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Predictive factors for preeclampsia in pregnant women: a unvariate and multivariate logistic regression analysis

Ashraf Direkvand-Moghadam[1,2], Afra Khosravi[3]✉ and Kourosh Sayehmiri[1,4]

[1]Psychosocial Injuries Research Center, Ilam University of Medical Sciences, Ilam, Iran; [2]Department of Midwifery, Faculty of Nursing and Midwifery, Ilam University of Medical Sciences, Ilam, Iran; [3]Department of Immunology, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran; [4]Department of Social Medicine, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran

Introduction: Several risk factors have been used to predict preeclampsia. The role of some risk factors as predictors associated with preeclampsia among Iranian women was analyzed in the present study using logistic regression. Materials and Methods: 610 women attending the obstetric ward of Mustafa hospital in Ilam were enrolled in this study. Demographic variables such as age, Body Mass Index (BMI), medical and obstetrics variables such as education, number of pregnancy, abortion and parity from May to September 2010 were analyzed. We used the unvaried and multiple logistic regression analyses to predict preeclampsia. Results: The history of preeclampsia, hypertension, and infertility showed to be good independent predicator variables for preeclampsia using multivariate logistic regression analysis (OR was 5.46, 2.34 and 3.07 respectively). Area Under the Receiver Operation Character (AUROC) was estimated to be 0.67 (95% CI 0.59–0.67, $p<0.01$) indicating the efficacy of the model for the prediction. Conclusion: The history of preeclampsia, hypertension and infertility predict preeclampsia with an increased odds ratio. Using such variables in regression analysis can help to diagnose preeclampsia beforehand and hence allow timely intervention.

Key word: independent predictive factors, preeclampsia, risk factors

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INTRODUCTION

Preeclampsia is a pregnancy-specific syndrome (Backes *et al*., 2011) characterized by the onset of hypertension and proteinuria after 20th week of gestation in women who previously were normotensive (Wagner, 2004). Preeclampsia complicates about 3% of all pregnancies (Conde-Agudelo *et al*, 2008). Although estimated incidence of preeclampsia in 6–10% of all pregnancies in the United States; the incidence is believed to be even higher in underdeveloped countries (Sibai, 2003)

Preeclampsia remains a major cause of maternal and prenatal mortality and morbidity (Duckitt & Harrington, 2005). Previous studies indicated that preeclampsia increases risk of subsequent cardiovascular disease (Bellamy *et al*., 2007) and the overall risk of cancer (Paltiel *et al*., 2004). Despite progress towards understanding the cause of preeclampsia and contributing circulating factors (Sibai *et al*., 2005), the etiology of preeclampsia remains unclear (Gilbert *et al*., 2008). Studies have suggested several risk factors for preeclampsia including nulliparity, family or own history of preeclampsia, diabetes, BMI higher than normal, multiple pregnancy, maternal age (less than 20 and greater than 35 years), renal disease, hydatidiform mole, hydrops fetalis, oocyte donation or donor insemination, chronic hypertension and chronic autoimmune disease (Mostello *et al*., 2002; Dekker & Sibai, 2001). Another study used multiple logistic regression analysis showed that history of preeclampsia in previous pregnancy (OR = 23.7, $p<0.001$), familiar history of preeclampsia (OR = 1.62, $p<0.08$) and BMI (OR = 1.60) were the main risk factors for preeclampsia (Gonzalez *et al*., 2000). As preeclampsia remains a serious and poorly understood complication of pregnancy, it is necessary to recognize the epidemiological and clinical risk factors to predict the disease before it threatens the survival of both mother and fetus. The present study was conducted to determine the predictive factors for preeclampsia in Iranian women in Mustafa Hospital of Ilam, Iran.

METHODS

The role of demographic, anthropometric, medical and obstetrics variables in prediction of preeclampsia among women attending the obstetric ward of Mustafa hospital of Ilam in the west of Iran, from May 2010 to September 2010, was evaluated performing this cross-sectional predictive study. All the pregnant women that were referred to the hospital during that period participated in the study except those who had abortion. Sample size was calculated according to systematic random sampling where P was 10% (prevalence of preeclampsia) and maximum estimate error was 2.4%.

Place of the study. Ilam province is one of the counties of Iran located in the west of the country with populations of over 500 000 and a mountainous geographical situation. As this part of the country is located close to the border of Iran and Iraq and had been exposed to bombardment during the war between these two countries is has a special health related concern and hence the importance of such studies.

MEASURES

Data collection and examinations were carried out by a face to face interview. Demographic data including age, education, and occupation and the anthropometrics data

✉e-mail: afra@medilam.ac.ir; afrakhosravi@yahoo.co.uk
Abbreviations: AUROC, Area Under the Receiver Operation Character; BMI, Body Mass Index.

including weight and height were obtained. Height and weight were measured employing Seca 220 (Germany) by a trained researcher when the subjects were minimally clothed without shoes before pregnancy or during the first trimester of pregnancy. The body mass index was calculated based on heights and weights [BMI = weight (kg)/(height (m)^2]. Based on BMI, women were grouped into different categories as recommended by the National Centre for Education in Maternal and Child Health. The clinical measures including the history of pregnancy, abortion, parity and medical conditions such as chronic hypertension, diabetes mellitus and renal disease were collected by an observational interview.

Subjects were divided into two groups: women without preeclampsia and women with preeclampsia at the time of referring to the hospital. Preeclampsia was defined as the development of hypertension (Blood Preassure 140/90 ≥ mm Hg) in pregnancy, after the 20th week of gestation, with proteinuria, with or without edema (Wagner, 2004)

Statistical analysis. Sample size was calculated using the following formula:

$$n = \frac{p(1-p)z_{\alpha/2}}{d^2}$$

The p was 0.1, α was 0.05 and d was 2.4.

Results were expressed as mean ± standard deviation. Kolmogrov-Smirno test was used to test the normality in continues variables. Independent *T*-test was used to compare the mean BMI and age in two groups (with preeclampsia *vs* without preeclampsia). To explore relationship between occupation, type of pregnancy, type of previous delivery, contraceptive method and preeclampsia Chi-square test was used. Both unvaried and multiple logistic regression analyses were used to indicate the association between the dependent (with preeclampsia *vs.* without preeclampsia) and independent variables. The P value was computed using Chi-square test to compare the variables between the preeclampsia and the normal group**s.**

The forward LR method was used to choose the best multivariate logistic regression model in independent variables such as education, BMI, number of pregnancy, abortion and parity. Predicted probability for preeclampsia was computed using multivariate logistic models. AUROC applied to compare the accuracy of models. A p-value less than 0.05 was considered as significant level throughout the study.

ETHICS

The Ethics Committee of Ilam University of Medical Sciences approved the study design. Written informed consent was obtained from the participants after comprehensive explanation of the procedure involved.

RESULTS

Totally 610 pregnant women participated in the study, of which 90.5% had normal blood pressure while 9.5% (95% CI 7.4–11.6%) had preeclampsia (1.3% mild and 8.2% severe). The socio-demographics, medical, obstetric and antenatal characteristics of all participants are presented in Table 1. A significant relationship was found between education and preeclampsia so that the risk of preeclampsia increased 4 times in illiterates women compared to women with Academic education. The mean age of the participants with preeclampsia was 28 ± 5.3 and 28.9 ± 4.8 for the normal group. There was no significant differences of the mean age between the two groups ($p = 0.170$). The results obtained from logistic regression analysis indicated that there was no significant relationship between age and preeclampsia (OR = 0.96, $p = 0.17$). Independent samples t-test indicated no significant difference of BMI of the two groups. There was no statistically significance association between the occupation, type of pregnancy, type of previous delivery or contraceptive method with preeclampsia (Table 1).

Univariate logistic regression analysis showed a significant association between preeclampsia and education (OR = 4.05 illiterate *vs.* academic), history of preeclampsia (OR = 7.7), history of hypertension (OR = 1.17) and history of infertility (OR = 3) (Table 2). Using multivariate logistic regression analysis, history of preeclampsia (OR = 5.46), history of hypertension (OR = 2.34), and history of infertility (OR = 3.07) were proved to be suitable independent prediction variables (Table 3). The multivariate logistic model between the probability of preeclampsia and the other covariates was estimated as: $\ln(\frac{p}{1-p}) = 0.74 - 1.016$ prior infertility -0.72 chronic hypertention -1.69 prior preeclampsia

Where P is probability of occurrence of preeclampsia. The coefficients of logistic regression models show that history of preeclampsia was the most important variable to predict preeclampsia. To compute the overall percentage of correct classification of the model, predicted values were compared to the observed values. The overall percentage of correct classification of the model is 90.7%. It means that, knowing the history of preeclampsia, history of hypertension, and history of infertility, the accuracy of the model to predict the actual situation of cases is 90.7%. An AUROC criterion was used to compute both the sensitivity and the specificity of the model. AUROC was estimated to be 0.67 (95% CI 0.59–0.76, asymptotic significance = 0.000). The area under the curve represents the probability that the model predicted for a randomly chosen positive case will exceed the result for a randomly chosen negative case. The asymptotic significance is less than 0.05, which means that using the model was a better means to predict preeclampsia compared to randomly prediction.

DISCUSSION

There was no significant relationship between the maternal age and preeclampsia ($p = 0.17$), which is in agreement with the results of some studies (Shamsi *et al.*, 2010; Ganesh *et al.*, 2010) while it was different from the results observed by another study (Macdonald-Wallis *et al.*, 2011). Such difference could be due to the specificity of each population and hospital of the attendant patients.

Although we reported that there was not significant relationship between the BMI and preeclampsia, another study reported opposite results (Ganesh *et al.*, 2010). This study determined that the history of preeclampsia, hypertension and infertility are important predictor factors for preeclampsia. Our study population consisted of 610 women, including 38 women who had history of preeclampsia and 572 women with no history of preeclampsia. A strong relationship between the history of preeclampsia and recurrence risk of preeclampsia has been reported by many researches (Mostello *et al.*, 2002b; Gonzalez *et al.*, 2000; Mostello *et al.*, 2008). One study reported that 65% of all studied women with a history of preeclampsia at the second trimester showed a recur-

Table 1. Comparison of the characteristics between groups

Characteristic	Groups		*p*-value
	Normotensive* = 552 (90.5%)	Preeclampsia n = 58 (9.5%)	
BMI** (kg/m²)			0.236
Lightweight (>19.8)	61 (16.95%)	7 (20.59%)	
Normal (19.8–25.9)	196 (54.45%)	20 (58.81%)	
Overweight (26–29)	56 (15.55%)	1 (2.94%)	
Obese (< 29)	47 (13.05%)	6 (17.64%)	
Education			0.041
Illiterate	37 (6.70%)	10 (17.24%)	
Reading and writing	53 (9.60%)	4 (6. 9%)	
Primary	75 (13.59%)	4 (6. 9%)	
Secondary school education	87 (15.77%)	7 (12.06%)	
High school	240 (43.48%)	29 (50%)	
Academic	60 (10.86%)	4 (6. 9%)	
Occupation			0.090
Homemaker	533 (97.26%)	52 (92.86%)	
Employed	15 (2.74%)	4 (7.4%)	
Pregnancy			0.001
Primigravida	267 (48.55%)	27 (46.55%)	
2–5 pregnancy	247 (44.91%)	29 (50%)	
>5 pregnancy	36 (6.54%)	2 (3.45%)	
Type of pregnancy			0.610
Acceptable pregnancy	442 (80.07%)	45 (77.59%)	
Unwanted pregnancy	110 (19.93%)	13 (22.41%)	
Prenatal care			0.003
Partially done	8 (1.45%)	1 (1.72%)	
Been completed	542 (98.55%)	57 (98.28%)	
Abortion			0.024
without	481 (88.26%)	50 (86.20%)	
1 abortion	59 (10.82%)	5 (8.62%)	
2 abortion	5 (.92%)	3 (5.18%)	
Parity			0.022
Primiparous	270 (49.54%)	30 (51.72%)	
2-5 parity	261 (47.89%)	28 (48.28%)	
>5 parity	14 (2.57%)	0 (0%)	
Newborn gender			0.430
Male	296 (54.81%)	27 (47.36%)	
Female	244 (45.18%)	30 (53.64%)	
Contraceptive method			0.202
Contraceptive pill	254 (57.20%)	17 (32.07%)	
Condom	60 (13.51%)	8 (15.09%)	
IUD	13 (2.93)	2 (3.77%)	
DMPA	7 (1.58%)	2 (3.77%)	
Withdrawal	87 (19.60%)	11 (20.75%)	
No method of contraception	23 (5.19%)	13 (24.54%)	
History of infertility			0.004
Yes	44 (8.07%)	12 (20.69%)	
No	505 (91.93%)	46 (79.31%)	
Relative of the partner			0.513
Yes	148 (26.96%)	16 (27.58%)	
No	401 (73.04%)	42 (72.41%)	
Medical disorders			
Cardiovascular disease			0.402
Yes	9 (1.64%)	0 (0%)	
No	540 (98.36%)	58 (100%)	
Diabetes mellitus			0.532
Yes	45 (8.2%)	5 (8.62%)	
No	504 (91.8%)	53 (93. 38%)	
Immune disorders			0.424
Yes	0 (0%)	0 (0%)	
Renal disorders			0.001
Yes	57 (10.38%)	8 (13.8%)	
No	492 (89.62%)	50 (86.2%)	
History of hypertension			0.000
Yes	50 (.91%)	14 (24.13%)	
No	499 (99.09%)	44 (75.87%)	
History of preeclampsia			
Yes	23 (4.21%)	15 (25.86%)	
No	523 (95.79%)	43 (74.14%)	

*Number; **Body Mass Index; The *p* value was computed using Chi-square test to compare the variables between the preeclampsia and the normotensive groups.

rent preeclampsia at their subsequent pregnancy (Sibai, 2003). In another study the recurrent risk of preeclampsia was inversely correlated with the gestational age at the first delivery and it was 38.6% in women whose previous delivery was at less than 28 weeks compared to 29.1% in women who had a previous delivery at 29–32 weeks (Mostello *et al.*, 2008). Chronic hypertension is a common problem in developing countries among non pregnant women and increases the incidence of preeclampsia (Macdonald-Wallis *et al.*, 2011).

Table 2. The association between preeclampsia and other variables using univariate logistic regression analysis.

Parameter	B	S.E.	OR (95% CI*)	*p*-value
Education				
Illiterate	1.40	0.63	4.05 (1.18–13.86)	0.026
Reading and writing	0.12	0.73	1.13 (0.270–4.75)	0.865
Primary	–0.22	0.73	0.8 (0.19–3.33)	0.759
Secondary school	0.19	0.65	1.21 (0.34–4.30)	0.772
High school	–2.71	0.52	1.81 (0.61–5.35)	0.282
Academic			1.0 (Ref.)	0.059
History of preeclampsia Yes *vs* No	2.1	0.36	7.70 (3.8–16.6)	0.000
History of hypertension Yes *vs* No	1.15	0.341	3.17 (1.62–6.2)	0.001
History of infertility Yes *vs* No	1.1	0.67	3 (1.49–6.1)	0.002

*Confidence Interval

Table 3. A association between preeclampsia and other variables using multivariate logistic regression analysis.

Parameter	B	S.E.	OR (95% CI)	*p*-value
History of preeclampsia Yes *vs* No	1.697	0.402	5.46 (2.48–12.1)	0.000
History of hypertension Yes *vs* No	0.729	0.389	2.34 (1.034–4.4)	0.001
History of infertility Yes *vs* No	1.016	0.382	3.07 (1.3–5.8)	0.002

We found that chronic hypertension is one of the main determinants of preeclampsia in our population, as women with history of hypertension had increased risk of preeclampsia by 38% compared to normotensive women. Our observation is in agreement with the results of several other studies (Mostello *et al.*, 2002; Dekker & Sibai, 2001; Qiu *et al.*, 2003). In another study the prevalence of chronic hypertension was higher in women who developed preeclampsia than in women who did not (12.1% *vs* 0.3%) (Duckitt & Harrington, 2005). Odegard and coworkers (2000) in a nested case-control study compared 323 preeclamptic women with 650 healthy women founding that the risk of development of preeclampsia in later pregnancy was significantly higher in women with a systolic blood pressure ≥ 130 mm Hg compared to a blood pressure < 110 mm Hg at the first visit before 18 weeks (OR = 3.6, 95% CI = 2.0–6.6) (Odegard *et al.*, 2000).

The risk factors of early and late onset preeclampsia has been investigated showing that history of chronic hypertension and family history of chronic hypertension were significantly associated with increased risk for both early ansd late onset preeclampsia. History of chronic hypertension (odds ratio 4.4; 95% confidence interval 2.1–9.3) was significantly associated with increased risk for only early-onset preeclampsia, while family history of chronic hypertension (odds ratio 18; 95% confidence interval 6–54) was significantly associated with increased risk for only late-onset preeclampsia(Aksornphusitaphong & Phupong, 2012).

In the present study, 10.81% (66/610) of participants become pregnant with assisted reproductive technology. The multivariate logistic regression analysis revealed an increased risk of preeclampsia in women who had been treated for infertility (OR = 3.07; 95% CI 1.3–5.8). This finding of the current study is in agreement with the finding of other (Lachmeijer *et al.*, 2001). In a recent study that investigated the effect of infertility on the risk of preeclampsia, it was revealed that the risk for preeclampsia was increased in those who were treated for infertility (Trogstad *et al.*, 2009). In another study the incidence of gestational hypertension was reported to be 8.9% (423/4762) among women without infertility treatments and 15.8% (55/349) among women undergoing infertility treatments. Compared to spontaneous pregnancies, the crude relative risk for gestational hypertension in pregnancies resulting from infertility treatments was 1.9 (95% confidence interval 1.4–2.6) (Hernández-Díaz *et al.*, 2007).

CONCLUSIONS

In view of the above findings, there are several risk factors for preeclampsia. It seems that history of preeclampsia, hypertension and infertility are some suitable independent predictor factors for preeclampsia. It is concluded that pregnant women at risk of preeclampsia could be diagnosed using some predictive analysis models allowing timely interventions to be performed.

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