Lipid Profile Changes in Pregnant Women with Pre-Eclampsia and Their Correlation with Severety of Pre-Eclampsia

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Abstract:

Objectives: To find out whether there is a lipid profile changes in pregnant women with preeclampsia and if we can use these lipid profile changes as markers of the severity of preeclampsia (for follow up to avoid leaving the patient reaching ecplamptic stage).

Design: A prospective case-control study.
Setting: AL- Kadhimiya Teaching hospital/department of Obstetrics and Gynecology.
Materials and Methods: The study included 120 pregnant women in the third trimester. They were divided into three groups. The study group consists of 60 preeclamptic and eclamptic women, 25 women had mild pre-eclampsia and 35 women with severe preeclampsia. The control group consists of 60 normotensive pregnant women. Blood sample was drown after 8-10 hours fasting. Triglyceride, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol levels were measured.
Results: Triglyceride and VLDL-C level of severe Preeclampsia group and mild Preeclampsia group was higher than the control group, but the difference between the severe PE group and the control group was statistically significant ($p<0.05$). Serum cholesterol in the severe PE group was significantly higher than in mild PE group and in the control group ($p<0.05$). LDL-C and HDL-C levels were determined similarly in all groups ($p>0.05$). A highly significant positive correlation between the level of proteinuria and serum cholesterol levels, LDL-C, TG and VLDL-C levels. While there was significantly negative correlation between proteinuria and HDL-C levels. Also, a significant positive correlation between the systolic-tension and serum cholesterol levels, TG, VLDL-C levels and among the diastolic-tension and with LDL-C, TG, VLDL-C levels.
Conclusion: Changes in levels of lipid profile are related with preeclampsia, especially with severe preeclampsia.

Key words: Lipid profile, pregnancy, severe pre-eclampsia

التغييرات في نسبة الدهون لدى النساء الحوامل اللاتي لديهن تسمم الحمل وعلاقتها مع شدَة تسمم الحمل

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الخلاصة:
أهداف البحث: التحري عن التغييرات في نسبة الدهون لدى الحوامل اللاتي يعانين من تسمم الحمل كدلائل على شدة حالة التسمم الحملي لديهن من أجل متابعة المريضات لتجنب الوصول إلى حالات الإختلاجات والتشنجات الحملية.
المرضى وطرق العمل: شملت الدراسة 120 إمراة حامل في الثلث الأخير من الحمل وتم تقسيمهن الى 3 مجاميع، ستون حالة تعاني من التسمم الحملي مقسمة الى 25 حالة تسمم حملي خفيفة، و 35 حالة تسمم حملي شديدة. عينات السيطرة كانت 60 حالة حمل لديها ضغط دم طبيعي. تم سحب عينات الدم بعد صيام 8-10 ساعات. تم قياس الدهون المركبة الثلاثية، والكولسترول بانواعه الثلاثة: عالية الكثافة، متوسطة الكثافة و قليلة الكثافة.
النتائج: كانت نسبة الدهون المركبة الثلاثية والكولسترول قليل الكثافة أعلى عند كافة المريضات مقارنة مع حالات السيطرة. وكانت نسبة الكولسترول في تسمم الحمل الشديد أعلى بنسبة دالة من الخفيف. الدهون العالية الكثافة والخفيفة الكثافة كانت غير مختلفة بين المجاميع. كانت هنالك علاقة إيجابية دالة بين نسبة البروتين في الإدرار والكولسترول، والدهون المتوسطة والقليلة الكثافة، بينما كانت العلاقة سلبية دالة بين بين نسبة البروتين في الإدرار والدهون عالية الكثافة. كذلك كانت علاقة إيجابية دالة بين ضغط الدم العالي والكولسترول والدهون الثلاثية المركبة والدهون الخفيفة الكثافة.
الإستنتاجات: إن التغييرات في نسبة الدهون لها علاقة وثيقة بتسمم الحمل وخاصة الحالات الشديدة منه.

لكلمات المفتاحية: نسبة الدهون، الحمل، تسمم الحمل.

Introduction

Preeclampsia (PE) is a syndrome unique to pregnancy characterized by the new onset of hypertension at least 140/90 mmHg and proteinuria following 20 weeks gestation in women whose blood-pressure that was normal and previously resolving completely by the sixth post-partum week[1-3].

Altered lipids in pre-eclampsia: serum triglycerides and free fatty acids concentrations were doubling in pregnant women with hypertension as compared to normal pregnant woman, and these conditions occur before, and so, they are not consequence of a clinically evident PE these are suggestive of the pathogenic role of dyslipidemia. Women had chronic hypertension in pregnancy don't usually display the dyslipidemia [4-7]. Serum TGAs correlates with serum malondialdehyde which is lipid-peroxidation product in pregnant women with PE [8]. This hypertriglyceridemia in PE is accompanied by higher prevalence of a smaller and denser LDL particles and a lower HDL and -cholesterol[9]. The mechanisms of this dyslipidemia in PE are not well explained. Increased insulin-resistance in PE might increase transfer of fatty acids from the adipocytes, increased production of the VLDL by the hepatocytes, and decreased the activity of lipoprotein lipase causing increased FFAs and TGAs [10-12]. Serum TGAs, cholesterols, and FFAs concent-rations highly reduced in pregnant women with hypertension in 24-48 hours [7].

Hypertriglyceridemia changes the spectrum of LDL subclasses to increases in the smaller, denser, and more atherogenic LDL molecules into the arterial wall and increased the adhesiveness to the arterial-intima, and these LDL molecules are of increased oxidation, the size of these LDL particles is highly decreased in PIH in relation to normal pregnancy [4,7]. All these changes are more common in pregnant women with hypertension [7]

The effect of abnormal lipid profile on the oxidative-stress in preeclampsia: these FFA increase might contribute to the endothelial dysfunction in PE [7].

Alternatively, free fatty acid mediated facilitation of cellular reactive oxygen species generation, and these ways might increase endothelial dysfunction in PE. Increased TGAs might affect the vascular function in many ways for example, TGA-rich lipoproteins have prothombotic effect [13].

Aim of the study

1- Evaluation of the concentrations of triglyceride, total cholesterol, high density lipoprotein-cholesterol, low density lipoprotein-cholesterol, very low-density lipoprotein-cholesterol antenatally of women diagnosed to have Pre-eclampsia in relation to those normotensive uncomplicated pregnancy.

2- To clarify the relationship between lipid profile changes and the severity of PE.

Patients

This study was a prospective case-control study conducted on 120 pregnant women admitted to the obstetrics and gynecology department at Al-Kadhymia Teaching Hospital, in cooperation with the laboratory department unit.

The study included 120 pregnant women, 60 pre-eclamptic and eclamptic women who were selected according to the patients' signs, symptoms & investigations and admitted to the obstetric ward for evaluation and 60 control normotensive pregnant women who were admitted to the labor ward for delivery and selected according to maternal age and gestational age.

Inclusion criteria:

1- pregnancy with singleton.

2- The gestational age from 32-40 weeks.

3- The criteria of diagnosing preeclampsia when the systolic and diastolic blood-pressure was equal or more than 140/ 90 mmHg in at least two readings 4 hr. apart or one measurement 160/110 or more.

Exclusion Criteria:

1. Multiple pregnancy
2. Systemic disorders including: Essential hypertension, DM, kidney disease, liver disease, epilepsy, hematological disorders, dyslipidemia, and thyroid diseases

The Study group: Included 60 singleton pregnant women presented with pre-eclampsia divided into two groups:

1- Mild preeclampsia Group (no.25) when blood-pressure equal or more than 140/90 on two consecutive readings four hours apart and + albumin.

2- Severe preeclampsia Group (no.35): when the blood pressure of $\geq 160/110$, a proteinuria $\geq +2$. Also, with continuous headache, disturbances in vision, abdominal pain, abnormal renal and liver functions test, eclampsia (generalized tonic clonic convulsion).

Control group: Included 60 singleton non hypertensive pregnant women composed the control group. Normotensive women their BP<140/90mmHg & proteinuria was nill.

Study design: All the cases included in the study were collected from labor and obstetrical ward of Al-Kadhymia Teaching Hospital.

Results

120 pregnant women participated in this study, 60 women had pre-eclampsia of these 25-women had mild preeclampsia and 35 women had severe preeclampsia their mean age was 31±6 years. The remaining 60 normotensive women were taken as control group, their mean age was 32±5 years.

The (Median±Standard error) of GW at labor of sever preeclampsia group, and mild preeclampsia group (35.4±0.7, 34.9 ± 0.9) was very low than control group (38.4 ± 0.3) there was a significant statistical difference with P value of ($P \leq 0.05$) .The

(Mean±Standard error) of birth weight , in sever preeclampsia group and mild preeclampsia group (2372.57±20.67, 3255.20±23.6) were very low than control group (3383.92±10.20) there was a significantly statistical difference, with a *P* value of ≤0.05.

Cesarean section ratio in sever pre-eclampsia group and mild pre-eclampsia group (68.6%, 56.0%) was higher than control group (26.7%) there was a significant statistical difference, with a P value of ≤ 0.001.

This study found that serum total cholesterol (TC) level in sever preeclampsia group (274.97±1.23) was higher than mild preeclampsia group (274.97±1.23) and the control group (235.82 ±0.59) the difference is statistically significant with a *P* value of (*P*< 0.05).

Serum triglyceride and VLDL-C levels in severe pre-eclampsia group (286.77±4.76, 62.66±0.49) and mild preeclampsia group (277.00±1.79, 55.60±1.24) were higher than control group (266.58±2.47, 53.17±0.19), but only the difference between severe pre- eclampsia group and control group was statistically significant (*P*< 0.05).

In addition, LDL level in severe preeclampsia group (128.34±4.99) was higher than mild preeclampsia and the control groups (118.60±3.43, 121.72±4.30) but the difference was statistically insignificant (*P*> 0.05).

However, HDL-C level was the highest in control group (58.42±0.26) than severe preeclampsia group and mild preeclampsia group (57.94±0.32, 59.16±0.42) but the differences was statistically insignificant since the P value was (*P*> 0.05).

On the other hand, systolic and diastolic blood pressure was higher in sever preeclampsia group and mild preeclampsia group relative to the control group the difference was statistically highly significant (*P* value<0.001). Also, protein-uria was reported in all women with preeclampsia which was significantly higher. As shown in table (1).

Table (1): Comparison of lipid profile and pre-eclamsia indicators among the Control and study groups (Median±Standard error)

	Control (Group:1) (n=60)	Pa	Mild PE (Group: 2) (n=25)	Pb	Sever PE (Group: 3) (n=35)	Pc
Total cholesterol (mg/dL)	235.82±0.59	>0.05	238.64±4.09	≤0.05	274.97±1.23	≤0.05
Triglycerides (mg/dL)	266.58±2.47	>0.05	277.00±1.79	>0.05	286.77±4.76	≤0.05
Very low-density lipoprotein (mg/dL)	53.17±0.19	>0.05	55.60±1.24	>0.05	62.66±0.49	≤0.05
Low density lipoprotein (mg/dL)	121.72±4.30	>0.05	118.60±3.43	>0.05	128.34±4.99	>0.05
High density lipoprotein (mg/dL)	60.42±0.26	>0.05	59.16±0.42	>0.05	57.94±0.32	>0.05
Protein in urine (mg/dl)	9.87±0.19	>0.05	117.00±4.90	>0.05	212.57±2.02	>0.05
Systolic BP (mmHg)	113.08±1.09	>0.05	148.20±1.04	>0.05	177.43±2.65	>0.05
Diastolic BP (mmHg)	70.50±0.96	>0.05	94.40±1.30	>0.05	107.06±2.01	>0.05

a- Comparison between Group:1and Group: 2

b- Comparison between Group: 2and Group: 3

c- Comparison between Group:1and Group: 3

Table (2) shows Pearson correlation analysis of lipid profile with proteinuria, systolic BP, diastolic BP. Significantly positively correlated among:
•The proteinuria and TC, TG, VLDL, and LDL (respectively, r: 0.767, 0.400, 0.582, 0.846) P≤ 0.001.

•The systolic-tension with TC, TGA, VLDL (respectively, r: +0.618, +0.263, +0.494) p < 0.01.
•The diastolic-tension with TGA, VLDL, LDL (respectively, r: +0.271, +0.502; +0.637) p < 0.01.
There was a significant negative correlation among the amounts of proteinuria and HDL (r: - 0,248; p≤ 0.05).

Table (2): Correlation values among the lipid profiles and the other parameters

	Total cholesterol	Triglycerides	Very low-density lipoprotein	Low density lipoprotein	High density lipoprotein
Protein in urine	0.367**	0.240**	0.282**	0.246**	-0.248*
Systolic blood pressure	0.418**	0.263*	0.394**	0.092	-0.156*
Diastolic blood pressure	0.103	0.271*	0.262**	0.273**	-0.123*

* Significant p≤0.05.   **Highly-significant p≤0.001.

Discussion

In normal pregnancy there is a high increase in the FFAs and also the complex lipids, with three-fold increases in TG and a 50% increase in VLDL-C, HDL is also increased. This hyperlipidemia in normal pregnancy is not pathogenic because the pattern of increase is not like that of atherogenic lipids [14,15]

Several previous studies showed that lipid profiles were higher in pregnant women with PE than in healthy pregnant [5, 6]. These changes cause activation of thrombocyte that leads to releasing thromboxane. This imbalance between prostocycline and thromboxane can account for the major clinical symptoms of pre-eclampsia [18].
A study done by Bodnar et al [19] (2005) asserted BMI as a strong and independent risk factor for PE development. In our study Systolic and diastolic blood pressure was higher in sever PE group and mild PE group relative to control group the difference was statistically highly significant (P value = 0.0001). The raised BP (systolic and diastolic) in PE is due to maternal endothelial cell activation/endothelial dysfunction which is due to release of placental anti-angiogenic factors and other multiple factors in plasma [3,11]. The finding of our study correlate with different other previous studies. Systolic and diastolic BP increased in studies done by, Mustafa Baki Cekman et al [21], Usha Adiga et al [22], Rubina aziz et al [23], Carl A Hubel et al [8] and Anne Cathrine staff et al [24]. The current study found that TG and VLDL-C levels in both groups of pre-eclampsia were higher compared to control group. The difference of TG and VLDL-C levels in sever PE group compared to the control group was significant ($P<0.05$), the difference of TG and VLDL-C levels in sever PE group compared to mild PE group was not significant. While their levels in mild PE group was higher than control group but the difference was not significant. This result was consistent with the result of Valmir et al [25] (2011) who found That the pre-eclamptic patients presented signify-cantly higher concentrations of TG and VLDL-C than shown by the healthy women

high triglyceride level seem to increase the risk of placental vascular disorder. Q Lei *et al* [26] (2011) found that the concentrations of TGs and FFAs were all higher in women with pre-eclampsia. Ray *et al* [27] (2006) In a review of 22 studies showed that women with high TGA level had twice the risk of PE. In contrast to our study Punthumapol C[28] (2008) found that there was no significant difference in lipid profile among normal pregnancy, mild, and severe PE women. Mikhail MS *et al* [29] suggested no direct-relationship between TG levels and severity of PE.

This study showed that the levels of cholesterol were significantly higher in the group of severe PEs compared with the group of mild PEs and the control groups (*P*< 0.05), but was similar in mild PE group and control group. These finding goes with different other previous studies. Serum cholesterol was raised in studies conducted by Faruh Khalid *et al* [30], Adiga Usha *et al* [22], Gohil J. T. *et al* [31],Sahu S. *et al* [32], and Uzun H. *et al* [33].

According to study done by Adiga Usha *et al*, it concluded that hypercholesterolemia leads to high lipid peroxidation and decreased in antioxidant activity leading to imbalance of peroxides and antioxidants that will lead to oxidative stress. In contrast to our study, Rubina Aziz[23], Punthumapol C[28], Islam NAF[34], concluded that normal pregnancy is characterized by an increase in TC.

In this study has found that HDL-C level was the highest in the control group, but by comparing it with the mild PE group and sever PE group the differences was not statistically significant. Like our study Sena *et al* [35] found that the level of HDL-C not differ significantly between pre-eclamptic and normal patients. In contrast to our study the decrease in HDL-C in pre-eclampsia patient is significant in study done by Jayanta De *et al* [36], Usha Adiga *et al* [22], Rubina aziz *et al* [23], and Faruh Khalid *et al* [30]. According to study done by Jayanta De *et al* [36] a significant lowering of HDL-C

was observed in preeclamptic and eclamptic women.

Oestrogen causes increase in TG and HDL and reduction of LDL, oestrogen levels fall in pre- eclampsia [37,38]. The Low level of HDL in pre-eclampsia is not only because of hypo- estrogenaemia but also due to increase in insulin resistance [39].

In addition, the current study has found that, though LDL-C level was higher in the sever PE group, the differences were not statistically significant. This result was consistent with the result of Punthumapol C[28] (2008) who found that there was no significant difference in serum LDL-C, total cholesterol, TG and HDL-C, among normal, mild, and severe pre-eclamptic women. In contrast to our study Jayanta De *et al* found that LDL-C level increases significantly in sever PE [36]. On the other hand, proteinuria in the current study was reported in all women with pre-eclampsia which was highly significant. This may be due to glomerular endothelial cell injury lead to increase permeability to albumin [39]. It's worth to mention that in this study, there was a significant and positive correlation between amount of proteinuria and the levels of TC, TG, VLDL-C, and LDL-C. However, there was an inverse correlation between proteinuria and HDL-C level, in addition, the systolic-tension correlated with TC, TG, VLDL-C and diastolic-tension correlated with LDL-C, TG, VLDL-C. Hypertension and proteinuria, are the most important diagnostic findings for PE, were significantly affected in relation with patients' lipid profile [15], this result goes with the study of Valmir Jose de Lima [25] (2011). Valmir Jose de Lima, observed that a significant positive correlation between proteinuria with TGA and VLDL levels high TGA could increase placental-vascular disorders, which causes endothelial dysfunction, thrombosis and athero-sclerosis [25].

Conclusions:
The changes in lipid profile were related with pre-eclampsia and especially in severe

pre-eclampsia. In a correlation analysis both hypertension and proteinuria are the most important diagnostic findings in PE, and they were found to be related to serum lipid profile. Hyperlipidemia could be an important cofactor in the pathogenesis of pre-eclampsia.

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