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ORIGINAL PAPER

Comparison of Hemodynamic and Biochemical Factors and Pregnancy Complications in Women with/without Preeclampsia

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ABSTRACT

Background: *Preeclampsia is the second most common cause of maternal mortality in the world after hemorrhage. The present study was conducted to compare the hemodynamic and biochemical levels and pregnancy complications in women with preeclampsia and normal blood pressure.*

Methods: *This cross-sectional descriptive study was conducted on two groups of healthy mothers and mothers with preeclampsia. The research sample included 147 people selected among all mothers referred to Kamali Educational and Medical Center of Alborz. The relationship of preeclampsia and its severity with indices such as age, maternal and fetal weight, body mass index, Apgar score, liver enzymes, laboratory indices, Doppler ultrasound, economic status and other hemodynamic and biochemical indices was examined.*

Results: *The mean age of patients with normal blood pressure and preeclampsia was 29.2 and 29.9 years, respectively. In the control group, no history of hospitalization in an intensive care unit (ICU) was reported, while in the case group, 28% of mothers were admitted to ICU. In the control group, 93% of the fetal middle cerebral arterial (MCA) index, 95% of UA index, 93% of SD index and 95% of CPR index were normal, while in the case group, 67% of MCA index, 65% of the umbilical arterial (UA) index, 70% of SD index and 36% of CPR index were normal. The mean uric acid was about 32% higher in the case group than the control group. The mean neonatal weight was about 20% higher in mothers with normal blood pressure (2836 g in the control group and 2345 g in the case group). In the multivariate logistic regression,*

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platelet (OR=1, P=.018), pulse rate of mother (OR=1.198, P=.044), uric acid (OR=2.057, P<.001) and LDH (OR=1.006, P=.015) were significant predictors of preeclampsia.

Conclusion: *By examining the indices at different ages of pregnancy, the occurrence of preeclampsia can be predicted at the appropriate time and its complications for both the mother and fetus can be thus prevented. Platelet, pulse rate of the mother, uric acid and LDH were significant predictors of preeclampsia, of which just uric acid was a strong predictor, with odds ratio (OR)=2.057 – for example, for one unit increase in uric acid, the odds of preeclampsia increase by about two times. Preeclampsia may cause low birth weight as well.*

Keywords: hemodynamic factors, blood pressure, uric acid, Doppler ultrasound, preeclampsia, pregnancy.

Abbreviations

PTT: partial thromboplastin time
PT: prothrombin time
Plt: platelet
BMI: body mass index
CT: computed tomography
PR: pulse rate
BP: blood pressure
LDH: lactate dehydrogenase
CPR: cerebroplacental ratio
S/D: systolic-diastolic
UA: umbilical arterial
MCA: fetal middle cerebral arterial
OR: odds ratio

INTRODUCTION

Globally, preeclampsia is the second most common cause of maternal mortality after hemorrhage and it accounts for 14% of maternal mortality worldwide. This disorder is specific to pregnancy and is diagnosed in women with hypertension and new proteinuria after the 20th week of pregnancy. Almost 10% of pregnancies around the world are affected by preeclampsia (1). Mothers with hypertension have a life-threatening factor and need to be hospitalized and monitored, because they have a greater risk for preterm delivery. In addition to the risks of pregnancy and motherhood hypertension, women with a history of hypertension are more susceptible to future cardiovascular disease (2). Diagnostic features of this disorder are blood pressure above 90/140 with proteinuria after 20 weeks of pregnancy. The majority of pregnant women with gestational hypertension have previous hemodynamic problems that are associated with or without difficulty in circulating the angiogenetic protein that regulates vascular function in early pregnancies (4). Hypertension occurs at different times during pregnancy, either alone or in combination with preeclampsia (5). The fetus may be affected by growth restriction and the mother may have some form of placental dysfunction, metabolic syndrome, or a family history of cardiovascular diseases. The effect of maternal and fetal history on hypertension is crucial and the diagnosis of these risks is one of the most important priorities of studies (6). Increased uric acid level is generally the beginning of increased blood pressure and proteinuria (7). Maternal complications of preeclampsia include eclampsia, premature placental abruption, and hematologic disorders that damage vital organs. Low birth weight, hypoxia, intrauterine death, and premature birth leading to premature birth are some of the fetal complications. Although the definitive treatment for preeclampsia is termination of pregnancy, careful prenatal care and appropriate treatment can improve the condition. In many cases, the result is satisfactory for both the mother and fetus (8). Therefore, conducting studies to identify people prone to the disease and early diagnosis of preeclampsia is a necessary step to reduce complications of the disease. Thus, the present study was an attempt to compare hemodynamic and chemical factors in women with normal blood pressure and hypertension during pregnancy. ❑

METHODS AND MATERIALS

The present cross-sectional descriptive study was conducted on two groups of healthy mothers and mothers with preeclampsia. The research sample included 147 persons selected among all mothers who were referred to Kamali Educational and Medical Center of Alborz. The relationship of preeclampsia and its severity with

indices such as age, maternal and fetal weight, body mass index, Apgar score, liver enzymes, laboratory indices, Doppler ultrasound, economic status and other hemodynamic and biochemical indices was examined. In coordination with the High-Risk Pregnancy and Emergency Ward of Kamali Hospital, two groups of mothers with preeclampsia and normal blood pressure were included in the study after obtaining their informed consent. Sampling was done using a convenience sampling method. A healthy group of mothers referred to the hospital emergency ward was selected and the group of mothers with preeclampsia referred to the high-risk pregnancy ward of the hospital was selected. Blood samples collected from a vein and uric acid, total protein, urea and creatinine, liver enzymes, red blood cell count were examined by Kamali Hospital laboratory. Blood samples were measured in special containers and after incubation at 37 °C for 30 minutes, the clot was removed, the remaining sample was centrifuged for 10 to 20 minutes and samples were measured in a dry and cool environment. Blood pressure and heart rate were measured after 15 minutes of rest under adequate temperature and humidity conditions and uterine artery pulsation was measured by Doppler ultrasound. Body mass index (BMI) before pregnancy was measured using maternal records.

Statistical issue

Mean and standard deviation (SD) were used to analyze the quantitative variables. Frequency and parentage were reported for qualitative variables. Additionally, independent t-test, chi-square and logistic regression were used to analyze the qualitative variables in SPSS 22. In all statistical analyses, a significance level of 0.05 will be considered.

Ethical issue

The present study was approved by the ethical committee of Avicenna Research Institute, Tehran, Iran (IR.ABZUMS.REC.1400.032). Written informed consent was obtained from all participants. ❑

RESULTS

Table 1 shows the demographic data of mothers in case and control groups based on age, BMI, neonatal weight, platelet count, uric acid, creatinine, PTT, white blood cells, SGOT and Systolic BP. The mean age of patients with normal blood pressure and preeclampsia was 29.2 and 29.9 years, respectively. In the control group, no history of ICU hospitalization was reported and in the case group, 28% of mothers were admitted to ICU. In the case of neonatal hospitalization at the NICU, only one case was reported in the control group. In the case group, 14 neonates (18%) were hospitalized in neonatal ICU (NICU). Among the Doppler ultrasound indices, four MCA, UA, SD and CPR indices were examined. There was a significant difference between the groups in all assessed indices. In the control group, 93% of MCA index, 95% of UA index, 93% of SD index and 95% of CPR index were normal, while in the case group, 67% of MCA index, 65% of UA index, 70% of SD index and 36% of CPR index were normal. In the postpartum hemorrhage or PPH index, only 1% of hemorrhage was reported in the control group, while in the case group, about 8% of mothers had hemorrhage. Regarding the number of abortions, the control and case groups were close to each other, with 15% and 19% of each, respectively reporting an abortion history. In the index of pregnancy of more than three cases, the two control case groups showed about 11.5% and 14% of the total sample members. In the control group, 28 cases included 36% of deliveries by cesarean section, while for the case group, this number was 49, accounting for 70% of deliveries. The mean systolic blood pressure was 109 mm Hg in the control group and 153 mm Hg in the case group, while diastolic blood pressure was 71 mm Hg and 95 mm Hg in each of the two groups. The mean value for white and red blood cell counts was very close in the case and control groups. The mean creatinine was about 7% higher in the case group than the control one. The value of urinary protein of mothers in the case group was about twice that of mothers in the control group. The mean uric acid was about 32% higher in mothers included in the case group than control subjects. The mean platelet count (PLT) was about 10% higher in mothers from the control group than those with preeclampsia. The mean neonatal weight is about 20% higher in mothers with normal blood pressure (2836 g in the control group and 2345 g in the case group). All assessed variable were statis-

tically different between the case and control groups except age and WBC (p>0.05) (Table 1).

In Table 2, all delivery-related data are presented and maternal hospitalization in ICU, neonatal hospitalization in NICU, MCA ultrasound, UA ultrasound, S/D ultrasound, and CPR were statistically different in case and control groups (P<0.001). Details of this table are presented below.

Delivery type

Cesarean section accounts for 70% of all deliveries in women with preeclampsia and in about 36% of those with normal blood pressure. Therefore, it can be concluded that preeclampsia may lead to a change in the type of delivery, which is also indicated by the p-value of 0.000.

Pregnancy

To group the data regarding the number of pregnancies, mothers who had three or more pregnancies were divided into one group and those who had less than three pregnancies into another group. As shown in Table 3, 15% of mothers who had more than three pregnancies in the case and control groups did not differ significantly; thus, considering a p-value of 0.632, it can be concluded that this variable does not play a determining role for our research.

TABLE 1. Mothers' demographic data

Variable		Mean	Standard deviation	P value
Age (year)	Control	29.2	6.1	0.514
	Case	29.9	6.8	
Body mass index	Control	25.26	4.5	<0.001
	Case	28.6	6.2	
Neonatal weight (g)	Control	2836	614	<0.001
	Case	2345	895	
Platelet count	Control	226794	225000	0.027
	Case	205179	202000	
Uric acid	Control	4.74	4,47	<0.001
	Case	6.29	6.14	
Creatinine	Control	.69	.70	0.032
	Case	.75	.70	
PTT	Control	25.68	25	0.035
	Case	26.25	25	
White blood cells	Control	11330	11700	0.311
	Case	11069	10900	
SGOT	Control	18.50	14	<0.001
	Case	28.07	20	
Systolic blood pressure	Control	109	110	<0.001
	Case	153.5	150	

Number of children

There were no significant differences in terms of number of pregnancies between the control and case groups, and considering the p-value of 0.630, it can be concluded that the parameter represented by the number of children does not play a determining role in creating a difference between the two groups of mothers.

Number of abortions

Similarly to the number of children and that of pregnancies, the number of abortions in the two groups of mothers with preeclampsia and normal blood pressure, respectively is not significantly different and it is observed that more than 80% of subjects in the control and case groups have no history of abortion. The p-value of 0.525 also confirms this issue. Thus, the variable of number of abortions does not play a determining role in creating a difference between the two groups.

Age of pregnancy

Regarding gestational age, mothers were divided into two groups of 37 weeks and more and less than 37 weeks. Although the gestational age less than 37 weeks was higher in mothers with preeclampsia, accounting for 62% of cases, the difference was not large enough to direct the p-value to less than 0.05 and the value of 0.230 cannot guarantee the significance of the gestational age variable to differentiate between the control and case groups. Therefore, this is also among the non-significant variables.

Postpartum hemorrhage

Postpartum hemorrhage (PPH) is another factor that was predicted to be effective in differentiating between mothers with preeclampsia and those with normal blood pressure. Although the rate of hemorrhage was only in 7.7% of mothers in the case group, it is different from that found among mothers in the control group (1.3%); thus, p-value became close to the threshold of 0.05.

Therefore, this variable can also be determining in differentiating the control and case groups.

Hospitalization of mothers in ICU and neonates in NICU

Hospitalization of mothers in ICU and neonates in NICU are two parameters that show significant differences between the two study groups. According to data summarized in Table 2, 28.2% of mothers with postpartum preeclampsia are hospitalized in ICU, which is zero in mothers with normal blood pressure. Also, 17.9% of neonates with maternal preeclampsia were under intensive care after birth, while this value was 1.3 for neonates whose mothers had normal blood pressure. The p-value also was 0.000. Therefore, it can be concluded that maternal hospitalization in ICU and neonatal hospitalization in NICU after birth are two significant parameters that are able to show the difference between two groups.

Variable		Total number	Type	N	%	P-value
Delivery type	Control	78	Vaginal	50	1.64	<0.001
			Cesarean section	28	9.35	
	Case	70	Vaginal	21	30	
			Cesarean section	49	70	
Pregnancy	Control	78	Less than 3	69	5.88	0.632
			More than 3	9	5.11	
	Case	78	Less than 3	67	9.85	
			More than 3	11	1.14	
Having children	Control	78	Child	40	3.51	0.630
			No child	38	7.48	
	Case	78	Child	43	1.55	
			No child	35	9.44	
Abortion	Control	78	Yes	12	4.15	0.525
			No	66	6.84	
	Case	78	Yes	15	2.19	
			No	63	8.80	
Pregnancy age (week)	Control	73	Less than 37	38	1.52	0.301
			37 and more	35	9.47	
	Case	71	Less than 37	44	62	
			37 and more	27	38	
Postpartum hemorrhage	Control	78	Negative	77	7.98	0.058
			Positive	1	3.1	
	Case	78	Negative	72	3.92	
			Positive	6	7.7	
Maternal hospitalization in ICU	Control	78	Negative	78	100	<0.001
			Positive	0	0	
	Case	78	Negative	56	8.71	
			Positive	22	2.28	
Neonatal hospitalization in NICU	Control	78	Negative	77	7.98	<0.001
			Positive	1	3.1	
	Case	78	Negative	64	1.82	
			Positive	14	9.17	
MCA ultrasound	Control	78	Normal	73	93	<0.001
			Abnormal	5	7	
	Case	70	Normal	47	67	
			Abnormal	23	33	
UA ultrasound	Control	78	Normal	74	95	<0.001
			Abnormal	4	5	
	Case	78	Normal	45	65	
			Abnormal	24	35	
S/D ultrasound	Control	69	Normal	73	93	<0.001
			Abnormal	5	7	
	Case	69	Normal	48	70	
			Abnormal	21	30	
CPR	Control	78	Normal	74	95	<0.001
			Abnormal	4	5	
	Case	69	Normal	25	36	
			Abnormal	44	64	

TABLE 2. Delivery-related data in the two study groups

Variable	B	S.E.	Wald	P-value	Odds ratio (OR)	95% CI for OR	
						Lower	Upper
BMI	.082	.050	2.688	.101	1.085	.984	1.196
Plt	.000	.000	5.608	.018	1.000	1.000	1.000
SGOT	-.017	.016	1.171	.279	.983	.952	1.014
PR	.181	.090	4.046	.044	1.198	1.005	1.429
Cr	.872	1.880	.215	.643	2.392	.060	95.323
Uric acid	.721	.199	13.179	<.001	2.057	1.393	3.036
LDH	.006	.003	5.954	.015	1.006	1.001	1.012
PTT	.300	.173	3.017	.082	1.350	.962	1.894

TABLE 3.
Prediction of preeclampsia using multivariate logistic regression

Ultrasound

Table 3 shows normal Doppler values of the umbilical artery (UA), midbrain, uterus and CPR, which are within normal range based on the week of pregnancy. After classifying the data, chi-square statistical analysis was performed for the parameter of normality of MCA, UA and CPR values, and the following results were obtained. In MCA ultrasound and based on Table 3.93% of the normal value was reported in the control group and 67% of the normal value in the case group. As shown in Table 3, p-value was 0.000, which indicates the association of MCA with the occurrence of preeclampsia in both case and control groups. In UA ultrasound, MCA-like values also show differences between the control and case groups. Abnormal values in the case group are 30% higher than the control group. According to the initial hypothesis, chi-square test was performed and the p-value for this statistical test also showed a significant relationship between UA and the occurrence of preeclampsia. The same results were reported in the SD data as in the MCA and UA data and abnormal values were by about 23% higher in the case group. The p-value indicates the significant relationship between this variable and the grouping of patients with preeclampsia and mothers with normal blood pressure. Cerebroplacental ratio or CPR is one of the most important indices that have always been tested in articles related to preeclampsia. Based on Table 3, CPR values and collected data, chi-square test was performed and the following results were obtained: CPR was 95% normal in the control group and 36% normal in the case group, with about 64% of mothers having an abnormal CPR. As seen, the p-value was 0.000, which indicated a strong association between this index and occurrence of preeclampsia among study subjects.

According to Table 3, among all variables in the univariate logistic regression, BMI, Plt, SGOT, PR, Cr, uric acid, LDH and PTT were significant, but in the multivariate logistic regression, plt (OR=1, P=.018), pulse rate of mother (OR=1.198, P=.044), uric acid (OR=2.057, P<.001) and LDH (OR=1.006, P=.015) were significant predictors of preeclampsia, of which just the uric acid was a strong predictor, with odds ratio=2.057 – *i.e.*, for one unit increase in uric acid, the odds of developing preeclampsia increase by about two times. ❑

DISCUSSION

In this study, 41 hemodynamic and biochemical factors with quantitative and ordinal values were investigated. After performing independent Mann-Whitney t-test, chi-square and Fisher's exact test, 21 factors reported a p-value or significance of less than 0.05. Some indices, including Doppler ultrasound, uric acid, creatinine and type of delivery, played a determining role in the development of preeclampsia and some of them, such as white and red blood cells, hematocrit and hemoglobin, were not involved in differentiating the two groups of mothers with preeclampsia and normal blood pressure. Bainbridge and Robert discussed the pathogenic role of uric acid in preeclampsia. In their research, higher uric acid levels were reported as a marker for disease occurrence and no relationship was noticed between disease severity and this index; by

examining the p-value between controls and cases, they found that the level of uric acid in the two groups was significantly different (7).

Another article has reported an increased risk of preeclampsia in women with a high BMI, showing that by increasing the BMI by 5 to 7, the risk of preeclampsia doubles. Our research has also revealed that the mean BMI in case group subjects was three units higher than the controls and the p-value for this statistical test was 0.000, indicating a strong relationship between BMI and the occurrence of preeclampsia (9). Two other indices that were found to be strongly associated with preeclampsia were Apgar and neonatal weight, which were also examined in another study (10). In the current research, we investigated the weight of mothers who suffered from severe preeclampsia and found that 65% of them gave birth to premature babies, with Apgar scores varying between 7 and 10. The p-value was less than 0.05 for the mentioned indices in our research. In the present study, the p-value was 0.005 for Apgar score and <0.001 for neonatal weight, and these two indices were different between case and control groups.

Coagulation indices also play a determining role in predicting the difference between the two groups. However, the use of PT and PTT is very helpful in cases where the platelet count cannot diagnose preeclampsia accurately. Also, investigating these factors is very helpful in cases of severe and mild preeclampsia (11). In our research, the p-value was 0.027 for PLT and 0.035 for PTT, which indicated the important role of these two factors in predicting preeclampsia. However, for PT index, the p-value is 0.1, which shows that there is no significant difference between the two groups. Urinary protein and creatinine are two other indices that have been examined in various studies on the role of preeclampsia. In one study, the role of 24-hour urinary protein in the diagnosis of preeclampsia and the ratio of protein to creatinine were examined (12). In our statistical studies, we obtained less than 0.05, which confirmed the initial hypothesis.

Research has shown that systolic and diastolic blood pressure in the first trimester of pregnancy was a predictor of preeclampsia. After statistical analysis and p-value determination for these two indices, values of <0.001 and <0.001 were obtained (13), which indicated a significant difference in systolic and diastolic blood pressures between controls and cases. Regarding the qualitative indices, the initial hypotheses based on previous studies was confirmed. In some studies, it was observed that mothers with a history of preeclampsia used cesarean section 2.5 times more frequently than women with normal blood pressure, and mothers with severe preeclampsia used cesarean section 3.3 times more often than women with mild preeclampsia (14).

Thus, the type of delivery was one of the qualitative factors. After performing statistical tests, p-value <0.001 was reported for this index, which confirmed the initial hypotheses.

Postpartum hemorrhage or PPH is also involved in differentiating control and case groups according to the initial hypotheses. A study conducted on 315 085 women in Norway, over five years, reported different types of postpartum hemorrhage. In all types of severe and moderate hemorrhage, the p-value for the groups with normal blood pressure and preeclampsia was less than 0.01 and confirmed the determining role of postpartum hemorrhage (15). In our research, as mentioned before, postpartum hemorrhage in the case group was about 6.5% more frequently encountered than the control group and the p-value was about 0.05. According to our data set, this value can confirm the effect of this index on differentiating control and case groups.

The next indices that were analyzed included maternal hospitalization in ICU and neonatal hospitalization in NICU. In a previous study, neonatal NICU hospitalization rates in mothers with preeclampsia were examined. It was found that hospitalization in NICU was associated with factors such as Apgar score, gestational age, and neonatal birth weight (16). Due to the significant difference between two control and case groups in the frequency of hospitalizations, predicting the effectiveness of these indices is not a difficult task. After performing the statistical test, the p-value for both maternal and neonatal hospitalization indices was <0.001, which confirmed the initial hypotheses. The last indices that were examined in this study were those related to Doppler ultrasound. The PI pulse index should be used to assess uterine artery resistance in preeclampsia screening. As reported in most studies, the best indices for evaluating the systole to diastole ratio (SD) are the resistance index (RI) and pulse index (PI), which can be used to de-

scribe the arterial flow velocity waveform. The pulse index is the most commonly used index. To convert quantitative variables in relation to ultrasound data, we divided the values into normal and abnormal categories. To classify data, a reference table was used for normal Doppler values of umbilical artery, midbrain, uterus and CPR. In all MCA, UA and CPR indices, the p-value shows the value of <0.001, which is in accordance with the initial hypotheses and indicates the predictive effect of these indices on the incidence of preeclampsia and its severity. ❑

CONCLUSION

Paraclinical factors, including Plt, pulse rate of mother, uric acid and LDH, were significant predictors of preeclampsia, of which just uric acid was a strong predictor, with odds ratio=2.057 – *i.e.*, for one unit increase in uric acid, the odds of preeclampsia increase by about two times. The important point is that the explored indices become significant when they are together. For example, changing uric acid levels alone may not be determining alone. Thus, based on the different data sets and different underlying diseases of mothers, different subgroups of these indices should be selected to prevent its effects on mother and fetus by early diagnosis of preeclampsia. Preeclampsia may cause low birth weight as well. ❑

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