampsia remains unclear many theories center on problems of placental implantation and the level of trophoblastic invasion [4] .

One of the most striking physiological changes is intense systemic vasospasm which is responsible for decreased perfusion of virtually all organ systems. [4]

Uterine vascular changes:

In contrast to normal pregnancy, endovascular trophoblast invasion remains superficial, rarely if ever reaching the myometrial segment, as a result the spiral arteries remain muscular, undilated and respond to vasomotor influence.[4]

Endothelial dysfunction:

Widespread disturbance of the maternal vascular endothelium is responsible for hypertension, altered vascular reactivity, activation of the coagulation cascade and the multisystem damage which accompany pre-eclampsia. Serum markers of endothelial dysfunction (e.g. von-willebrand factor, and fibronectin) are increased and may precede the onset of clinical disease by weeks or months.[4]

Circulating factor: [5]

Lipid per oxidation degradation product and reactive oxygen species (ROS): lipid peroxidation and oxidative damage is increased in the placenta of women with per-eclampsia . lipid peroxide and ROS , particularly the super oxid anion radical , are know to cause endothelial dysfunction .

Maternal contribution:

A-Genetic influences: [6]

Daughters of women with PE are 4-5 times more likely to develop the syndrome then daughters in law.

2 kinds of genetic model have been suggested :
*A simple recessive model with genes acting in the mother
* dominant model with incomplete pentrance

B- Abnormal lipid metabolism: [5].

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 wks gestation.

Lipid changes in normal pregnancy:

During the course of normal pregnancy, plasma triglyceride and cholesterol concentration rise by 200-400% and 25-50% respectively [7]

In an earlier study of pregnant women silliman *et al*[8] showed that the raised concentrations of plasma triglyceride are accompanied by a reduction in mean LDL size. Those women who experienced the greatest increase in plasma triglyceride exhibited the most significant shrinkage in their LDL particle

Relationship between serum estradiol and lipoprotein:

From 10 weeks to 35 weeks of pregnancy mean serum estradiol concentration increased steadily and there was a strong relationship between the rise in estradiol and the increment in plasma triglyceride and plasma cholesterol. [9].

Oxidized low – density lipoprotein (Oxidized LDL) and the risk of pre-eclampsia:

The Oxidative conversion of low density lipoprotein (LDL) to Oxidized LDL is considered to be a key event in the biological process that initiates and accelerates the development of the early atherosclerotic lesion, the " fatty streak. Women with pre-eclampsia are more likely than normotensive pregnant women to experience metabolic disturbances that are similar to those seen in non pregnant patient with coronary heart disea**se.**[10]

Aim of study

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

Patient and Methods

This prospective study was conducted on 100 pregnant women admitted to AL- mauanii hospital in AL – Basra city .

The following inclusion criteria were followed:

Pre – eclampsia was diagnosed by blood pressure elevation , equal or more that 140/90 mmhg in combination with proteinuria after 20 weeks gestation in previously normotensive non proteinuric patient.

Age group from 14 – 44 years.

Parity less than 10.

Gestation from 27 – 40 weeks.

Singleton pregnancy.

The exclusion criteria were.

Multiple pregnancy .

History of essential hypertension , diabetes mellitus , renal disease , hepatic disease , blood disease , epilepsy and other medical disease.

History of chronic drug intake.

Women in this study were divided into 3 group :

1-25 pregnant women with severe pre – eclampsia which was indicated by a systolic blood pressure equal or more than 160 mmhg and diastolic pressure of equal or more than 110 mmhg with proteinuria

2- 25 pregnant women with mild – moderate pre – eclampsia which was evidenced by a systolic pressure of 140 – 159 mmhg and diastolic blood pressure of 90 – 109 mmhg with proteinuria .

3- 50 apparently healthy pregnant women of comparable age , parity and stage of pregnancy as control group .

Blood pressure was recorded in the study in the sitting position with cuff that is large enough for the subjects arm on at least two occasions 6 hours apart.

Korotkoff phase 5 (k5) .which is now universally recommended for diagnosing diastolic hypertension is used to detect diastolic pressure. [11]

One24_hours urine collection with total protein excretion of 300 mg or more or two clean catch _ mid stream or catheter urine specimens with 2+ (1g albumin/L) or more on reagent strip or1+(03 g albumin/L) if specific gravity less than 1030 and ph 3)

Blood samples were drawn from all the subjects following a fasting for 8-10 hours. Blood was aspirated , lipoprotein aspirated by spinning

serum for long time in high speed centrifuge (ultracentrifuge). The most dense classes will settled toward the bottom , the least dense toward the top.

Following centrifugation the quantity of each lipoprotein class was determined based on its movement in an electrical field and analyzed for serum triglycerides (TG) total cholesterol (TC), and high density lipoprotein (HDL) .

Serum LDL was calculated by Frederick son Fredwalds formula according to which:

LDL cholesterol = total cholesterol – (HDL + VLDL)

VLDL was calculated as 1/5 of triglyceride .

Statistic analysis

The results were expressed as mean ± SD or as percentage, as suitable. The significance of comparison between pairs of groups was tested using student t-test or chi-square test as appropriate.

A level of P- value < 0.005 was considered as the lower limit of statistical significance .

highly significant if < 0.001

Results

Table (1) Show the demographic characteristics of the studied groups. In this table most of patients were nilliparous women 25 (50%) , 15(30%) in case and control groups respectively No significant difference in both group regarding patient age, gestational age and antenatal care(ANC).

Table (2)Study the changes in lipid profile in PE compared to control group. It shows that women with PE had significantly higher level of VLDL, LDL, and TG than women in control group and there is decrease in mean level of HDL among PE women in comparison with control group. While there is no significant difference in the mean level of serum cholesterol among both group.

Table (3) Study the relation ship of mean level of lipid concentration with severity of PE. Show the pregnant women with severe PE had a significantly higher level of TG and VLDL in comparison with mild PE women. While there were no statistically significant differences in the level of CH, HDL, and LDL in both group of hypertensive women.

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

Variable	Case group N=50	Control group N= 50	Significant P-value
Age (years) Mean ± SD Range	 26.60 ± 7.97 14-44	 26.90 ± 8.15 14-44	 NS
Parity / No. (%) Nulliparous Parity (1-4) Parity 5 and a bove	 25(50%) 19 (38%) 6 (12%)	 15(30%) 21(42%) 14(28%)	 NS
Gestational age (week) Mean ± SD Rang	 33.88 ± 3.70 27-40	 34.20± 3.96 27-40	 NS
ANC Inadequate <3 Adequate ≥ 3	 16 (32%) 34 (68%)	 20 (40%) 30 (60%)	 NS

NS= Non significant

Table (2)The changes in the mean level of lipid profile among women under study.

Parameters (mg/Dl	Case group N=50	Control group N=50	Significance P-value
HDL (mean ± SD)	40.82± 4.06	49.80 ± 3.24	0.001 S
VLDL (mean ± SD)	48.68 ± 2.7	40.46 ± 3.33	0.001 S
LDL (mean ± SD)	118.91 ± 7.93	107.89 ± 7.90	0.001 S
Chol estrol (mean ± SD)	201.20 ± 9.81	197.42 ± 8.29	0.054 NS
T.G (mean ± **SD)**	233.28 ± 23.03	202.10 ± 16.91	0.001 S

S= significant , NS= Non significant

Table(3)The relationship of mean level of lipid concentration with severity of PE.

Severity of PE	No	HDL Mean ± SD	VLDL Mean ±SD	LDL Mean ±SD	Ch Mean ±SD	T.G Mean ± SD
Mild PE BP ≥ 140/90	25	42.16±3.61	42.56±2.39	115.60±6.84	199.16±10.58	212.80±12.04
Sever PE BP≥160/110	25	39.48±4.11	50.80±2.00	112.28±8.57	203.24±8.71	253.76±8.04
Significance P-value		0.014 NS	0.001 S	0.127 NS	0.133 NS	0.001 S

S= significant
NS= Non significant

Discussion

Pre-eclampsia a vascular disorder of pregnancy is a leading cause of maternal morbidity as well as perinatal morbidity and mortality.Complications of hypertension are the third leading cause of pregnancy-related death after hemorrhage and embolism.[12]

Disturbed lipid metabolism, including hypertriglyccridemia, which is primary due to enhanced entery of TG rich lipoproteins (especially VLDL) in to the circulation rather than to diminish removal, was noted to be a feature of pre-eclampsia over 60 years age [13].

Therefore our study was designed to ascertain whether there is any change in the level of lipid profile in pre-eclampsia group in comparisom to those with normal uncomplicated pregnancy.

It has been shown from the results of (Table 1) that both studied group have approximately the same age range (14 - 44 years) and approximately the same gestational age rang (27-40 weeks), but half number of our patients (50%) were nulliparous, this is because the hypertensive disorder in pregnancy is more common in first pregnancy [14].

Our data demonstrate that there was a significance increment in the level of TG and VLDL in women with PE in comporism with those who had normal uncomplicated pregnancy, this finding goes with different other previous studies [15,16,17]

The mechanisms underlying abnormal elevation of TG and VLDL in PE are poorly understood. One possibility; heightened gestational insulin resistance in PE probably increase The mobilization of fatty acid from visceral adipocytes , fuelling over production of VLDL by the liver, and suppresses the activity of lipoprotein lipase, culminating in elevated serum TG concentration which is major risk factor for vascular dysfunction in PE. [17]

In our study we found that there is lower level of HDL in PE patient in comparsim to normal pregnancy, this finding is in agreement with other study[18]

In normal pregnancy HDL increase slightly due to the effect of estrogen which are known to elevate HDL[19])

Normal pregnancy is characterized by gestational increase in TG and LDL concentration followed by progressive decrease during puerperim [20].

There is general consensus that these lipids are not further increased in patient with PE , in our study level of LDL concentration were significantly higher in PE patient than in normal pregnancy and there is no significant difference in the level of CH in both groups our findings were in agreement with other studies [18, 21].

In regard to the severity of PE, we found that the only serum TG and VLDL concentration were significantly higher in sever PE group in comparison with mild PE group, while there is no significant difference on other lipid parameters (CH, LDL, and HDL). In this aspect our finding was in agreement with that of Cong-KJ *et al* [22]

While Mikahail-Ms *et al* [23] found that there was no direct relation ship between the TG level and severity of PE.

Kokia-E *et al* [24] found that the TG and LDL level were significantly higher in severely PE group .He also conclude that the lipid profiles in hypertensive pregnant women could be associated with enhancement of pathological lipid deposition in predisposed vessels such as uterin spiral arteries.

Further more, the hypertriglyceridemia in PE may be associated with the hypercoaglobility reported in PE [24].

Conclusion

From the presented study, we conclude the followings:

The serum TG, LDL , VLDL, but not the CH concentrations are increased markedly in PE. The serum HDL concentrations are decreased markedly in mild and severe PE in comparison to control group.

The serum TG and VLDL only are markedly increase in sever PE, these may result in a rise of lipid peroxide which is very toxic compound and this may contributes to endothelial cell dysfunction and oxidative stress in severe PE.

Recommendation

There may be a role for lipid profile in early prediction of pre-eclampsia especially high risk group so may be used as a screening test.

Further study are needed to evaluate the type changes in lipid profile according to the age of patient and gestational age.

Further studies are needed to identify maternal lifestyle characteristic that are determinants of elevation of LDL ,triglyceride and VLDL . Knowledge from such studies may contribute to developing behavioral and medical intervention aimed at reducing the occurance of pre-eclampsia.

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