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Comparison of Abdominal Aorta Intima-Media Thickness, Serum Level of Leptin, and Lipid Profile between Maternal Preeclampsia and Neonatal Outcomes

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Abstract

Background

Pre-eclampsia is one of the main causes of morbidity and mortality among pregnant women. This study was done with the objective of measuring abdominal aorta intima-media thickness, serum level of leptin, and lipid profile in neonates of pre-eclampsia mothers and comparing them with neonates of mothers without pre-eclampsia (control group).

Materials and Methods

Ninety neonates of pregnant mothers, who delivered their babies at Imam Reza Hospital of Kermanshah University of Medical Sciences, were included. They were divided into mild pre-eclampsia (15 neonates), severe pre-eclampsia (15 neonates), and control group (60 neonates). Their blood samples were delivered to the laboratory to assay leptin and lipid profile. Also, echocardiography was done to determine the thickness of intima-media of the abdominal aorta. The data were analyzed by SPSS software using Pearson correlation test and analysis of variance (for variables with normal distribution) and Spearman coefficient test and Kruskal-Wallis tests for variables with non-normal distribution.

Results

The minimum and maximum ages of mothers in all groups were 20 and 35 years, respectively. There was no significant difference between the mild pre-eclampsia, severe pre-eclampsia, and those without pre-eclampsia regarding serum leptin level and lipid profile ($P> 0.05$). However, there was significant difference between the groups regarding intima-media thickness ($P< 0.05$). Mean (± standard deviation) intima-media thickness was the highest in severe pre-eclampsia group (0.629±0.034) and the lowest in control group (0.472±0.058).

Conclusion

Neonates of mothers with pre-eclampsia had higher measurements of abdominal aorta intima-media thickness compared to control group.

Key Words: Aorta, Leptin, Lipid Profile, Intima-Media Thickness, Pre-Eclampsia.

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1- INTRODUCTION

Blood pressure disorders during pregnancy are common and along with infection and hemorrhage constitute three most common causes of morbidity and mortality in pregnant women. Timely diagnosis and treatment of these disorders can decrease maternal and fetal complications (1, 2). Pre-eclampsia in which blood pressure of more than 140/90 mmHg is a major characteristic is a type of syndrome which occurs during pregnancy. It is one of the main causes of morbidity and mortality among pregnant women. Pre-eclampsia is divided into mild and severe forms. It can virtually affect all bodily systems such as cardiovascular system, hematologic and coagulation systems, kidney, liver, and central nervous system. It can affect the fetus as well and hence it is considered a high risk pregnancy with dangerous consequences for both mother and her fetus (3-5).

The incidence rate of pre-eclampsia is 5%, but a wide range has been reported. Factors such as parity, ethnicity, genetic factors, etc. can affect this wide range of incidence rate (1, 2, 6). The diagnosis of pre-eclampsia is made by the presence of hypertension along with proteinuria, edema or both of the latter (7). Another report from Iran described the prevalence of pre-eclampsia in a range of 1 to 8% (8).

Considering the importance of pre-eclampsia in pregnancy, several studies have been performed to investigate its risk factors. Factors such as nulliparity older age, race, genetic factors, environmental factors such as living in high altitudes, obesity, poverty, chronic hypertension, and multiple pregnancies all have been advocated as possible risk factors for pre-eclampsia. In some other studies, factors such as mother being employed, having sister with history of pre-eclampsia, urinary tract infection during pregnancy, lower educational level of mother, long interval with previous pregnancy, history of preterm labor and Intra-uterine growth retardation inappropriate prenatal care (IUGR), season, blood group, and low weight upon birth have been reported as risk factors as well (3-5, 9-13). Most complications and some risk factors of pre-eclampsia can be diagnosed and prevented. Although, the definitive treatment of pre-eclampsia is termination of pregnancy, appropriate prenatal care can provide suitable lieu for both mother and fetus (14). Neonates born to mother with pre-eclampsia are likely to develop lipid disorders and consequent cardiovascular disorders. Many cardiovascular disorders which occur later in adulthood stem from infancy and childhood. For instance, children who are IUGR, which is one of the main complications of pre-eclampsia, develop hypertriglyceridemia and have higher risk of increased aorta thickness and atherosclerosis (13, 15, 16).

Leptin is a protein hormone derived from adipocytes which has role in lipid metabolism. This hormone also plays role in reproduction, maturity, energy homeostasis, and pregnancy. Irregularity in leptin activity during pregnancy can be a risk factor for abortion, gestational diabetes, pre-eclampsia, and IUGR. In some studies, the possible role of leptin as atherogenic risk factor has been reported (16). Several studies have been performed in order to develop diagnostic tests for pre-eclampsia. However, at the moment no reliable and cost-effective screening test exists for pre-eclampsia.

Only with proper health care services provided during pregnancy, pre-eclampsia can be diagnosed in early stages. In developing countries, due to insufficient access to health care services, many patients present at advanced stages of pre-eclampsia. Therefore, many of these patients face severe complications and higher rate of morbidity and mortality. Since diagnosis and providing appropriate medical care for neonates born to mothers

with pre-eclampsia, this study was done with aims of measuring abdominal aorta intima-media thickness, serum level of leptin, and lipid profile in neonates of mild and severe pre-eclampsia mothers and comparing them with neonates of mothers without pre-eclampsia.

2- MATERIALS AND METHODS

2-1. Study design and population

In this case-control study, the study population involved neonates who were born at Imam Reza Hospital, Kermanshah, Iran from January to December 2015. Imam Reza Hospital is a university referral center for three provinces of Kermanshah, Ilam, and Kurdistan. Three groups were studied including neonates of mothers who experienced mild pre-eclampsia, those with severe pre-eclampsia, and neonates of mothers who did not have pre-eclampsia (control group). Mild pre-eclampsia was defined as blood pressure of 140/90 mmHg, proteinuria of +1, and no poor signs including headache, blurred vision, or epigastric pain. Severe pre-eclampsia was defined as blood pressure of 160/100 mmHg, proteinuria of +3, and presence of poor signs (1).

The primigravida mothers of neonates in control group had gestational age of more than 28 weeks with an uneventful pregnancy with no systemic diseases, and did not take any medications. To select control group, for each neonate whose mother had pre-eclampsia, one delivery before and one delivery after that particular delivery without pre-eclampsia were selected. Considering the mean (± standard deviation [SD]) intima-media thickness as 0.45 (±0.03) mm and 0.39 (±0.04) mm in two groups (16), the sample size, using the formula of comparing means, with confidence of 95% and power of 90% was calculated as 15 cases per group (a total of 45 neonates). Considering other objectives of the study, the sample size in control group was increased to 60 subjects and the total sample size became 90 neonates. The sampling method was of convenient method.

2-2. Ethical Consideration

The study protocol was approved by the Ethics Committee of Kermanshah University of Medical Sciences. The objectives of the study were explained for the mothers and their consent was obtained for obtaining umbilical cord blood samples and performing echocardiography.

2-3. Inclusion and Exclusion Criteria

Inclusion criteria consisted of primigravida mothers with age range of 20 to 35 years who had singe pregnancy with gestational age of more than 28 weeks. Exclusion criteria were taking any medication, chronic hypertension, systemic diseases, Addiction to illegal drugs, or immunosuppressive disorders. Also, neonates whose mothers had hypercholesterolemia, were smokers, had systemic disorders, or were taking any particular medications and neonates with congenital malformations were excluded.

2-4. Laboratory Measurements

Five ml of the umbilical cord blood was taken to measure serum leptin and lipid levels. The blood samples were transferred, while keeping in ice bags, to the laboratory. Leptin level was assayed using radio-immunoassay method (Webster Inc., TX). The abdominal aorta intima-media thickness was measured using ultrasound by a pediatric cardiologist for all the studied neonates.

2-5. Data Analysis

The data gathered were analyzed using the SPSS software (version 20.0). The results of the Kolmogorov-Smirnov test showed normal distribution of lipid profile and intima-media thickness ($P > 0.05$), but serum leptin level did not have normal distribution ($P < 0.05$). To investigate the relationship between serum leptin level

and intima-media thickness, the Spearman (for variables with non-normal distribution) and Pearson correlation coefficient (for variables with normal distribution) test (considering the results of the Kolmogorov-Smirnov test) were used. In order to compare intima-media thickness and other variables according to the presence of pre-eclampsia, the independent t test and Mann-Whitney U test were used. Kruskall-Wallis test and ANOVA was done to compare intima-media thickness and other variables based on pre-eclampsia severity.

3- RESULTS

Age range of mothers was 20 to 35 years. Mean age in the three groups was comparable as it was 26.7 (±4.6) years in control group, 27.5 (±4.4) years in mild pre-eclampsia group, and 27.4 (±4.2) years in severe pre-eclampsia group. The minimum gestational age was 36 weeks and the maximum was 41 weeks. The data regarding neonate gender and delivery type are presented in **Table.1**.

Mean (±SD) aorta intima-media thickness measurements were 0.62 (±0.03) mm in severe pre-eclampsia, 0.53 (0.05) mm in mild pre-eclampsia, and 0.47 (±0.05) mm in control group. There was no significant difference between the three groups in terms of serum leptin level and lipid profile (P> 0.05). However, there was significant difference between the groups regarding aorta intima-media thickness (P= 0.001); **Table.2**.

The results of two-by-two comparisons of the groups using the post-hoc Tukey's test regarding intima-media thickness showed that there were significant differences between the three groups (P< 0.001). Mean intima-media thickness was significantly lower in control group than mild and severe pre-eclampsia mothers (P< 0.001). Also, this value was significantly higher in severe pre-eclampsia than in mild group (P< 0.001).

The results of the Pearson correlation test showed that in mild pre-eclampsia group, no significant relationship existed between intima-media thickness with serum leptin level or lipid profile (P> 0.05). However, in severe pre-eclampsia group, intima-media thickness had positive and significant relationship with serum leptin level and lipid profile (P< 0.05); **Table.3**.

Table-1: Demographic data based on the study group

Variables		Control	Pre-eclampsia	
			Mild	Severe
Gestational age		39.07 (1.31)	37.53 (1.25)	36.93 (1.1)
Maternal age		26.72 (4.59)	27.53 (4.38)	27.4 (4.24)
Neonate gender	Girl	26 (43.3%)	6 (40%)	6 (40%)
	Boy	34 (56.7%)	9 (60%)	9 (60%)
Delivery type	Natural	16 (26.7%)	2 (13.3%)	0
	Cesarean	44 (73.3%)	13 (86.7%)	15 (100%)

Table-2: Mean (standard deviation) of major variables in the three study groups

Variables	Control	Pre-eclampsia		P-value
		Mild	Severe	
Intima-media thickness, range	47.23 (±5.76), 38-60	53.93 (±5), 42-59	62.87 (±3.4), 59-69	0.001
Serum leptin level	15.02 (±16.38), 1-89	20.37 (±23.30), 1-84	17.85 (±15.36), 3-47	0.595
low-density lipoprotein	24.52 (±10.13)	30.33 (±14.76)	23.93 (±8.2)	0.877

High-density lipoprotein	27.17 (10.15)	25.93 (7.74)	26.13 (11.64)	0.347
Triglyceride	47.82 (25.51)	51.67 (32)	36.67 (17.61)	0.584
Cholesterol	71.95 (23.25)	77.73 (24.91)	69.27 (21.49)	0.365

Table-3: The correlation between abdominal aorta intima-media thickness with serum leptin and lipids levels

Parameters	Abdominal aorta intima-media thickness			
	Mild pre-eclampsia		Severe pre-eclampsia	
	r	P value	r	P value
Serum leptin level	-0.234	0.402	-0.607	0.016
Lipid profile	0.116	0.680	0.660	0.007

r= Pearson correlation coefficient.

4- DISCUSSION

In this study which was done with the objective of investigating the relationship between abdominal aorta intima-media thickness with serum leptin level and lipid profile, 90 neonates of pregnant mothers who gave birth at Imam Reza Hospital were studied. The results showed that intima-media thickness of the abdominal aorta was the highest in severe pre-eclampsia group and the lowest in control group. The analyses showed that significant difference existed between control group, mild, and severe pre-eclampsia groups regarding intima-media thickness. In a former study, it was reported that mean intima-media thickness was higher in neonates born to mothers with pre-eclampsia than control group (17). Likewise, in Koklu et al. study the thickness of aorta intima-media had a mean value of 0.45 (0.03) mm in pre-eclampsia group and it was 0.39 (0.04) mm in control group with a significant difference (16). Sodhi et al. studied the intima-media thickness of abdominal aorta and carotid artery in neonates with normal size vs. those who were small for gestational age (SGA). They noted that intima-media thickness of both aorta and carotid artery was significantly higher in SGA group (18). Similarly, Iwashima et al. did not find any significant association between gestational age and intima-media thickness of the aorta, but reported that there was significant relationship between intima-media thickness and subsequent development of cardiovascular diseases (19). In this study, mean serum leptin level was not different between the three study groups. A previous study reported that umbilical cord blood leptin level in neonates born to mothers with pre-eclampsia had significant association with gestational age and this was higher in pre-eclampsia group. But pre-eclampsia severity did not have significant association with intima-media thickness (20). Increased level of umbilical cord leptin level can be the result of conditions that cause fetal stress such as hypoxemia. Some studies have noted that the placenta can have effect on increased leptin level in mothers and fetuses and can be responsible in the pathogenesis of pre-eclampsia (20).

However, we did not find significant difference regarding umbilical cord leptin level between pre-eclampsia and the control group. In another study, neonates born to mothers with pre-eclampsia had lower levels of leptin compared to control group (21) which is not compatible with our results. There is controversy in the literature about the leptin level and pre-

eclampsia (22). However, maternal serum leptin has been implicated as an important biomarker in the onset of pre-eclampsia (23, 24). There was no significant difference between the three studied groups (mild pre-eclampsia, severe pre-eclampsia, and control group) regarding lipid profile. However, in a former study, triglyceride level was higher in neonates born to mothers with pre-eclampsia (17). Also, in the mentioned study, high-density lipoprotein (HDL) was lower in pre-eclampsia group than in control group. In Koklu et al. study, leptin and insulin-like growth factor levels were lower in IUGR group than in control group. IUGR can be the result of pre-eclampsia. In IUGR patients, higher rate of increased intima-media thickness occurs (16).

5- CONCLUSION

Neonates born to mothers with pre-eclampsia had higher likelihood of lipid disorders. The results obtained here can be used to study epidemiologic aspects of cardiovascular diseases in adulthood and their relationship with pre-eclampsia. Also, risk stratification for development of cardiovascular diseases can be addressed by the results presented here.

6- CONFLICT OF INTEREST

Authors declare no conflict of interest.

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