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Value of Several Risk Factors for Predicting Gestational Hypertension

Gestational hypertension is the most common cause of maternal morbidity, fetal morbidity and mortality worldwide, so it is important to predict this complication of pregnancy. The purpose of the study was to evaluate the value of several risk factors in predicting gestational hypertension. The study involved a total of 200 pregnant women, 59 of whom were diagnosed with preeclampsia and 60 women with gestational induced hypertension (PIH) who were compared with a control group of 80 normotensive pregnant women, adjusted for gestational age 24-34 weeks of pregnancy. A prospective Case-Control study was undertaken in the Obstetrics and Gynecology Clinic at the University Clinical Center of Kosovo. Pregnant women with a family history of preeclampsia have 18 times a significantly greater chance of developing gestation hypertension than pregnant women without family history of preeclampsia (OR-18.7320, 95.0%, CI 2.475-141.778, $p < 0.05$ (Pearson Chi-square 14.5912, $p=0.0001330$). The age less than 30y were protective than pregnant women with more of 30y of developing gestation hypertension (95.0%, CI 0.002-0.091, $p < 0.05$ (Fisher exact, 2 tailed $p=0.000000$). A statistically significant association between gestational hypertensions and with partner less/more than a year coexistence and was register for $p < 0.05$ (Fisher exact, 2 tailed $p=0.001924$). A statistically significant association between multiparity and gestational hypertensions was register for $p < 0.05$ (Fisher exact, 2 tailed $p=0.000000$). In conclusion, the results of numerous analyzes in this study revealed that the following patient characteristics are predictive factors for gestational hypertension: family history of preeclampsia, previous history of preeclampsia, which are characteristics of patients at risk for gestational hypertension and older less than 30 which is a protective feature.

Keywords: gestational hypertension, pregnancy, risk factors, pregnancy induced hypertension (PIH), preeclampsia (PE)

Introduction

Gestational hypertension is the most common cause of maternal morbidity, fetal morbidity and mortality worldwide [1]. The study of normal and complicated pregnancies with preeclampsia provides important and useful information to find a potential predictor of preeclampsia. Identification of this clinical entity and effective management play an important role in the outcome of pregnancy for both mother and child. In developing countries, in a pregnancy with insufficient care, this entity persists and many cases remain undisclosed until major complications prevail [6]. Predictor identification will help ensure closer case surveillance and reduce the negative consequences of hypertensive disorders in pregnancy.

Hypertensive disorder in pregnancy respectively is not a totally preventable disease. However, some patient characteristics present specific “high risk” factors leading to gestational hypertension be identified in an individual. Not all studies reported the same risk, but a way of categorizing different risk factors is presented:

- # Primipara: Young or old (first exposure to choral villas)
- # New partnership (<1 year of marriage or cohabitation with the designated partner)
- # Family history: hypertension, preeclampsia as a mother, sister
- # Obesity: $BMI > 35 \text{ kg/m}^2$
- # Preeclampsia in previous births
- # Maternal age <20 or > 35, etc.
- # Multiple pregnancy
- # Pre-existing diseases (*chronic hypertension, renal disease, pre-gestational diabetes, SLE*) [1, 6, 7].

One the most important risk factors is the presence of preeclampsia in a previous pregnancy. The recurrence rate of preeclampsia varies from study to study, but a recurrence rate of over 65% has been described [8]. The incidence of preeclampsia in hospital practice varies widely from 5% to 15%. The incidence in primipara is about 10% and in multipara 5% [6].

Young and nulliparous women are particularly vulnerable to developing preeclampsia, whereas older women are at greater risk for chronic hypertension with superimposed preeclampsia. In several worldwide studies reviewed by Staff and coworkers (2014), the incidence of preeclampsia in nulliparous populations ranged from 3 to 10 percent [2].

There are several other risk factors associated with preeclampsia.

The relationship between maternal weight and the risk of preeclampsia is progressive. It increases from 4.3 percent for women with a body mass index ($BMI < 20 \text{ kg/m}^2$) to 13.3 percent in those with a $BMI > 35 \text{ kg/m}^2$ [1].

Women with preeclampsia in the first pregnancy are at greater risk in a second pregnancy compared with women normotensive during their first pregnancy [4].

Prevention of preeclampsia would make a major contribution to obstetrics. Prevention is classified into primary, secondary and tertiary, where:

- Primary prevention includes avoiding the occurrence of illness.
- Secondary prevention is the interruption of disease progression before the appearance of clinical signs.
- Tertiary prevention is the prevention of complications through treatment [9].

Secondary prevention should focus on identifying women at high risk for preeclampsia, then carry out a medical intervention so that the disease does not occur or delay its onset [9].

For this reason we decided to investigate some of the characteristics of patients and their role in predicting gestational hypertension, in order to intervention in time with adequate treatment before the disease becomes serious.

Materials and Methods

This prospective Case-Control study was undertaken in the Obstetrics and Gynecology Clinic at the University Clinical Center of Kosovo. A total of 200 pregnant women who received medical service in our hospital between October 2018 and June 2019 were enrolled into this study. The study involved a total of 200 pregnant women, 59 of whom were diagnosed with preeclampsia and 60 women with gestational induced hypertension (PIH) who were compared with a control group of 80 normotensive pregnant women, adjusted for gestational age 24-34 weeks of pregnancy. All patients provided a signed informed consent before the investigation.

Inclusion Criteria

The study population will be divided into three groups:

Group I: normotensive pregnancies

Group II: include patients with Pregnancy Induced Hypertension and

Group III: Include patients with preeclampsia

Case group: both groups with PE and PIH between 24-34 weeks of pregnancy together form the case group. This group will exclude multiple pregnancies, IVF pregnancies and other ART methods.

Control group: This will include normotensive pregnant women between 24-34 weeks of gestation, without any of the risk factors for preeclampsia such as: primipara, preeclampsia in previous births, multiple pregnancy, family history of preeclampsia as mothers, sisters, cohabitation with partner less than

a year, BMI>35, family history of preeclampsia, who are using any anti-eclampsia drug hypertensive or on any diuretic.

Both groups will exclude patients with hypertension before pregnancy, patients with diabetes and other endocrine diseases, with history suggesting thrombophilia or coagulopathy, urinary tract infection, patients with renal disease and other chronic diseases.

All women were clinically evaluated at the time of booking to exclude the exclusion criteria and would then undergo routine clinical examination such as: history (name, surname, age, BMI, number of births, number of abortions, duration of cohabitation with partner, previous history of preeclampsia, family history of preeclampsia, history of other illnesses). General examination: edema (especially in the face and upper extremities) nausea, vomiting, headache, visual disturbances, right upper quadrant pain, convulsions. Arterial blood pressure (mmHg) is measured and monitored. All of these women have been followed up until birth. At each visit, they will be evaluated for the history of symptoms of preeclampsia and adjacent eclampsia such as edema, vomiting, epigastric pain, decreased urine output, and visual disturbances.

Statistical Analysis

Statistical programs Stat Soft STATISTICA 10.0; SPSS 20.0 were used for the statistical analysis; collected data was processed using the following statistical methods:

- Database was formed by using specific computer software and was processed by using standard descriptive and analytical methods.
- Attribute statistical data were analyzed by determination of rates and percentages and statistical significance between detected differences – Difference test.
- In numerical series with two variables, the significance of the difference is tested by t-Test.
- Pearson chi-squared test was used to determine the associative relations and Fisher exact, 2 tailed test.
- Receiver operating characteristic (ROC), or ROC-curve was used for analysis.
- Univariate Logistic Analysis and Multiple regression analysis was used to determine the relationship between the dependent-criterion variable and the system of predictor variables of interest.
- Correlational relations were performed using Pearson's correlation coefficient (r).
- For CI (confidence interval \pm 95% CI) was defined statistical significance at level of standard error less than 0.05 (p).

The results are shown in the following tables.

Results

The study population will be divided into three groups:

Group I: normotensive pregnancies.

Group II: include patients with pregnancy induced hypertension and

Group III: include patients with preeclampsia

Table 1. *Distribution of the Patients According to Which Groups they Belong to*

groups	Count	Percent
I - normotensive	80	40.0
II - PIH syndrome	61	30.5
III - preeclampsia	59	29.5
total	200	100.0

All patients in the group I: are in the age group between 20-30y. In the group II: 45.9% of patients belong to the age group 20-30, 49.2% are in 31-40y group and 4.9% are in the age group over 41y. In the group III: 52.5% of patients belong to the age group 20-30y, 42.4% are in 31-40y group and 5.1% are in the age group over 41y (Table 2). The percent between age groups between I and III groups are no significant for $p > 0.05$.

Table 2. *Distribution of the Patients According Age Groups*

I		
age	Count	Percent
20-30	80	100.0
II		
20-30	28	45.9
31-40	30	49.2
>=41	3	4.9
III		
20-30	31	52.5
31-40	25	42.4
>=41	3	5.1

13.7% of the patients in the first group were obesity, much more were register 31.1% of the patients in II group and 32.2% of the III group which were obesity too. The percentage difference of obesity which were register between I group versus II and III groups are statistical significant for $p < 0.05$ (Difference test, $p = 0.0123$; $p = 0.0087$), other percentage differences are not significant (Table 3).

Table 3. *Distribution of the Patients According BMI*

BMI / I group	Count	Percent
underweight <18.5	0	
normal 18.5-24.9	5	6.3
overweight 25-29.9	64	80.0
Obesity > 30 or greater	11	13.7
BMI / II group		
underweight <18.5	0	
normal 18.5-24.9	0	
overweight 25-29.9	42	68.9
Obesity > 30 or greater	19	31.1
BMI / III group		
underweight <18.5	0	
normal 18.5-24.9	0	
overweight 25-29.9	40	67.8
Obesity > 30 or greater	19	32.2

All of the patients according cohabitation with partner, in the first and second group were more than a year, in the third group were 78.0% more than a year and 22.0% less than a year (Table 4).

Table 4. *Distribution of the Patients According Cohabitation with Partner Less than a Year*

I group	Count	Percent
>1	80	100.0
II group		
>1	61	100.0
III group		
>1	46	78.0
<1	13	22.0

All of the patients in the first group were multipara. In the second group were 78.7% multipara and 21.3% primipara. In the third group were 54.2% multipara and 45.8% primipara (Table 5). The difference between second versus third groups are statistical significant for $p < 0.05$.

Table 5. Distribution of the Patients According Parity

I group	Count	Percent
multipara	80	100.0
II group		
multipara	48	78.7
primipara	13	21.3
III group		
multipara	32	54.2
primipara	27	45.8

77.5% of the patients in the first group have not abortions, in the second group 63.9% and in the third group were 74.6% (Table 6). The difference between the groups are not statistical not significant for $p > 0.05$

Table 6. Distribution of the Patients According Number of Abortions

number of abortions	Count	Percent
I group		
no	62	77.5
1	14	17.5
2	4	5.0
II group		
no	39	63.9
1	13	21.3
2	7	11.5
3	1	1.6
4	1	1.6
III group		
no	44	74.6
1	12	20.3
2	1	1.7
3	2	3.4

No pregnant women in the normotensive group had preeclampsia in previous pregnancies. 29.5% of the patients from II group and 28.8% of the III had previous birth preeclampsia (Table 7).

Table 7. *Distribution of the Patients According Previous Birth Preeclampsia*

I group	Count	Percent
no	80	100.0
II group		
no	43	70.5
yes	18	29.5
III group		
no	42	71.2
yes	17	28.8

100.0% in the first group, 80.3% in the second group and 81.3% in the third group of the patients had no family history for preeclampsia. Family history for preeclampsia had in the second (19.6%) and third group (18.7%) (Table 8). Ten patients (16.4%) from second group had family history for preeclampsia-mother was with preeclampsia, in one (1.6%) patients was register that sister was with preeclampsia and in one (1.6%) patients was register that sister and mother were with preeclampsia. During the study 9 (15.3%) patients from third group had family history for preeclampsia- mother was with preeclampsia, and in 2 (3.4%) patients was register that sister and mother were with preeclampsia.

Table 8. *Distribution of the Patients According Family History for Preeclampsia*

I group	Count	Percent
no	80	100.0
II group		
mother was with preeclampsia	10	16.4
sister was with preeclampsia	1	1.6
mother and sister was with preeclampsia	1	1.6
no	49	80.3
III group		
mother was with preeclampsia	9	15.3
mother and sister was with preeclampsia	2	3.4
no	48	81.3

By univariate analysis, the single statistically significant predictors of gestation hypertension of some characteristics of patients are family history of preeclampsia, previous history of preeclampsia, BMI over 30, and ageless of 30y are not risk (protective) for gestational hypertension (Table 9). Pregnant women with a BMI>30 have three times a significantly greater chance of developing gestation hypertension than pregnant women with a BMI<30 (95.0% CI 1.382-6.114) (Table 9). The age less than 30y were protective than pregnant

women with more of 30y of developing gestation hypertension (95.0% CI 0.002-0.091) (Table 9). Pregnant women with a previous preeclampsia have 16 times a significantly greater chance of developing gestation hypertension than pregnant women without previous preeclampsia (95.0% CI 3.738-68.991) (Table 9). Pregnant women with a family history of preeclampsia have 18 times a significantly greater chance of developing gestation hypertension than pregnant women without family history of preeclampsia (95.0% CI 2.475-141.778) (Table 9).

Table 9. Univariate Logistic Analysis View for Some Characteristics of Patients in Prediction of Gestation Hypertension

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)		
							Lower	Upper	
Step 1	bmi>30	1.067	.379	7.912	1	0.005	2.907	1.382	6.114
	Constant	-1.240	.342	13.110	1	0.000	0.289		

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)		
							Lower	Upper	
Step 1	age<30y	-4.403	1.023	18.532	1	0.000	0.012	0.002	0.091
	Constant	0.292	0.172	2.878	1	0.090	1.339		

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)		
							Lower	Upper	
partner cox.	-20.912	11147.611	0.000	1	0.999	0.000	0.000		
	Constant	20.621	11147.611	0.000	1	0.999	903052256.745		

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)		
							Lower	Upper	
Step	multiparity	-21.203	6355.067	0.000	1	0.997	0.000	0.000	
	Constant	0.000	0.158	0.000	1	1.000	1.000		

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)		
							Lower	Upper	
Step	previous preeclampsia	2.776	0.744	13.934	1	0.000	16.059		
	Constant	-2.862	0.727	15.499	1	0.000	0.057		

Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)		
							Lower	Upper	
Step	family preeclampsia	2.930	1.033	8.051	1	0.005	18.732		
	Constant	-3.135	1.022	9.422	1	0.002	0.043		

Multivariate logistic analysis includes predictors that are significant with the univariate method and with which we evaluate gestational hypertension. Multiple analysis confirmed previous preeclampsia, family history of

preeclampsia are predictors of gestational hypertension and protective age less than 30y (tab 10). No association was observed between abortions (have or and no) and gestational hypertensions for $p > 0.05$ (Pearson Chi-square 1.6719, $p=0.196005$).

A statistically significant association between age (less and over 30y) and gestational hypertensions was register for $p < 0.05$ (Fisher exact, 2 tailed $p=0.000000$).

A statistically significant association between BMI(less and over 30) and gestational hypertensions was register for $p < 0.05$ (Pearson Chi-square 8.3300, $p=0.003899$).

BMI over 30 increases the chance of gestational hypertensions by three times (OR-2.9069 (1.38209-6.1142)). A statistically significant association between with partner less/more than a year and gestational hypertensions was register for $p < 0.05$ (Fisher exact, 2 tailed $p=0.001924$).

A statistically significant association between multiparty and gestational hypertensions was register for $p < 0.05$ (Fisher exact, 2 tailed $p=0.000000$).

A statistically significant association between previous preeclampsia and gestational hypertensions was register for $p < 0.05$ (Pearson Chi-square 22.6386, $p=0.000000$).

The previous preeclampsia increases the chance of gestational hypertensions by 16 times (OR-16.0588 (3.7379-68.9926)).

A statistically significant association between family history of preeclampsia and gestational hypertensions was register for $p < 0.05$ (Pearson Chi-square 14.5912, $p=0.0001330$).

The family history of preeclampsia increases the chance of gestational hypertensions by 18 times OR-18.7320 (2.4748-141.7834).

Table 10. Multivariate Logistic Analysis View Patients in Prediction of Gestation Hypertension

		Variables in the Equation							
		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1 ^a	Previous preeclampsia	1.934	0.808	5.737	1	0.017	6.919	1.421	33.687
	bmi>30	0.577	0.467	1.526	1	0.217	1.780	0.713	4.443
	age<30	-3.892	1.034	14.181	1	0.000	0.020	0.003	0.155
	family preeclampsia	2.487	1.083	5.274	1	0.022	12.019	1.440	100.348
	Constant	-4.325	1.354	10.203	1	0.001	0.013		

Multiple analysis confirmed previous preeclampsia, family history of preeclampsia are predictors of gestational hypertension and protective age less than 30y (Table 10).

Discussion

Gestational hypertension is the most common cause of maternal morbidity, fetal morbidity and mortality worldwide, so it is important to predict this complication of pregnancy [1]. Preeclampsia is a vasospasm. The fundamental pathophysiological changes involve systemic arteriolar spasm, loss of function of endothelial cells, and systemic target organ damage as well as different clinical signs due to blood flow decreased [10, 11, 12]. Although the etiology and pathogenesis are unclear yet, it is generally deemed that as an idiopathic systemic disease in duration of pregnancy, although preeclampsia has been generally believed that multiple factors are jointly involved in its pathogenesis. Epidemiological studies have increased the people's understanding of the risk factors for preeclampsia. Primipara (young or old, first exposure to choral villas), new partnership (<1 year of marriage or cohabitation with the designated partner), family history (hypertension, preeclampsia as a mother, sister), obesity (BMI>35 kg/m²), preeclampsia in previous births, maternal age <20 or >30 have been considered to be high risk factors for preeclampsia. One of the most important risk factors is the presence of preeclampsia in a previous pregnancy. The recurrence rate of preeclampsia varies from study to study, but a recurrence rate of over 65% has been described [8]. The incidence of preeclampsia in hospital practice varies widely from 5% to 15%. The incidence in primipara is about 10% and in multipara 5% [6]. In some certain populations, the incidence can be triple increased. In this study pregnant women with history of previous preeclampsia have 16 times a significantly greater chance of developing gestation hypertension than pregnant women without previous preeclampsia. The OR value was 16.0588, 95.0%, CI 3.738-68.991, p<0.05) for pregnant women with history of previous preeclampsia. Women whose mothers had a history of hypertension (p=0.003), preeclampsia (p=0.007) or eclampsia (p=0.038) were at increased risk of severe preeclampsia. The risk of preeclampsia was greater when the woman had a sister with a history of hypertension (OR 2.60, 95% CI 1.60-4.21, p<0.001), preeclampsia (OR 2.33, 95% CI 1.58-3.45, p<0.001), or eclampsia (OR 2.57, 95% CI 1.28-5.16, p=0.008). The risk of preeclampsia was also higher for women who had both a mother and sister with a history of hypertension (OR 3.65, 95% CI 1.65-8.09, p=0.001) [13]. In this study family history of preeclampsia increases the chance of gestational hypertension by 18 times (OR-18.7320, 95.0% CI 2.4748-141.7834, p <0.05). The relationship between maternal weight and the risk of preeclampsia is progressive. It increases from 4.3 percent for women with a body mass index (BMI) < 20 kg/m² to 13.3 percent in those with a BMI>35 kg/m² [1]. Obese women had a mild increased risk of preeclampsia (OR=1.81; 0.73-4.52); women in the other BMI categories had risks similar to that of normal BMI subjects. In contrast, risk of transient hypertension was substantially decreased among underweight women (OR=0.35; 0.14-0.87) and substantially increased among obese women (OR=3.43; 2.27-5.21). Higher than expected gestational weight gain did not increase the risk of preeclampsia. In contrast, risk of transient hypertension was

increased over twofold among women in the highest quartile of the weight gain index (OR=2.55; 1.66–3.92) [3]. In this study, pregnant women with a BMI>30 increases the chance of gestational hypertensions by three times (OR=2.9069, 95.0% CI 1.382-6.114, $p<0.05$). The age less than 30y were protective than pregnant women with more of 30y of developing gestation hypertension ((95.0% CI 0.002-0.091, $p<0.05$ (Fisher exact, 2 tailed $p=0.000000$)).

In this study, after these risk factors were analyzed by univariate analysis, was conducted and revealed that the single statistically significant predictors of gestational hypertension are: family history of preeclampsia, previous history of preeclampsia and ageless of 30y are not risk (protective) for gestational hypertension. Multiple analysis confirmed previous preeclampsia, family history of preeclampsia, BMI over 30 are predictors of gestational hypertension and protective age less than 30y. No association was observed between abortions (have or and no) and gestational hypertensions for $p>0.05$ (Pearson Chi-square 1.6719, $p=0.196005$). The incidence of preeclampsia in hospital practice varies widely from 5% to 15%. The incidence in primipara is about 10% and in multipara 5% [6]. Young and nulliparous women are particularly vulnerable to developing preeclampsia, whereas older women are at greater risk for chronic hypertension with superimposed preeclampsia. In several worldwide studies reviewed by Staff and coworkers (2014), the incidence of preeclampsia in nulliparous populations ranged from 3 to 10 percent [2]. Women with preeclampsia in the first pregnancy are at greater risk in a second pregnancy compared with women normotensive during their first pregnancy (McDonald, 2009) [4]. PIH was more frequent in nulliparous than multiparous women (relative risk [95% confidence interval], 1.30 [1.24 to 1.37]) and increased linearly with advancing maternal age after 35 years and also with increasing pre-pregnancy BMI [5]. In this study, a statistically significant association between multiparity and gestational hypertensions was register for $p<0.05$ (Fisher exact, 2 tailed $p=0.000000$).

As well in this study a statistically significant association between age (less and over 30y) and gestational hypertensions was register for $p<0.05$ (Fisher exact, 2 tailed $p=0.000000$) between gestational hypertensions and with partner less/more than a year cohabitation was register for $p<0.05$ (Fisher exact , 2 tailed $p=0.001924$).

Conclusion

In conclusion, the results of numerous analyzes in this study revealed that the following patient characteristics are predictive factors for gestational hypertension: family history of preeclampsia, previous history of preeclampsia, which are characteristics of patients at risk for gestational hypertension and older less than 30 which is a protective feature.

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