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Evaluation Of Some Common Risk Factors Associated With Preeclampsia Syndrome.

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ABSTRACT

Preeclampsia affects 3–8% of pregnancies and contributes to 20-80% of maternal-fetal mortality. It is necessary to identify risk factors associated with preeclampsia in order to predict and prevent it. This case-control study conducted in two groups of pregnant women (n=150 in each group). The target group defined according to diagnostic criteria of preeclampsia. The first criterion was systolic blood pressure ≥140mmHg and diastolic blood pressure ≥90mmHg after 20th week of gestation. The second criterion is excretion of 300mg protein in 24h urine or 30mg/dl of protein in random urine. The control group had healthy and alive child, and normal blood pressure. Then, the two groups compared in terms of maternal age, BMI and hemoglobin, gestational age, preeclampsia season and child weight at birth. Statistical analysis was performed using the T-test, Mann-Whitney test and the chi-square test. The maternal age, gestational age, maternal hemoglobin and maternal BMI were significantly associated with risk of preeclampsia (P≤0.0001), while the preeclampsia season did not reach the statistically significant in this regard (P=0.914). Since the current study did not fully overlapped with other studies, further investigations are required to fully understand the risk factors associated with preeclampsia syndrome.

Key words: Pregnancy, hypertension, preeclampsia, risk factors.

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INTRODUCTION

Hypertension is one of the most important clinical symptoms in pregnancy and preeclampsia is the most common clinical symptoms associated with this period that has been considered by the World Health Organization as one of the main problems of women's health [1]. Its prevalence in women, who are not pregnant, is about 3-7% and in women, who have been pregnant several times, is about 1-3% [2]. The incidence of preeclampsia is approximately 4-7% of pregnancies in Western countries [1] and in Iran is estimated approximately 3-7% [3-6]. According to various studies, about 20-80% angiogenesis and maternal and fetal deaths are associated with preeclampsia [7, 8].

The disease usually develops after the twentieth week of pregnancy, with an increase in blood pressure along with edema or *proteinuria* (or both) and more in the last months of pregnancy. Systolic blood pressure of ≥140mmHg and diastolic blood pressure of ≥90 mmHg associated with *proteinuria* of 300mmHg 24-*hour urine protein* or 30 mg/dl in a random urine sample after the twentieth week of pregnancy is defined as preeclampsia [9]. Various mechanisms have been discussed of the reason for the incidence of preeclampsia, including the lack of sufficient blood flow to the uterus, vascular wall injury, genetic factors and disorders of the immune system, but overall, the main cause of preeclampsia remains unknown that is why it is called as the *disease of theories* [10, 11].

Due to the high importance of this disease, many studies have been conducted on its risk factors, and factors such as genetic issues, race, some of coagulation disorders, lack of pregnancy, high age, chronic blood pressure, and twin or multiple pregnancies, and environmental factors like living in the heights and poverty are known as risk factors [12-15]. In some other studies, factors such as family history of preeclampsia [16], obesity, long distance with a previous pregnancy, and season of the disease have been identified as risk factors [17].

Given that several studies of the relationship between the mentioned factors with the disease have been conducted in the world, the purpose of this study was to investigate the relationship between factors such as pregnancy weeks, BMI, maternal hemoglobin, the season of pregnancy occurrence and the baby's weight with preeclampsia syndrome with the use of statistical modeling in order to use its results in the promotion of understanding, predicting and preventing the incidence of this disease in our country.

MATERIALS AND METHODS

This retrospective case-control study was performed in Imam Khomeini and Razi hospitals in Ahvaz during February 2013 to March 2014. One hundred and fifty women with preeclampsia were selected as a target group and 150 women, who had a history of at least one alive and healthy child and no history of high blood pressure during pregnancy as well as no history of chronic kidney disease, diabetes, autoimmune diseases and cardiovascular diseases, were considered as controls. Based on references 3 and 18, with a confidence interval of 95% and a power of 80% a sample size of 150 patients in each group (in total, 300 samples) was calculated [3, 18].

In this study the patient's medical records information was used and then, according to the gynecologist ‘s detection and the profile inserted in the file as well as a profile taken by a researcher, the target group was identified and based on this, exclusion criteria carefully were determined.

After stating the objectives and the nature of the research and obtaining the informed consent of the women admitted to the women's ward of Imam Khomeini and Razi hospitals, the questionnaire was completed by the researcher through interviews and a visit to the patients’ files. This questionnaire contained the information of file’s number; maternal age; gestational age at the time of entry into the study; the mother's weight; height; systolic and diastolic blood pressure; registration of protein excreted in the urine; the baby's weight at birth; the amount of hemoglobin in the beginning of pregnancy; occurrence season; pregnancy history; history of the blood pressure; family history of preeclampsia; recording the history of diseases such as cardiovascular diseases; diabetes; kidney dysfunction and *antiphospholipid antibody syndrome* (APS). Given that the majority of women were at the end of the age of pregnancy and the time of collecting the samples for the variable season of occurrence lasted for in 4 seasons and about 11 months, the baby's weight recorded in the file was considered in the calculations.

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The first criteria for diagnosis of the target group, was a diastolic blood pressure recorded of ≥90 mm Hg and a systolic blood pressure of ≥140 mm Hg from the start of the 20th week of pregnancy and the weeks after it (the blood pressure was measured at least two times and also for at least four to six hours apart from each other). In addition, *proteinuria* of 300mmHg 24-*hour urine protein* or with the concentration of 30mg/dl in a random urine sample (either +1 or + 2 on the dipstick) was second diagnostic criteria (this amount of protein was recorded in at least two random urine samples that were taken for 4 to 6 hours apart from each other). Each of the first and second criteria alone, were considered a sign of preeclampsia [9].

Due to the influence of some diseases and various factors that are associated with a preeclampsia syndrome [19], exclusion factors were: a history of chronic kidney disease before pregnancy, pre-pregnancy bleeding, diabetes mellitus, multiple pregnancies, smoking, history of preeclampsia, patients with autoimmune diseases, age over 35 and under 18 years.

Then, patients in the two groups were compared in terms of BMI, the week of pregnancy at the time of entry into the study, the rate of hemoglobin at the time of pregnancy, the season of preeclampsia occurrence and, the baby weight with each other.

Data collected were analyzed using SPSS version 21.00 and in order to check the results the t-test, Mann-Whitney and chi-square tests were used and a P-value of ≥0.05 was considered as significant.

RESULTS

Table 1: Sample number according to season of occurrence of preeclampsia

Season of Occurrence	Normal group	Preeclampsia group	Total
Spring	43	41	84
Autumn	33	38	71
Summer	36	36	72
Winter	38	35	73
Total number	150	150	300

Quantity of samples was obtained based on the season of preeclampsia occurrence as follows (table 1). To examine the relationship between the sample type and the season of preeclampsia occurrence the *Pearson's Correlation Coefficient* and *Chi-square test* were used. The results did not show a correlation between the sample type and the season of preeclampsia occurrence (P =0.914).

Table 2: Descriptive statistics for studied variables

Variables	Sample type	)N(	)Mean(	)Std. Error Mean(
Maternal age(year)	Normal	150	25.32	0.395
	Preeclampsia	150	28.46	0.351
Gestational age(weak)	Normal	150	36.52	0.084
	Preeclampsia	150	35.35	0.183
Child weight at birth(gr)	Normal	150	2934.8	30.412
	Preeclampsia	150	2586.6	34.895
Maternal hemoglobin(gr/dl)	Normal	150	11.714	0.080
	Preeclampsia	150	10.013	0.061
Maternal BMI(kg/m^2)	Normal	150	27.254	0.121
	Preeclampsia	150	30.074	0.161

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The results of the studied quantitative variables for the two groups obtained using the descriptive statistics are separately shown in table 2. According to the findings, mean age (± SD) in the patients with preeclampsia (28.46± 4.2) was significantly different from normal subjects (25.32 ± 4.8). In addition, in patients with preeclampsia, maternal BMI average (30.07) was significantly higher than normal controls (27.25) (P≤0.0001)). Average weight of infants born to people with preeclampsia (25860.60) was significantly lower than normal population (2934.80) (P≤0.0001)).

Table 3: The results of Mann-Whitney Test for studied variable

Variables	Mann-Whitney (U)	Z	Sig.(2-tailed)= P-value
Maternal age(year)	8227.500	-4.032	0.000
Maternal BMI(kg/m^2)	2713.000	-11.364	0.000
Gestational age(weak)	7392.000	-5.261	0.000
Child weight at birth(gr)	5624.000	-7.492	0.000
Maternal hemoglobin(gr/dl)	4724.000	-8.694	0.000

The results obtained showed that the mean hemoglobin (registered in the first week of disease) of individuals with preeclampsia (10.01) was significantly lower than normal controls (11.71) (P≤0.0001).

Mann-Whitney test shows that there were significant differences between the variables of maternal age, maternal BMI, pregnancy weeks, birth weight and hemoglobin of mothers in two groups (table 3). This table shows that the P-value for all mentioned variables is the same that is indicative of a significant relationship between these variables (P≤0.0001).

Table 4: The results of T-Test for studied variables

Variables		Levene's Test for Equality of Variances		t-test for Equality of Means			
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference
Maternal age(year)	EV assumed	0.736	0.391	-4.052	298	0.000	-2.140
	EV not assumed			-4.052	293.997	0.000	-2.140
Gestational age(weak)	EV assumed	24.474	0.000	5.789	298	0.000	1.167
	EV not assumed			5.789	208.896	0.000	1.167
Child weight(gr)	EV assumed	11.442	0.001	7.523	298	0.000	348.200
	EV not assumed			7.523	292.540	0.000	348.200
Maternal Hb(gr/dl)	EV assumed	15.696	0.000	10.246	298	0.000	1.0327
	EV not assumed			10.246	278.827	0.000	1.0327
Maternal BMI(kg/m^2)	EV assumed	7.540	0.006	-13.983	298	0.000	-2.8202
	EV not assumed			-13.983	277.038	0.000	-2.8202

EV(Equal Variances)

Similar to the Mann-Whitney test, results of T-Test shows that the P-value is the same for all mentioned variables (table 4), which indicates a significant relationship between these variables (P≤0.0001).

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DISCUSSION

In several studies different factors have been examined as risk factors for preeclampsia. In a study, factors such as a urinary tract infection (UTI) during pregnancy, low education level, BMI higher than 30, smoking and being exposed to diethylstilbestrol in uterus were risk factors for preeclampsia [20]. In another study it was observed that preeclampsia in the previous pregnancy, the history of family, chronic hypertension and high BMI are risk factors for incidence of preeclampsia [21]. In this study, maternal age, BMI of mother, pregnancy weeks, birth weight and hemoglobin of mothers were risk factors for preeclampsia. In this research like the study conducted by Su *et al.,* there was a statistically significant difference between the mean age of the case and control groups, indicating that age increases along with increase in the risk of preeclampsia [22]. In the study conducted by Mittendorf *et al.*, average age higher than 35 years was associated with incidence of preeclampsia [20], while in the study conducted by Salonen, no relations was not proven between age and incidence of preeclampsia [23]. Given that relationship between preeclampsia with increased age higher than 35 years has been proven in the numerous studies [14, 25], the findings of the present study indicate that along with increasing age, the likelihood of incidence of preeclampsia also increases. So because only people with an age range of 18-35 years (the ideal society in the age of pregnancy) participated in this study, it can be said that in each of the age range (young or old), the probability of incidence of preeclampsia increases along with increased age.

In this study it was observed that increasing body mass index (BMI) increases the risk of preeclampsia that is consistent with the study conducted by Rudra as well as the study conducted by Sibai [24, 25].

Like in a study conducted by Kashanian *et al.,* in the present study, the reduced amount of hemoglobin has been seen in people with preeclampsia that shows the relationship between anemia and preeclampsia [3]. While in the study conducted by Hershkovitz *et al.*, there was not much difference between preeclampsia and the level of hemoglobin in the control group [26].

In a study conducted by Allahyari *et al.*, the average age of pregnancy in the preeclampsia group was significantly lower than the case group [27], while in the current study, the age of pregnancy in women with preeclampsia was significantly higher.

In a study, Mostello *et al.* examined an issue with the question of whether gestational age at delivery in previous pregnancy that was associated with preeclampsia, can affect the incidence of preeclampsia in the second pregnancy? The result was that the lower the gestational age at birth in previous pregnancies, the risk of preeclampsia in the next pregnancy is rising, which indicates that there is a strong determining factor in the incidence of the disease [28].

In this study there was no significant association between the seasons of occurrence of preeclampsia. In the study conducted by Mahaba *et al.*, the occurrence of preeclampsia has been reported mostly in the summer season [17], while in the study conducted by Kashanian *et al.*, winter season was associated with a higher frequency of preeclampsia [3].

When in the different studies and societies there are different risk factors for the disease, probably other unknown genetic factors or underlying issues are involved in the incidence of this disease. For this reason, studies of this nature should be investigated in detail in the various societies in order to make a general conclusion about the influential factors in the disease.

In a study, Lawler *et al.* concluded that the rate of preeclampsia has had a downward trend during five years, and it seems that a review of the reductions in preeclampsia in various countries according to risk factors associated with this disease is essential. Therefore, it is suggested that a study be done in Iran during this period and even more [29].

Due to the influence of some immune system cells, such as lymphocytes of T, B and NK in the course of pregnancy has been proven [30-32], so, by investigating the factors, along with the mentioned risk factors we can achieve an interesting relationship in terms of intensity of the effects of these factors on preeclampsia.

It should be noted that the criteria for diagnosing women at risk is only based on clinical and epidemiological risk factors that this show the importance of reviews of these risk factors. When we obtain a sufficient understanding of these risk factors during pregnancy, the patient should be monitored from the beginning of pregnancy on a regular basis, and as a result, we can have a better prediction of the disease and so, better control can be done in relation to the disease prevention.

CONCLUSION

It seems increased maternal age, BMI and gestational age as well as reduced maternal hemoglobin enhances the risk of preeclampsia syndrome in pregnant women. Further studies required in order to fully understand about the risks factors associated with preeclampsia syndrome.

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