Research Article

Evaluation of lipid profile and lipid peroxidase level in pregnant women with pregnancy induce hypertension ,preeclampsia and eclampsia in their third trimester of pregnancy versus normotensive pregnant women in the same trimester

Esraa H. AL-Maini *F.I.B.O.G, C.A.B.O.G,* **Abdilkarim Y. Alsammariae** *Ph.D,* **Anfal I. Semeet** *M.B.Ch.B*

Date Submitted: 22/9/2014
Date Accepted:19/1/2015

Address for Correspondence:
Dr. Esraa Hameed AL-Maini, Assis. Prof. College of Medicine/Al-Mustansiriya University/Consultant Obs. & Al-Yarmouk Teaching Hospital

Abstract

Background: The association of altered lipid profile in essential hypertension is well documented.. The pathophysiology of the underlying mechanism is unknown. Disorder of lipoprotein metabolism may contribute to endothelial dysfunction. Oxidative stress and decreased antioxidant defense enhance free radical-mediated membrane lipid peroxidation and possibly vascular endothelial damage
Objective: To assess the relationship between lipid level and lipid peroxidase with occurrence of hypertension in pregnant women in their third trimester of pregnancy.
Study design: Case control study.
Patient and Method: A total of one hundred twenty five pregnant women in their third trimester of pregnancy were enrolled in this study. Fifty normotensive pregnant women, thirty pregnant women with pregnancy induce hypertension (PIH), thirty pregnant women with preeclampsia and fifteen pregnant women with eclampsia. The four group were comparable for maternal age, body mass index and gestational age. Blood samples were taken for measurement of serum lipid and lipid peroxidase from the four groups and correlate with occurrence of pregnancy induce hypertension, preeclampsia and eclampsia.
Result: There was a significant and direct correlation between occurrence of preeclampsia and total cholesterol in comparison to the control group .There was a significant and direct correlation between preeclampsia and triglyceride, high density lipoprotein, low density lipoprotein /cholesterol level. There was a significant correlation between malondialdehyde level and preeclampsia in comparison to the control group. Also there is recognized relation between the malondialdehyde level and eclampsia.
Conclusion: abnormal lipid metabolism may play a role in the development of preeclampsia and eclampsia, can be used as a measure for early prediction of this disorder.

Key words: lipid profile, lipid peroxidase, hypertension with pregnancy.

INTRODUCTION

Hypertension is the most common medical problem encountered during pregnancy, its complicate 6-12% of all pregnancy [1], it include 2 relatively benign condition (chronic and gestational hypertension) and the more severe conditions of preeclampsia and eclampsia. International society for the study of hypertension in pregnancy classified it as [2- 4]: **A.** Gestational hypertension and / or protein urea developing during

pregnancy, labor or the peurperium in a previously normotensive non protein uric woman.

1. Gestational hypertension PIH (without protein urea): Is a new hypertension presenting after 20 weeks gestation without significant proteinuria.

2. Gestational protein urea (without hypertension) occur after 20 weeks gestation

3. Gestational protein uric hypertension (pre-eclampsia) new onset of hypertension and proteinuria after 20 weeks of gestation in a woman whose blood pressure was previously normal .

B. Chronic hypertension before 20th week of pregnancy and chronic renal disease (protein urea before the 20th week of pregnancy)

1.Chronic hypertension (without protein urea).
2.Chronic renal disease (protein urea with or without hypertension).
3.Chronic hypertension with superimposed pre-eclampsia (new onset protein urea).

C.Unclassified hypertension and /or protein urea.

D.Eclampsia It's an extremely severe form of Preeclampsia characterized by the sudden onset of generalized tonic-clonic seizure.

Pre-eclampsia may be subdivided further into mild and severe forms. The distinction between the two is made on the basis of the degree of hypertension and proteinuria, and the involvement of other organ systems ([5-7]).

Pathophysiology of preeclampsia:

There is an increasing evidence that endothelial dysfunction is the primary pathophysiological mechanism which cause preeclampsia [(8)].

However pathway mediating endothelial cell layer dysfunction still remain unclear. One hypothesis receiving amplified attention is that endothelial dysfunction may be the result of increased oxidative stress [(8)].

Oxidative stress is the imbalance of pro-oxidants and antioxidants leading to the formation of oxygen free radicals and lipid peroxides. Lipid peroxidation is a process generated naturally in small amount in the body, mainly by the effect of several reactive oxygen species, these reactive oxygen species readily attack the polyunsaturated fatty acids of the fatty acid cell membrane, initiating a self – propagating chain reaction. Since lipid peroxidation is a self –propagating chain-reaction, the initial oxidation of only a few lipid molecules can result in significant tissue damage [(9)].Lipid peroxides and oxygen free radicals are directly toxic to the endothelial cells and increase the release of cytokines, which cause damage to the endothelial lining of blood vessel walls [(10)].Lipid peroxidation mediated by free radical is considered to be the major mechanism of cell membrane destruction and cell damage (endothelial damage), and is a key contributing factor to the pathophysiologic condition of preeclampsia [(11)]. Lipid profile: is the results of a blood tests that measure the levels of lipids, or fats.It including: cholesterol(TCH),triglycerides (TG),high density lipoprotein(HDL),low density lipoprotein(LDL), and very low density lipoprotein (VLDL)[(12)]. Factors such as age, sex, and genetics influence lipid profile. Certain aspect of life style, including diet, level of physical activity, level of diabetic control, and smoking status, also affect lipid profile and some medical conditions can lower or raise lipid profiles [(12)], and pregnancy induce hypertension may cause dyslipidemia [(13)].

Lipid metabolism during normal pregnancy and pregnancy complicated with Pre_eclampsia. During pregnancy hepatic and adipose tissue metabolism alter circulating concentration of Triglycerol, fatty _acid, and phospholipid. After an initial decrease in the 1st eight weeks of pregnancy, there is steady increase in triglyceride, fatty acids, lipoprotein and phospholipid. The principle modulator of this hypertriglyceridemia is estrogen as pregnancy is associated with hyperoestrogenemia. Estrogen induce hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL, this process may be modulated by, hyperinsulinism found in pregnancy[(14)].Furthermore increase in free fatty acid , triglycerides, LDL, HDL, total lipid, cholesterol and VLDL values are increased during preeclampsia. Lipid peroxidase and cytokines increase secondary to an increase in levels of plasma lipid. Increased triglyceride found in pregnancy induce hypertension is likely to be deposited in the predisposed vessels such as ,uterine spiral arteries and contribute to the endothelial dysfunction both directly and indirectly through generation of small dense LDL[(15)].

There is significant increase in triglyceride, which is explained by: preeclampsia is very frequently associated with aggravated hepatic damage which inhibit the enhanced de novo synthesis of triglyceride in the liver [(6).] Moreover VLDL which carries the endogenous triglyceride is also synthesized in the liver and the increase in triglyceride in pregnancy induce hypertension is related to increase both synthesis and secretion of VLDL-TG as a result of increase in lipolysis due to increase insulin resistance, leading to increased flux of fatty acids to the liver promoting the synthesis of VLDL-TG concentration [(16)] so in pregnancy the increase in TG is estimated mainly in the VLDL estimated mainly in

the VLDL. Lipid levels increase parallel to the severity of the disease being normal in normotensive group compared with the gestational hypertensive, chronic hypertension, preeclampsia and worst in the eclampsic group. This is also parallel with the prognosis of the disease.

This study was conducted to compare lipid profile and lipid peroxidation in women with gestational hypertension, pre-eclampsia and eclampsia versus normotensive pregnant women during third trimester of pregnancy.

PATIENTS AND METHODS

A case-control study was conducted at Al-Yarmouk Teaching Hospital during the period of one year October 2012 to October 2013.The study was approved by ethical committees of AL-Yarmouk Teaching Hospital. A total of one hundred twenty five women were included in this study and were divided into four groups:Control group: fifty normotensive pregnant women. Study group: thirty women with pregnancy induce hypertension, thirty women with preeclampsia weather mild or severe types of PE [(7)] fifteen women with eclampsia.

The women in this study were selected while attending the antinatal care(ANC) for assessment or from the inpatient ward, all women were pregnant in their 3rd trimester of pregnancy (32-41) completed weeks of gestation (according to the reliable Last Menstrual period and first and early second trimester ultrasound scan (u/s) .The control group were selected as a healthy pregnant women with age range between 15 – 45 year old with normal blood pressure and the gestational age, BMI that were comparable with study group.

Exclusion criteria :
1-Women with renal disease
2-Diabetes
3- Hypertension prior to pregnancy or cardiovascular diseases
4-Women treated with drugs that may influence lipid profile were excluded from this study in both study and control groups

All the participants were told about the nature of the study and only those who agreed to participate in the study were included. Verbal consent was obtained from all pregnant women in the study. Information's about the age of the patient ,LMP, gestational age, were taking from all participant. Regarding patient with hypertension history was taken about the type of hypertension, and the time of their onset and type of medication taken.

Past medical history include question about pre-existing condition associated with hypertension, drug history and family history. Examination include the measurement of height, weight and BMI, Ultrasound for viability and gestational age. All the patient's blood pressure were measured two times 6 hours a part, the systolic pressure is recognized by disappearance of the radial pulse. the Korotkoff v(disappearance of the sound) or Korotkoff IV (muffling of the sound) was used to determine diastolic blood pressure. Every patient had under gone the following investigations:
-Mid-stream specimen for albumin
-Renal function test ,Liver function test ,complete blood picture, Coagulation profile , 2hours post prandial blood sugar
-Lipid profile (TG, TCH ,LDL ,HDL and VLDL),Lipid peroxidase : Malondialdehyde (MDA)

Sample collection, processing for assessment of lipid profile and lipid peroxidation:

The blood was collected after at least 12 hours fasting. A five millilitre of venous blood were collected in plain tube. The samples were transferred to first allowed to clot and then centrifuged at 3000 rpm for 5 minutes.
All the specimens were clearly labelled with names of cases and controls along with the date and time of collection. The test were done in biochemistry laboratory at AL-Yarmouk hospital.
-Lipid profile (TG, TCH ,LDL ,HDL and VLDL) and Lipid peroxidase(MDA) were statistically analysed using ANOVA and student-t-test

Pearson correlation with its t-test was used for testing the significance of correlation between variable. The correlation coefficient value (r) either positive (direct correlation) or negative (inverse correlation) with value <0.3 represent no correlation, 0.3-<0.5 represent weak correlation, 0.5-<0.7 moderate strength, >0.7 strong correlation. P value ≤ 0.05 was considered significance.

RESULT

In this study the Control group was comparable in age, BMI and gestational age with the hypertensive group. As shown in table 1: there is significantly higher level of TCH, TG, HDL, LDL and VLDL in hypertensive groups in comparison to control group. Table 2 shows significantly higher level of MDA in hypertensive groups in comparison to control group, and higher level in PE and Eclampsia groups in comparison to PIH group. **Regarding MDA level**: the maternal age and parity shows no significant difference between control and hypertensive group.Regarding the level of TCH, TG , HDL , LDL , VLDL all show no significant difference regarding MDA level between the hypertensive patients in comparison to control group ,the there is a significant correlation between MDA level and TCH in patient with eclampsia in comparison to control group as shown in table 3.

Table 1. The level of lipid profile in patient with PIH, Pre-eclampsia , Eclampsia and control groups included in the study.

	Preeclampsia	Eclampsia	PIH	Control	P value
TCH (mmol/l)	6.41±0.18 (6.035-6.734)	7.49±0.20 (7.174-7.770)	6.33±0.21 (5.957-6.630)	6.18±0.18 (5.724-6.579)	0.0001#
TG (mmol/l)	3.33±0.27 (2.660-3.791)	4.13±0.27 (3.830-4.722)	3.61±0.09 (3.392-3.764)	2.61±0.44 (1.902-3.325)	0.0001#
HDL/C (mmol/l)	1.61±0.12 (1.425-1.813)	2.37±0.07 (2.305-2.486)	1.96±0.22 (1.554-2.305)	1.09±0.11 (0.829-1.425)	0.0001#
LDL/C (mmol/l)	4.92±0.64 (3.445-6.035)	5.62±0.31 (5.128-6.061)	4.07±0.30 (3.263-4.792)	3.94±0.36 (3.186-4.584)	0.0001#
VLDL/C (mmol/l)	1.10±0.13 (0.803-1.269)	1.85±0.16 (1.502-2.072)	0.85±0.09 (0.570-0.984)	0.83±0.12 (0.518-1.010)	0.0001#
#Significant using ANOVA test for difference among four independent means at 0.05 level.					
-Data were presented as Mean±SD (Range)					

Table 2. The oxidant status (MDA) level in patient with PIH, Preeclampsia, Eclampsia and control group included in this study.

MDA	Preeclampsia	Eclampsia	PIH	Control
NO.	30	15	30	50
Mean±SD	13.57±1.48	13.80±1.61	12.73±1.31	5.72±1.84
Standard Error of Mean	0.270	0.416	0.239	0.260
Mode	13.0	13.0	12.0	6.0
Range	11.0-17.0	11.0-17.0	11.0-15.0	2.0-9.0
Percentile 5^{th}	12.0	11.0	11.0	3.0
25^{th}	12.0	13.0	12.0	4.0
50^{th} (Median)	13.0	14.0	13.0	6.0
75^{th}	15.0	15.0	14.0	7.0
95^{th}	17.0	17.0	15.0	9.0
99^{th}	17.0	17.0	15.0	9.0
P value compared to control	0.0001*	0.0001*	0.0001*	-
P value compared to PIH	0.024*	0.022*	-	-
P value compared to eclampsia	0.631	-	-	-
P value comparing all groups	-	-	-	0.0001#
*Significant using Students-t-test for difference between two independent means at 0.05 level.				
#Significant using ANOVA test for difference among four independent means at 0.05 level.				

Table 3. The correlation between oxidant status (MDA) level and lipid profile in patient with PIH, Preeclampsia, Eclampsia and control group

		MDA			
		Preeclampsia	Eclampsia	PIH	Control
Age (years)	R	0.006	0.030	0.054	-0.014
	P	0.976	0.915	0.775	0.926
Parity	R	0.102	0.076	-0.133	-0.041
	P	0.591	0.789	0.482	0.778
TCH (mmol/l)	R	0.155	0.667**	0.116	0.118
	P	0.413	0.007	0.541	0.416
TG (mmol/l)	R	-0.290	-0.134	0.230	0.024
	P	0.120	0.633	0.222	0.870
HDL/C (mmol/l)	R	0.111	-0.126	0.289	-0.041
	P	0.560	0.654	0.122	0.779
LDL/C (mmol/l)	R	-0.104	0.211	-0.067	-0.047
	P	0.585	0.449	0.726	0.748
VLDL/C (mmol/l)	R	0.182	-0.016	0.118	0.043
	P	0.335	0.956	0.535	0.764
***Correlation is significant at the 0.05 level.**Correlation is significant at the 0.01 level**					

DISCUSSION

Normal human pregnancy results in physiologic hyperlipidemia involving gestational rise in blood triglyceride (TG) and cholesterol Increased TG, found in pregnancy induce hypertension markedly observed in patient with preeclampsia and eclampsia . TG is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contribute to the endothelial dysfunction [17]. A question arose , as to weither

discernible difference would be observed in lipid and MDA levels in pregnant women with preeclampsia compared with women with normal pregnancy.

In the current study there was a significant increase in the TCH and TG level in women with PIH, Preeclampsia and Eclampsia, when compared with the control group the p value was ≤0.0001. William et al in 1997[18] was reported the same result regarding the TG level and Garactose E, 2003[19] found significant elevation in TCH level in pregnant women with hypertension. Our result disagree with Cekmen et al in 2003: his result did not show a significant rise in TCH levels in hypertensive groups [20].

Our study which show a significant rise in LDL-C among pregnant women with hypertension (PIH, Preeclampsia and Eclampsia) when compared with normotensive pregnant women ,the P value was ≤0.0001.

Gractacose E 2003[19], found a significant rise in LDL-C in women, his result support the result of our study.In this study the level of HDL-C raise in pregnant women with hypertension and raise more in patient with eclampsia and decrease in control group the difference was statistically significant p ≤0.0001

This finding is consistent with Potter et al(21), he report a rise in HDL-C level in patient with preeclampsia ,but disagree with Dutta DC 2001(22) ,and Bradley R 1995(23) they found a significant decrease in the level of HDL-C in pregnant women with preeclamptic and eclamptic as compared to normotensive pregnant women (controls), this low HDL-C level might be due to increase insulin resistance in patients with PE. Excessive lipid peroxidation occurring in preeclampsia can be attributed to hypercholesterolemia.Hypercholesterolemia promotes the formation of free radicals. Different study showed there was a significant difference in the serum MDA levels between pregnant women with hypertension and normotensive The result of these study suggest that the extent of lipid peroxidation probably correlates with the severity of hypertensive disorder. The increase in MDA is strongly related to lipid peroxidation caused by oxidative stress and is expected to affect various tissues and organ system, including vascular endothelium,during these processes, other molecules involved in vasodilatation such as nitric oxide are inhibited by high lipid peroxide concentration[18,19] . The current study which demonstrate significant rise in MDA level in PIH, Preeclampsia and eclampsia groups same result was obtained by Aydin et al[7] he demonstrate significant rise in MDA level in preeclampsia when compared to healthy pregnant women p≤0.001.

In our study MDA levels were highest in patient with preeclampsia and eclampsia than patient with PIH P≤(0.024, 0.022) respectively in agreement with Jain and wise, 1995[24]

Esterbauer H 1990[25], measure the MDA levels preeclamptic women and normotensive women in their third trimester , he found significant positive association of MDA with both systolic and diastolic blood pressure in preeclamptic women p≤0.001. Moreover the same study demonstrate that MDA had more significant correlation with TCH in control group p≤0.001 While in this study a significant association was found between MDA level and TCH level in eclamptic women p≤0.007, and no positive relation is present between MDA and TCH in PIH , preeclamptic and control groups and no significant association were found between MDA level and TG, HDL-C, LDL-C, VLDL-C in women with hypertension nor in control group.

The age of the pregnant women that included in this study had no significant correlation with level of MDA p≤0.091 same result was obtained by Erel et al., 1999[26], regarding parity no significant association was found in our study.

In conclusion, the current study suggest that an abnormal lipid metabolism and particularly high level of TCH ,TG/C , LDL/C VLDL/C and lipid peroxidase may contribute to the promotion of oxidative stress and vascular dysfunction seen in PIH and preeclampsia.It is, therefore, measurement of blood lipid concentration and lipid peroxidase could be evaluated in pregnant women during antenatal care since it could be helpful in the early detection and prevention of obstetric complications such as PIH..

REFERENCES

1. Legro RS; Strauss JF (September 2002). "Molecular progress in infertility: polycystic ovary syndrome". Fertility and Sterility 78 (3): 569–576\
2. Diamanti-Kandarakis E; Kandarakis H, Legro RS (August 2006). "The role of genes and environment in the etiology of PCOS". Endocrine 30 (1): 19–26
3. Goldenberg N, Glueck C (2008). "Medical therapy in women with polycystic ovary syndrome before and during pregnancy and lactation". Minerva Ginecol 60 (1): 63–75
4. Boomsma CM, Fauser BC, Macklon NS (2008). "Pregnancy complications in women with polycystic ovary syndrome". Semin. Reprod. Med. 26 (1): 72–84.
5. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO (June 2004). "The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population". Journal of Clinical Endocrinology & Metabolism 89 (6): 2745–9.
6. Gennarelli G, Holte J, Berglund L, Berne C, Massobrio M,Lithell H Prediction models for insulin resistance in polycystic ovary syndrome. Hum Reprod. 2000; 15(10):2098-102.
7. Kajaia N, Binder H, Dittrich R, Oppelt PG, Flor B, Cupisti S. Low sex hormone-binding globulin as a predictive marker for in insulin resistance in women with

hyperandrogenic syndrome. Eur J Endocrinol. 2007; 157: 499–507.

8. Kalra A, Nair S, Rai L. Association of obesity and insulin resistance with dyslipidemia in Indian women with polycystic ovarian syndrome. Indian J Med Sci. 2006; 60(11):447-53.
9. Cibula D, Skrha J, Hill M, Fanta M, Haaková L, Vrbíková J et al. Prediction of insulin sensitivity in nonobese women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2002 , 87(12):5821–5.
10. Wongwananuruk T, Rattanachaiyanont M, Indhavivadhana S, Leerasiri P, Techatraisak K, Tanmahasamut P et al. Prevalence and clinical predictors of insulin resistance in reproductive-aged thai women with polycystic ovary syndrome. Int J Endocrinol. 2012; 2012:529184. 53.
11. Mor E, Zograbyan A, Saadat P, Bayrak A, Tourgeman DE, Zhang C et al. The insulin resistant subphenotype of polycystic ovary syndrome: clinical parameters and pathogenesis. Am J Obstet Gynecol. 2004; 190(6):1654-
12. Ducluzeau PH, Cousin P, Malvoisin E, Bornet H, Vidal H, Laville M et al. Glucose-to-insulin ratio rather than sex hormone-binding globulin and adiponectin levels is the best predictor of insulin resistance in nonobese women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2003; 88(8):3626-31.
13. Golbahar J, Al-Ayadhi M, Das NM, Gumaa K. Sensitive and specific markers for insulin resistance, hyperandrogenemia, and inappropriate gonadotrophin secretion in women with polycystic ovary syndrome: a case-control study from Bahrain. Int J Womens Health. 2012; 4:201-6.