Prediction of mild and severe preeclampsia with blood pressure measurements in first and second trimester of pregnancy

Predykcja łagodnego i ciężkiego stanu przedrzucawkowego przy pomocy pomiarów ciśnienia tętniczego w I i II trymestrze ciąży

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Abstract

Objectives: *The study was designed to determine the accuracy of using systolic (SBP) and diastolic blood pressure (DBP), mean arterial pressure (MAP), and increase of blood pressure (BP) to predict Preeclampsia (PE).*

Materials and Methods: *We examined 300 normotensive and 100 PE pregnancies divided in two subgroups: mild (n=67) and severe (n=33) PE. The patients had a BP check in first and second trimester (SBP, DBP, and MAP).*

Results: *We found out significant difference between the groups, but what is more important is that the difference in BP values (especially diastolic and MAP) existed before the pathological increase of the BP above the normal values. This was happening most often after 31 wg (at 92.5%) and less often after 26 wg (at 7.5%) at the pregnancies with mild PE while at the pregnancies with severe PE, 18,2% had increased tension after 21 wg; 24% in the period of 26-30 wg and 57.58% after 31 wg.*

Conclusion: *Based on the results we could conclude that when BP is measured in the first or second trimester of pregnancy, the MAP is a better predictor for PE than SBP and DBP.*

Key words: **preeclamsia** / **prediction** / **blood pressure measurements** /

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Streszczenie

Cel pracy: *Ocena przydatności pomiarów ciśnienia skurczowego (SBP) i rozkurczowego (DBP), średniego ciśnienia tętniczego (MAP) i wzrostu ciśnienia tętniczego (BP) w przewidywaniu stanu przedrzucawkowego.*

Materiał i metody: *Zbadano 300 ciężarnych z prawidłowym ciśnieniem tętniczym oraz 100 ze stanem przedrzucawkowym, które podzielono na dwie podgrupy: z łagodnym i ciężkim stanem przedrzucawkowym. Pacjentkom mierzono ciśnienie tętnicze w I i II trymestrze ciąży (SBP, DBP i MAP).*

Wyniki: *Znaleziono istotne różnice pomiędzy badanymi grupami. Co więcej różnica wartości ciśnienia rozkurczowego i średniego ciśnienia tętniczego istniała już przed patologicznym wzrostem ciśnienia powyżej wartości prawidłowych. W ciążach z łagodnym stanem przedrzucawkowym najczęściej zaburzenie to występowało po 31 tyg. ciąży (92,5%), najrzadziej po 26 t.c.(7,5%). Podczas gdy w przypadkach z ciężkim stanem przedrzucawkowym, 18,2% miało podwyższone ciśnienie po 21 t.c., 24% w okresie 26-30 t.c. a 57,58% po 31 t.c.*

Wnioski: *W oparciu o wyniki naszej analizy można powiedzieć, że MAP jest lepszym predykatorem stanu przedrzucawkowego niż SBP czy DBP.*

Słowa kluczowe: **stan przerzucawkowy** / **predykcja** / **ciśnienie tętnicze** /

Introduction

Preeclampsia (PE) is a multisystem disorder of unknown aetiology, unique to pregnancy. Women with PE usually develop raised blood pressure after 20 weeks of gestation, but the condition is also associated with abnormalities of the coagulation system, disturbed liver function, renal failure and cerebral ischemia [1, 2]. It complicates an estimated 2–30% of pregnancies and is a major cause of maternal morbidity, prenatal death and premature delivery, although for most women the outcome is good [3-5].

The pathogenesis of preeclampsia is complex. It has been suggested that preeclampsia is a two-stage disease [6]: Stage 1: asymptomatic, characterized by abnormal placental development during the first trimester resulting in placental insufficiency. This in turn leads to symptomatic, stage 2, wherein the pregnant women develops characteristic hypertension, renal impairment, and proteinuiria and is at risk for the HELLP syndrome, eclampsia and other endorgan damage [6, 7].

The PE is associated with low birth weight and preterm delivery, but can also develop at term, during labour, or even post partum. It has been shown that women destined to develop pre-eclampsia have higher mean arterial pressures in the first and second trimester and even before pregnancy than women with normal pregnancies [8, 9].

Women with PE generally have a good outcome. The risks to them and their baby increase only if they progress to PE, or have very high blood pressure [9, 10].

Objectives

Blood pressure (BP) measurement is a screening test routinely used in antenatal care to detect or predict hypertensive disease. Studies investigating the predictive accuracy of BP measurement report conflicting results. In view of these conflicting reports it is uncertain whether BP measurement should be used routinely as a predictive test or should only be used to diagnose hypertensive disorders in pregnancy once they are suspected. The aim of this study is to examine the performance of screening for PE and to compare systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP) measured by validated devices in pregnant women.

Materials and Methods

The research was conducted in the Clinical Hospital ”Dr Trifun Panovski” in Bitola, Macedonia (FYROM), Department of gynaecology and obstetrics. These patients had been admitted during the period of May 1st 2008 to August 1st 2009. This study protocol was approved by the Director of Clinical Hospital in Bitola, and the Ethics committee of School of Medicine University of Belgrade, Serbia. A written consent was provided by all participants. The research was conducted in the Antenatal Care Ambulance which is part of the Gynecology-Obstetric Department. Approximately, this ambulance provides treatment to 900-1000 patients annually, while at the Gynecology-Obstetric Department approximately 1600 pregnancies are delivered annually.

The study included 400 participants. Considering the recommendations of the Ethics committee, this prospective study is based on 300 normotensive pregnants and 100 preeclamptic pregnants.

The preeclamptic women later on, based on clinic and laboratory parameters, were divided in two subgroups: women with mild and severe preeclampsia. This study wasn’t limited by any timelines and when we reached the demanded numbers of patients, we concluded the research.

The research was conditioned with the following criteria:

The criteria to determine the exact pregnancy stage is based on the following criteria: anamnestical, obstetrical and ultrasound scan, which means that the information of the last period is corresponding with the results from the obstetrical examination and the ultrasound scan. The first examination was performed in the period of 6-12 week of gestation (wg).

The participants were healthy women with normal BP (on their first visit they didn’t have artery pressure above 120/80 mmHg), with no history of any chronic disease, with singleton pregnancy, without chromosomal or congenital abnormalities, with exact date of the last menstrual period and regular menstrual period.

We reviewed age, parity, smoking status, week of preeclampsia onset, duration of preeclapmpsia, duration of pregnancy, and birth weight in percentile. Smoking status and level of education was determined by self-report.

All subjects were followed until delivery. The gestational age at delivery, obstetric complications if any, and neonatal outcome were recorded. For those subjects who were subsequently delivered in another hospital, the obstetric information was obtained by telephoning the subject or via contact with the staff in the other hospital. Birth weight (to the nearest gram) was classified into five categories: very low birth weight (<5th percentile), low (5-9,9), normal (10-89.9), high (90-94.9) and very high (>95). Intrauterine growth restriction (IUGR) is defined as birth weight less than the 10th percentile based on the Alexander growth standard [11].

Pre-pregnancy or at booking body mass index (BMI) was based on measured height and maternal weight at the initial visit (6-12 w.g.) and maternal self report of pre-pregnancy weight. Height was measured by using a portable stadiometer, accurate to 1 mm. Pre-pregnancy BMI was categorized as: underweight (<19.9), normal (20.0-24.9), overweight (25.0-29.9) or obese (>30.0) [12]. Total maternal weight gain during pregnancy was recorded on admission to delivery ward.

BP measurements were performed using a mercury sphygmomanometer according to a standardized published protocol, and all urine specimens were assessed for protein by dipstick. MAP (in mmHg) was calculated using the equitation: MAP= (SBP+ 2xDBP)/3 [13].

Mild PE was defined by the occurrence of two or more SBP ≥140mmHg and/or DBP ≥90mmHg, with the first elevated BP occurring after 20 weeks' gestation up to 24 hours after delivery [14].

Severe PE was defined as a SBP ≥160mmHg and DBP ≥110mmHg on at least two occasions at least 4 hours apart or on one occasion if antihypertensive therapy was administered. Severe proteinuria was defined with a 24-hour urine sample containing ≥3.5 g of protein or two urine samples of "3+ protein" or greater taken at least 4 hours apart [14].

During the research the methods used were descriptive statistics, the relative numbers, chi-quadrate test, Student t-test, multivariate analysis and post-hoc test was used to determine the statistical differences between groups. A p value <0.05 was considered statistically significant.

Table I. Description of maternal characteristics and pregnancy outcome by study groups.

Characteristics	Controls n=300	Mild preeclampsia n=67	Severe preeclampsia n=33	P value
Maternal age (years)	27.5±5.04 (17-42)	27.4±5.9 (17-42)	29.2±5.8 (16-43)	
<20	5.3 (16/300)	8.96 (6/67)	9.1 (3/33)	
20-25	29.0 (87/300)	40.3 (27/67)	12.1 (4/33)	p>0.05†
26-30	40.0 (120/300)	19.4 (13/67)	42.4 (14/33)	
31-35	21.0 (63/300)	19.4 (13/67)	24.2 (8/33)	
>35	4.7 (14/300)	11.9 (8/67)	12.1 (4/33)	
Parity (%)				
Primipara	46.7 (140/300)	65.7 (44/67)	60.6 (20/33)	p<0.05†
multipara	53.3 (160/300)	34.3 (23/67)	39.4 (13/33)	
Smoking status	10.33 (31/300)	1.49 (1/67)	30.3 (1/33)	<0.05‡
BMI	22.7±1.7 (19.1-27.6)	25.53±1.6 (21.8-27.9)	25.8±2.2 (21.7-29.1)	
<19.99	1.7 (5/300)	0 (0/67)	0 (0/33)	
20.0-24.99	87.3 (262/300)	23.9 (16/67)	30.3 (10/33)	<0.01§
25.0-29.99	11.0 (33/300)	76.1 (51/67)	69.7 (23/33)	
Weight gain (kg)	13.9±3.1 (7-29)	19.6±3.8 (13-31)	20.2±7.4 (10-39)	
Duration of pregnancy	39.6±0.9 (37-42)	39.1±0.9 (37-40)	37.5±2.0 (32-40)	
≤32	0 (0/300)	0 (0/67)	3.03 (1/33)	<0.01†
33-36	0 (0/300)	0 (0/67)	18.2 (6/33)	
>37	100 (300/300)	100 (67/67)	78.8 (26/33)	
Birth weight (g)	3427.8±332.4	2989.3±256.2	2582.4±407.9	<0.01†
Birth length (cm)	50.7±1.2	48.7±1.3	46.4±2.4	<0.05†
Birth weight (percentile)				
<10	3 (9/300)	29.9 (20/67)	63.6 (21/33)	<0.01†
10-90	93.3 (280/300)	70.2 (47/67)	36.4 (12/33)	
>90	3.7 (11/300)	0 (0/67)	0 (0/33)	

Data are given as mean, standard deviation and range or % unless otherwise specified;
n – number of subjects; † – multivariate analysis; ‡ – chi-squared test

Results

Table 1 shows the demographic and clinical characteristics of the women studied. The significant difference in the frequency of categories and age groups was tested with a method of multivariate analysis for proportion. The difference was not statistically significant p>0.05, which clearly shows that the groups are a priori similar and comparable.

The significant difference in the frequency of categories and parity groups was tested with a method of multivariate analysis for proportion. The difference was statistically significant p<0.05. We found a decreased risk of mild and severe PE among women who smoked during pregnancy.

Women who developed preeclampsia had higher rates of overweight prior to pregnancy and gained more weight during pregnancy. The majority of women who developed preeclampsia were overweight, but not obese (p<0.01).

The newborns from the hypertensive pregnancies had lower birth weight vs. neonates from normotensive pregnancies.

The severe vs. mild PE, occurs earlier in pregnancy 30.4±4.5 (21-38 w.g.) vs. 34.5±2.7 (26-38) and the hypertension is long lasting (8.0±4.3 vs. 4.8±2.6). Early beginning of the hypertension during the pregnancy is associated with longer lasting and more severe conditions of PE. Early development of hypertension is also associated with more severe conditions of PE. The results are presented in Table II.

Table II. Characteristics of mild and severe preeclampsia.

Variables	Mild preeclampsia (n=67)	Severe preeclampsia (n=33)
Onset of PE**‡ (week of gestation)	**34.5±2.7 (26-38)**	30.4±4.5 (21-38)
Gestational age during the PE onset (%)**‡		
≤25	**0**	18.18
26-30	**7.5**	24.2
≥31	**92.5**	57.6
Duration of PE§ (weeks)**	**4.8±2.6 (1-14)**	8.0±4.3 (2-16)
MP – group with mild preeclampsia; SP – group with sevre preecampsia; * Data are given as median, standard deviation and range; ** p<0.01; ‡ – chi-squared test; Student's t test.		

Table III. Values of systolic blood pressure, diastolic blood pressure and mean arterial pressure.

Characteristics	Normal pregnancies n=300	Mild preeclampsia n=67	Severe preeclampsia n=33	P value*
SBP (mmHg)				
8-12 wg	102.2±7.4	111.8±8.7	114.2±10.5	>0.05
13-16 wg	103.9±7.5	113.7±8.3	118.3±8.9	>0.05
17-20 wg	104.9±7.8	117.3±5.3	121.8±7.1	<0.05*
25-27 wg	107.6±6.5	121.3±10.2	133.3±15.3	<0.05
postpartum	117.8±3.3	120.8±5.3	122.1±6.1	>0.05
DBP (mmHg)				
8-12 wg	63.7±4.9	73.4±7.5	75.5±8.2	<0.05**
13-16wg	65.1±4.7	74.9±7.2	78.2±7.0	<0.05)
17-20 wg	65.9±5.0	77.8±5.7	80.9±6.9	<0.05
25-27 wg	67.9±4.7	80.5±7.2	88.0±11.9	<0.05
postpartum	74.3±4.4	78.1±5.0	79.7±3.7	>0.05
MAP (mmHg)				
8-12 wg	76.5±5.4	86.2±7.66	88.4±8.6	<0.05
13-16wg	78.1±5.4	87.8±7.3	91.6±7.5	<0.05
17-20 wg	78.9±5.78	90.9±5.35	94.5±6.86	<0.05
25-27 wg	81.1±5.2	94.1±7.99	103.1±12.85	<0.05
postpartum	88.8±3.5	92.3±4.53	93.8±4.2	>0.05
Data are given as mean and standard deviation; n – number of subjects; SBP – Systolic blood pressure; DBP – Diastolic blood pressure; MAP – Mean arterial blood pressure; wg – week of gestation;);* two way ANOVA; **control vs. severe preeclampsia;				

During the regular checkups every patient had BP measured. Table III shows the results of measured systolic (SBP), diastolic pressure (DBP) and mean arterial pressure (MAP) in the following periods: 8-12, 13-16, 17-20, 25-27 week of gestation (w.g.) and postpartal values maximum one week postpartum.

Here we found that statistical difference between groups, before pathological increase of pressure exists ($p<0,05$). Both DBP and MAP were significantly higher in the first and second trimester for pregnants who later developed PE.

Discussion

Preeclampsia is a major cause of maternal and neonatal morbidity and mortality worldwide. Some studies are concluding that the major phenotype of PE, hypertension and proteinuria, may be due to an excess of circulating anti-angiogenic growth factors, most notably soluble fms-like tyrosine kinase 1 (sFlt1) and soluble endoglin (sEng) [15, 16].

Generally, to identify particular potential factors in cases of PE in some population requires a lot of effort. Some factors have proven cause connection for PE; however at most of the cases we couldn't prove any connection. The main focus of PE and its symptomatology is the hypertension. Diastolic pressure as a relation to arteriolar spasm is a permanent damage of the blood circulation and has primary influence. Values of systolic pressure are affecting the vegetative irritable, reaction for external sensation and mental perception [17].

The importance of BP measurement during pregnancy has been recognized for more than a century (Seligman, 1987) and is a fundamental part of antenatal care. For many women their pregnancy will be the first point of medical contact and they may have been unaware of any pre-existing hypertension up to the third point [18].

In the present study, the lower birth weight and length at birth, underline the severity of the disease in the preeclamptic groups. Also, these results, too, are same as from the associated literature in this area [18, 19].

Our study includes data of smoking status. It is well known that smoking is a strong and common risk factor for low birth weight. Smoking seems to be negatively associated with PE. Thus, smoking would increase rather than decrease the effect of PE in infants' size [20].

During our research we were measuring the SBP and DBP and calculating the MAP during the pregnancy. Based on the BP measurements, we found out significant difference between the group of hypertensive and normotensive pregnancies, but what is more important is that the difference in BP values (especially diastolic and MAP) existed before the pathological increase of the artery pressure above the normal values. This was happening most often after 31 wg (at 92,54%).

Based on the results that we got during our research we could conclude that in the first and the second trimester of pregnancy, MAP has higher predictability, while with SBP statistically significant difference is obvious with SP group related pregnancies. After the manifested imbalance, significant difference between the groups was noticeable at the DBP values. SBP has the lowest predictable values. The values of SBP even before the PE manifestation at the hypertensive pregnancies are slightly higher than the measured values at the normotensive pregnancies; however the value is not statistically significant.

We also recorded difference in the diastolic pressure in the same period of pregnancy. Statistically significant difference is obvious between the normotensive and hypertensive pregnancies at the level of $p<0,05$; however there was not difference between the MP and SP.

In relation to the calculated values of MAP, the average values in the periods of 8-12, 13-16 and 17-20 wg. The statistical difference between the groups is obvious on a level of $p<0,05$.

Cnossen SJ. Et al.(2008), worked on 34 studies in which 60599 women were observed, of which 3341 had preeclampsia. Their hypothesis was based on the diastolic average, but not on the systolic pressure. They concluded that the diastolic blood pressure over 75mmHg in the period of 13-20wg has predictive importance. They also concluded that in the same period the MAP values over 85-90 mmHg also has predictive importance for the development of PE, which was also the case in our research, too [21].

The importance of the regular measurement of the blood pressure and the MAP values was emphasized by other authors, too. Walsh AC. and Baxi VL. (2008), find out that values of DBP over 75 mmHg, have limited predictive importance for pre-eclampsia, also the MAP values in the second quarter are better predictor in relation to PE, as well as DBP and even more on SBP [22].

After childbirth, blood pressure between groups did not differ. This proves that the deliveries are only real cure for pre-eclampsia.

At the hypertensive pregnancies with an easier form of PE the hypertension was commencing in the period of 34,5±2,7 wg and it lasted in average of 4,8±2,6 weeks. With the pregnancies with severe forms, PE was commencing around 30,4±4,5wg and lasted in average of 8.0±4.3 weeks. Our results concluded the same facts that the hypertension that is manifested earlier and lasts longer, affects the level of unbalance.

With easier forms of PE, at the largest part of the pregnancies (92,5%) the defect was manifested after 31 wg, while at 7,46% the unbalance development happened in the period of 26-30 wg. At the severe forms at 18,2% pregnancies the unbalance was developed before 25 wg, at 24,2% in the period of 26-30 wg, and in 57,6% after 31 wg.

Early diagnosis of PE has important implication for the management and prognosis of both the mother and the fetus. It depends on the accurate measurement of BP, as hypertension is often the only early sign of impending PE. It is not, however, necessarily indicative of PE or indeed eclampsia [21] .

Based on all that we can conclude that measuring the BP from the beginning of the pregnancy and knowing the values of the artery pressure before the conception, we can divide a group of pregnancies that are below the risk of PE. In the period within 20 w.g. the values of MAP over 85-90mmHg and values of DBP over 75mmHg are important predictive indicator for determination the risk of hypertensive disorders in pregnancy, especially PE [23]. To reduce the level of prenatal morbidity and mortality in PE, it's necessary to insist on regular and organized control for every pregnancy, because it is proven that with better antenatal protection, we can influence prenatal morbidity and mortality [24, 25]. Screening for preeclampsia with blood pressure measurement is recommended for all pregnant women at the first prenatal visit and periodically throughout the remainder of pregnancy.

The optimal frequency for measuring blood pressure in pregnant women has not been determined and is left to clinical discretion it is most efficient to measure blood pressure on women who are being seen by their clinicians for other reasons. The collection of meaningful blood pressure data requires consistent use of correct technique and a cuff of appropriate size [26].

Future research should concentrate on the development of algorithms that combine biochemical and biophysical markers, including blood pressure measurement – a diagnostic process used in clinical care. These may help improve the predictive accuracy of the tests to clinically important values [8, 24, 26].

An integrated first hospital visit at first trimester combining data from maternal characteristics and history and maternal blood pressure measurement can define the patient at risk for PE [24, 25].

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