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Evaluation of Systolic, Diastolic and Mean Arterial Blood Pressure in the First Trimester of Pregnancy as an Indicator for Predicting the Occurrence of Preeclampsia

Z. Bouzari (MD)[1], S. Mahabadi (PhD)[2], Sh. Yazdani Cherati (MD)*[3], S. Talebi (MD)[4], K. Hajian (PhD)[5]

1.Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran
2.Departement of Biochemistry & Clinical laboratories, Faculty of Medicine, Tabriz Univercity of Medical Sciences, Tabriz, I.R.Iran
3.Infertility and Reproductive Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran
4.Clinical Research Development Unite of Rouhani Hospital, Babol University of Medical Sciences, Babol, I.R.Iran
5.Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran

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ABSTRACT

BACKGROUND AND OBJECTIVE: Preeclampsia is a common disease during pregnancy that may be associated with maternal and fetal mortality. Since the pathogenic process of preeclampsia begins during the first trimester of pregnancy, it is very difficult to identify biomarkers of early detection of preeclampsia. The aim of this study was to determine the predictive validity of systolic, diastolic and mean arterial blood pressure in the first trimester of pregnancy in the diagnosis of preeclampsia.

METHODS: This case-control study was performed on 200 pregnant women referred to Ayatollah Rouhani Hospital in Babol within a historical cohort. The data of the records of 100 pregnant women with preeclampsia diagnosis (case group) and 100 healthy women (control group) were filled in special forms and compared.

FINDINGS: According to ROC curve analysis, in the first trimester for systolic blood pressure at the cut-off point of 117.5, sensitivity of 56% and specificity of 70%, for diastolic blood pressure at the cut-off point of 72.5, sensitivity of 68% and specificity of 63% and for mean arterial pressure at the cut-off point of 87.5, sensitivity of 67% and specificity of 66% were calculated. Based on the area under the ROC curve, the diagnostic power was 0.706, 0.663 and 0.709, respectively ($p<0.001$).

CONCLUSION: The results of the present study indicate that arterial pressure can be used as an effective method in identifying women at risk for preeclampsia as a selection criterion in testing, treatment or prevention.

KEY WORDS: *Preeclampsia*, *Systolic Blood Pressure*, *Diastolic Blood Pressure*, *Mean Arterial Pressure*.

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***Corresonding Author: Sh. Yazdani Cherati (MD)**
Address: Ganjafrooz Stree, Babol University of Medical sciences, Babol, I.R.Iran
Tel: +98 11 32238301
E-mail: shahla_yazdani_1348@yahoo.com

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Introduction

Preeclampsia is a common complication in late pregnancy that affects an average of 3 to 5% of pregnancies in different communities and is involved in maternal and fetal mortality. Several predisposing factors have been suggested for its occurrence. Preeclampsia is usually characterized by high blood pressure and proteinuria in pregnancy. Systolic blood pressure equal to or greater than 140 mm Hg and diastolic blood pressure greater than 90 mm Hg with a protein excretion of 300 mm Hg in 24-hour urine or +1 in the urine test strip after the twentieth week of pregnancy is called preeclampsia. In fact, preeclampsia is one of the three leading causes of death in pregnant women worldwide (1, 2).

Despite numerous studies in this field, the pathophysiology of preeclampsia is still not fully understood. The pathogenic process of preeclampsia begins during the first trimester before the onset of clinical symptoms, so it is very difficult to identify early biomarkers of preeclampsia (3-5). Therefore, this disease can be identified only by clinical manifestations and is often diagnosed late (6-10).

In people with preeclampsia, oxidative stress causes vascular dysfunction, inflammation, apoptosis, and structural damage (11-16). On the other hand, hypertension occurs as a result of vasoconstriction and decreased peripheral vascular compliance. Since hypertension is an early sign of preeclampsia that can be considered as a marker of early diagnosis (17, 18), there is still no reliable criterion for early diagnosis of preeclampsia. There are several clinical, biophysical and biochemical tests to identify women at risk for preeclampsia, and the results of studies indicate that their predictive value in the early diagnosis of preeclampsia is low (19).

Various studies and research that measure blood pressure have had conflicting results. Because of these conflicting results, it is still unclear whether blood pressure can be used as a routine screening test for prognosis or it is only a diagnostic criterion for hypertensive pregnancy in susceptible individuals (20). Preeclampsia is one of the leading causes of maternal mortality and is now a major challenge in modern obstetric care. Therefore, identifying pregnancies at risk of preeclampsia and the necessary measures to improve the condition of the pregnant mother is very important (21). Due to the importance of this disorder and maternal and infant mortality, the lack of a definitive test to predict preeclampsia, the cheapness and feasibility of this test and the lack of a study in this area, the purpose of this study was to determine the validity of the prediction based on systolic, diastolic and mean arterial blood pressure in the first trimester of pregnancy in the occurrence of preeclampsia..

Methods

This nested case-control study was performed within a historical cohort among pregnant women referred to the clinic of Ayatollah Rouhani Hospital in Babol for perinatal care and termination of pregnancy from September 2011 to April 2015 after obtaining permission from the Ethics Committee of Babol University of Medical Sciences with the code MUBABOL.REC.1393.21. People with chronic hypertension, diabetes, kidney disease, smoking, taking drugs that affect blood pressure, and people whose perinatal tests were not performed at Ayatollah Rouhani Hospital were excluded from the study. According to previous studies and using statistical estimates at 95% confidence level and 80% test power, to identify the standardized effect of blood pressure of 0.28 units (on a standard scale), 200 people were considered for the two groups; 100 people in the preeclampsia group (case) and 100 people in the group without preeclampsia (control).

The control group was matched with the case in terms of age while information about the level of education and prenatal care of the two groups was collected. In this study, preeclampsia refers to gestational hypertension and proteinuria. The patient is diagnosed with hypertension when the blood pressure recorded under normal conditions has systolic greater than 140 mm Hg and diastolic greater than 90 mm Hg at intervals of at least 6 hours and at most one week. Proteinuria refers to the presence of at least 300 mg of protein in a liter of 24-hour urine or a protein concentration of at least 30 mg from two random urine samples prepared within at least 6 hours interval. In this study, blood pressure was measured after at least 5 minutes of rest in a sitting position. Blood pressure was measured in both hands and excluded if there was a difference in blood pressure. Mean arterial blood pressure was obtained based on the following equation:

Mean arterial blood pressure= ([2×diastolic blood pressure+systolic blood pressure]) ÷ 3

People who were hospitalized with a diagnosis of preeclampsia by a gynecologist, the necessary preeclampsia tests (liver test, platelet, kidney test) were performed for them and if they met the inclusion

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criteria, these people were included in the case group (preeclampsia). Among the samples who were hospitalized with normal blood pressure for delivery, if they had inclusion criteria, they were selected as a (healthy) control group and information was collected. Statistical analysis of data was performed by Chi-square, T-Test and Mann-Whitney tests using SPSS V22. The area below the ROC curve was considered as a criterion for diagnostic accuracy for the data and $p<0.05$ was considered significant.

Results

The mean age of pregnant women was 27.14±5.67 years (minimum age was 16 years and maximum age was 44 years). The mean age was 27.49±5.77 in the case group and 26.80±5.58 in the control group (Table 1).

Table 1. Demographic information of the participants in the study in case and control groups in the first trimester of pregnancy

Variable	Preeclampsia Mean±SD or N(%)	Without preeclampsia Mean±SD or N(%)	P-value
Parity			
Nulliparous	76(76)	62(62)	0.01
Multiparous	24(24)	38(38)	
Education			
Illiterate	2(2)	10(10)	
Primary	3(3)	2(2)	
Middle school	10(10)	12(12)	
High school	26(26)	21(21)	0.25
High school diploma	28(28)	28(28)	
Associate degree	31(31)	27(27)	
College education	2(2)	10(10)	
Prenatal care			
Received	100	99	1
Did not receive	-	1	

The mean body mass index at the beginning of pregnancy was 25.96±4.00 and at the time of hospitalization was 32.32±4.59. None of the women in the study reported a history of smoking. Women with preeclampsia had higher weight and BMI (p=0.001). Healthy pregnant women and women with preeclampsia were similar in terms of age, level of education, and prenatal care. Systolic, diastolic and mean arterial blood pressure in pregnant women with preeclampsia were significantly different from pregnant women without preeclampsia (p=0.001) (Table 2).

Table 2. Comparison of systolic, diastolic and mean arterial blood pressure in the first trimester of pregnancy in the two preeclampsia and healthy groups

Blood pressure (mm Hg)	Preeclampsia	Without preeclampsia	P-value
First trimester systolic	118.37±9.25	110.95±9.60	0.001
First trimester diastolic	76.15±5.63	71.80±7.30	
First trimester mean arterial	90.22±6.04	84.85±7.32	

The ROC curve was used to determine the appropriate cut-off point for systolic, diastolic and mean arterial blood pressure (Figure 1). For systolic blood pressure of the first trimester (area under the curve= 0.706), the cut-off point of 117.5 mm Hg, sensitivity of 56% and specificity of 70% were calculated.

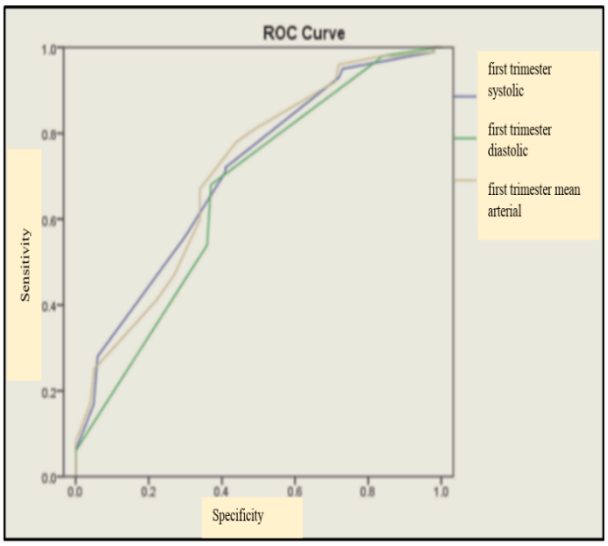

Figure 1. ROC curve of systolic, diastolic and mean arterial blood pressure in the first trimester in the diagnosis of preeclampsia

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For the diastolic blood pressure of first trimester (area under the curve= 0.663), the cut-off point of 72.5 mm Hg, sensitivity of 68% and specificity of 63% were calculated. This rate was calculated for the mean arterial pressure of the first trimester (area under the curve= 0.709); cut-off point of 87.5 mm Hg, sensitivity of 67% and specificity of 66% (Tables 3 and 4).

Table 3. Optimal cut-off point and sensitivity and specificity of PPV, NPV, LR^+, LR^- with 95% confidence interval of systolic, diastolic and mean arterial blood pressure in the first trimester of pregnancy in the diagnosis of preeclampsia

Blood pressure (mm Hg)	Optimal cut off point	Sensitivity (%)	Specificity (%)	LR^-	LR^+	NPV	PPV
First trimester systolic	117.5	56	70	0.63 0.49-0.81	1.87 1.32-2.64	61% 52%-70%	65% 55%-0.75%
First trimester diastolic	72.5	68	63	0.51 0.37-0.70	1.84 1.38-2.45	66% 57%-76%	65% 56%-74%
First trimester mean arterial	87.5	67	66	0.50 0.37-0.68	1.97 1.45-2.68	67% 57%-76%	66% 57%-76%

Table 4. Diagnostic power of systolic, diastolic and mean arterial blood pressure in the first trimester of pregnancy in the diagnosis of preeclampsia and 95% confidence interval

Blood pressure	AUC	CI 95%	P-value
First trimester systolic	0.706	0.635-0.777	0.001
First trimester diastolic	0.663	0.587-0.736	0.001
First trimester mean arterial	0.709	0.78-0.636	0.001

Discussion

In this study, the results showed that in the first trimester of pregnancy at 11-13 weeks, mean systolic and diastolic blood pressure and mean arterial pressure were significantly higher in women with preeclampsia than in healthy pregnant women. The study of Nzleu et al. in the UK divided 586 pregnant women with chronic hypertension into three groups during the first trimester of pregnancy. Group 1: blood pressure < 90/140 mmHg without antihypertensive drug, group 2: blood pressure < 90/140 mmHg with antihypertensive drug and group 3: systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. The mean gestational age in the study was 10 weeks (ranging between 9.1 and 11 weeks). The results showed that in groups 2 and 3, compared to group 1, body mass index and history of preeclampsia in previous pregnancies were significantly higher. Moreover, pregnant women with high blood pressure in group 3 had a significant increase in the incidence of severe hypertension, early preeclampsia (starting at < 37 weeks of gestation) compared to groups 1 and 2 (22), which is consistent with the present study. In a study of pregnant women during the first trimester of pregnancy, Turri et al. reported that mean systolic and diastolic blood pressure in the preeclampsia group were 122.2±0.0 and 76.10±7.00, respectively. Our study observed a slight difference in systolic blood pressure. However, diastolic blood pressure was approximately equal in the two studies (23). Another similar study showed that systolic blood pressure in the first trimester of pregnancy is a risk factor for preeclampsia. Accordingly, the rate of systolic blood pressure in the study in the group with preeclampsia was equal to 112.1±0.0 and in the control group was equal to 110.16±0.0. Similar to our study, there was a significant difference between the two groups. However, the mean diastolic blood pressure in Myatt's study was approximately equal in the two groups, which is not consistent with the results of this study. Mean systolic and diastolic blood pressure in the first trimester in our study was higher than in Myatt's study. It is also worth noting that the women participating in Myatt's study were younger than ours. Studies have shown that age over 35 increases the risk of preeclampsia in pregnant women. None of the women in our study were smokers, but in Myatt's study about 15% of women smoked during pregnancy (24). Thus, slight differences in the samples participating in the study can explain the differences in the results of the present study with the study of Myatt et al. (24). Their study also showed that systolic pressure is higher than the diastolic and mean

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arterial pressure based on the area under the curve and has a higher predictive value, which is different from our study in this regard. The results of a similar study by Sonek et al. showed that screening for preeclampsia based on clinical markers, including maternal blood pressure in the first trimester of pregnancy, is very important in diagnosing preeclampsia. In fact, late screening results in very poor performance in identifying cases of preeclampsia (25). In another study conducted by Iwasaki et al., the evidence showed that at 5-13 weeks of gestation, blood pressure in the two preeclampsia and healthy groups was 94.2±10.0 and 82.3±10.8, which is almost similar to the values obtained in our study (17).

In the study of bullarbo et al., diastolic blood pressure at the cut-off point of 80 mmHg had a sensitivity of 30.6% and a specificity of 92%, which in the present study had a higher sensitivity and lower specificity. However, in the bullarbo's study, it was mentioned that most people with preeclampsia, both during and before the disease, have a 15 mmHg increase in diastolic blood pressure. If these two parameters are combined, the sensitivity increases from 30.9% to 92% and specificity decreases from 93% to 44% (26).

Evidence shows that in the first trimester, mean arterial blood pressure at the cut-off point of 88 mmHg had a sensitivity of 78% and a specificity of 62%, which had higher sensitivity than our study and almost equal specificity. Also in this study, systolic blood pressure at the cut-off point of 120 mmHg had a sensitivity of 57% and a specificity of 69%, which was approximately equal to our study (27). On the other hand, according to previous studies, there is a significant relationship between weight and body mass index at the beginning of pregnancy and at the time of hospitalization with the risk of preeclampsia, which is consistent with the study of Sohlberg in this regard. However, in this study, it was stated that the body mass index of pregnant women is more associated with the group with mild preeclampsia than severe preeclampsia. In our study, preeclampsia was not classified based on severity (19). The results of Styen et al.'s study also showed that systolic blood pressure and mean arterial blood pressure in the preeclampsia group were much higher than the control group in the study and there was a significant difference, but systolic blood pressure was higher in the mentioned study compared to our study, which could be due to differences in the statistical population. Also in this study, diastolic blood pressure in the preeclampsia group started to increase from the second trimester and there was a significant difference with diastolic blood pressure in the control group. In our study, diastolic blood pressure was significantly different in the two groups from the beginning of pregnancy. Therefore, mean arterial blood pressure was slightly different in our study and Styen's study (18).

The results of the present study indicate that arterial hypertension can be used as an effective method in identifying women at risk for preeclampsia as a selection criterion in testing, treatment or prevention. It seems that screening, including mean arterial pressure with a combination of clinical trials, can be used to diagnose preeclampsia early. However, other studies with larger statistical communities and consideration of intervening factors are recommended to obtain definitive results in this field.

According to the findings of this study, the use of mean arterial pressure in the first trimester of pregnancy is more valuable than systolic and diastolic blood pressure for screening and predicting preeclampsia. Since the measurement of mean arterial pressure is a non-invasive method, it is very cheap and applicable, it is recommended to use this method in prenatal care to take a useful step in reducing the incidence of preeclampsia.

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