

## Brief Report

## Risk Factors for Pre-Eclampsia: A Study in Tehran, Iran

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## Abstract

This study evaluated some risk factors for pre-eclampsia, which is one of the most problematic complications of pregnancy. This was a retrospective case control study conducted on 318 pre-eclamptic women (case group) and 318 women who were normotensive at the time of delivery as the control group. Evaluated factors were: maternal age, gestational age, nulliparity, mother's educational status, maternal body mass index (BMI), maternal hemoglobin and blood Rh, familial history of pre-eclampsia, history of pre-eclampsia in a previous pregnancy, marital relations, urinary infection (UTI) during the present pregnancy, season of delivery, and method of contraception. Risk factors for pre-eclampsia were: UTI ( $P=0.04$ ); history of pre-eclampsia during previous pregnancy ( $P=0.003$ ), and winter season ( $P=0.001$ ). Maternal age of more than 20 years, high educational status of mother, parity more than one, and oral contraceptive pills were protective for pre-eclampsia. After adjusting for all possible confounding factors using multiple logistic regression, only preexisting pre-eclampsia ( $P=0.004$ ) was a risk factor, whereas parity more than three ( $P=0.007$ ) and anemia ( $P=0.01$ ) were protective for pre-eclampsia. The rate of cesarean delivery was more common in the pre-eclamptic group (245 cases, 77%) than the control group (85 cases, 26.7%). The one minute Apgar score of neonates less than 8 was more common in the case group (28.6% vs. 47.4%,  $P<0.001$ ). Gestational age at the time of delivery was lower in the case group ( $36.48\pm3.4$  weeks vs.  $37.12\pm3.3$  weeks,  $P<0.001$ ). Awareness of risk factors of pre-eclampsia can help to monitor patients, ensure earlier diagnosis and predict which patients are more likely to develop pre-eclampsia.

**Keywords:** gestational age; pregnancy induced hypertension; pre-eclampsia; risk factors

## Introduction

Hypertensive disorders are one of the most important complications of pregnancy and in combination with hemorrhage and infection make a lethal triad which cause the majority of pregnancy-related maternal morbidity and mortality conditions,<sup>1,2</sup> occurring in about 3.7% – 5% of pregnancies.<sup>1,3</sup> The etiology of pre-eclampsia is not completely understood<sup>4,5</sup> and immunological factors appear to underlie the placental disease, whereas genetic arrangements determine maternal susceptibility.<sup>6</sup> Considering the high importance of this disorder, a large number of studies have been performed to evaluate risk factors of nulliparity, high maternal age, race, genetic factors, environmental factors (high altitude), obesity, poverty, chronic hypertension, and multi-fetal pregnancy, all of which are considered contributory.<sup>1,7-9</sup>

Other studies have suggested risk factors such as: occupation and stress,<sup>8,10</sup> a sister with a history of pre-eclampsia,<sup>11</sup> urinary tract infection (UTI), mother's poor educational status, in utero diethylstilbestrol exposure,<sup>12</sup> long interval between pregnancies, history of preterm delivery, and intra-uterine growth restriction (IUGR), inadequate prenatal care,<sup>13</sup> season and blood group,<sup>14</sup> low maternal weight at birth,<sup>15</sup> and smoking.<sup>16</sup>

At the present time, at risk women are diagnosed according to epidemiological and clinical risk factors.

This study evaluated a number of potential risk factors between pre-eclamptic women and those who were normotensive at the time of delivery.

## Material and Methods

This was a retrospective case-control study conducted in Akbarabadi Teaching Hospital in Tehran, Iran between 2005 – 2006. Totally, we enrolled 318 pre-eclamptic women and 318 pregnant women who were normotensive at the time of delivery (control group). Pre-eclampsia was defined as blood pressure higher than 140 mmHg systolic and 90 mmHg diastolic, and proteinuria greater than 300 mg/24 hr. Exclusion criteria were: over 35 years of age or below 18 years of age, history of any maternal disease including diabetes, chronic hypertension and renal disease, any drug use, multi-fetal pregnancy, smoking, erythroblastosis fetalis, and non-Iranian.

Patients of the two groups were compared for the following factors: maternal age, UTI, history of pre-eclampsia in relatives, BMI, history of pre-eclampsia in previous pregnancy, pre-existing hypertension, nulliparity, blood Rh, pre-existing diabetes, educational status of mother, maternal Hb and anemia, season, method of contraception, gestational age at the time of diagnosis of pre-eclampsia, and marital status.

Statistical analysis was performed using SPSS (Version 15). Chi-square and Mann-Whitney tests and univariate analysis were used for comparisons.

## Results

Characteristics of the two groups of patients are shown in Table 1. In Table 2 we report the estimation the risk of pre-eclampsia during pregnancy considering some known factors through univariate analysis. Risk factors of UTI, history of pre-eclampsia during previous pregnancy and winter were risk factors for pre-eclampsia whereas maternal age greater than 20 years old, mother's high educational status, parity more than one and oral contraceptive pill were protective for pre-eclampsia (Table 2).

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**Table 1.** Patient characteristics.

Characteristic	Pre-eclampsia (+)		Pre-eclampsia (-)	
	Number (N)	Percentage	Number (N)	Percentage
Mother's age, (years)				
15 – 20	59	9.3	44	6.9
21 – 30	151	23.7	187	29.4
≥31	108	17	87	13.7
Education level				
Illiterate	22	6.1	39	3.5
Elementary	129	23	146	20.3
Secondary	163	19.8	126	25.6
University	4	1.1	7	0.6
Parity				
1	150	23.6	116	18.2
2	54	8.5	93	14.6
3	40	6.3	58	9.1
≥4	74	11.6	51	8
Pre-existing diabetes				
No	309	48.6	312	49.1
Yes	9	1.4	6	0.9
Anemia				
No	235	36.9	216	34
Yes	83	13.1	102	16
Pre-existing eclampsia				
No	300	47.2	316	49.7
Yes	18	2.8	2	0.3
Pre-existing hypertension				
No	305	48	313	49.2
Yes	5	2	5	0.8
Mother's Rh				
Negative	30	4.9	26	4.3
Positive	277	45.4	277	45.4
Contraceptive				
No	252	39.6	234	36.8
OCP	11	1.7	22	3.5
IUD	12	1.9	10	1.6
Barrier	4	0.6	7	1.1
Gestational age at first antenatal visit (weeks)				
≤20	1	0.2	2	0.3
21 – 35	86	13.7	62	9.9
≥36	227	36.2	249	39.7
Family history of pre-eclampsia				
No	313	49.2	317	49.8
Yes	5	0.8	1	0.2

After adjusting for all possible confounding factors with multiple logistic regression, only preexisting pre-eclampsia was considered a risk factor. Parity more than three and anemia were protective for pre-eclampsia.

Although preexisting diabetes, preexisting hypertension and UTI showed an increased risk for pre-eclampsia, the results, however, were not statistically significant and were probably due to the low numbers of cases in these groups (Table 3).

There were 245 pre-eclamptic women (77%) who had cesarean deliveries compared to 85 controls (26.7%),  $P=0.000$ . The one minute Apgar score of neonates less than 8 was more common in the case group (28.6% vs. 47.4%,  $P=0.000$ ). Finally, gestational age at delivery was less in the case group ( $36.48\pm3.4$  weeks vs.  $37.12\pm3.3$  weeks,  $P=0.006$ ).

## Discussion

In different studies, various factors have been evaluated as possible risks for pre-eclampsia. Trostad et al.,<sup>17</sup> have studied the recurrent risk of pre-eclampsia in the second pregnancies. They determined a higher risk compared to women with first-time pregnancies, and concluded that there was a polygenic liability model for pre-eclampsia.

The greater likelihood of pre-eclampsia among sisters of women with a previous pre-eclamptic pregnancy<sup>11</sup> is consistent with a pathophysiologic role for genetic and/or behavioral factors that cluster in families.

In another study,<sup>7</sup> a history of pre-eclampsia in a previous pregnancy, familial history of pre-eclampsia and high BMI were risk

factors for pre-eclampsia. Researchers in one study<sup>10</sup> determined that moderate to high levels of physical activity at work were associated with a 2-fold increase in the risk of severe pre-eclampsia.

UTI during pregnancy, nulliparity, poorer standard of education, exposure to diethylstilbestrol in utero, BMI>30 and cigarette smoking were other risk factors in another study,<sup>12</sup> which is mostly consistent with the present study. Another study found that pre-eclampsia in a previous pregnancy, familial history of hypertension and high BMI were risk factors.<sup>8</sup>

Mostello et al.<sup>13</sup> performed a study to determine whether gestational age at delivery in the first pregnancy increased the risk of recurrent pre-eclampsia. They concluded that the relative risk of recurrent pre-eclampsia increased when earlier gestational age at delivery of the first pregnancy was complicated by pre-eclampsia. Lawler et al.<sup>18</sup> showed that the incidence of pregnancy-related hypertensive disorders slightly decreased in their population during the last five years with a decline in the rate of pre-eclampsia that accounted for this change. They concluded that further analysis might provide additional insights into the population-based incidence of pre-eclampsia with respect to risk factors. In one study<sup>19</sup> the concentration of erythropoietin was higher among patients with pre-eclampsia, but hemoglobin and hematocrit levels were similar to controls. The sample size of this study was low (22 pre-eclamptic and 19 normotensive) and they suggested that further prospective studies should investigate the association between pre-eclampsia and erythropoietin levels.

In a study by Mahaba,<sup>14</sup> pre-eclampsia was more common in blood group B, Rh- cases and during the summer. In contrast, another study<sup>20</sup> noted that blood group O, Rh- cases had HELLP syn-

**Table 2.** The crude Odds Ratio (OR) of risk factors in Pre-eclampsia.

Characteristics of factors	With pre-eclampsia n (%)	Without pre-eclampsia n (%)	OR (95% CI)	P-value
Mother's age , years				
15 – 20	59 (9.3)	44 (6.9)	Reference	Reference
21 – 30	151 (23.7)	187 (29.4)	0.6* (0.3 – 0.9)	0.02
≥31	108 (17)	87 (13.7)	0.9 (0.5 – 1.4)	0.75
Education level				
Illiterate	22 (6.1)	39 (3.5)	Reference	Reference
Elementary	129 (23)	146 (20.3)	0.6 (0.3 – 1.1)	0.12
Secondary	163 (19.8)	126 (25.6)	0.4* (0.2 – 0.7)	0.004
University	4 (1.1)	7 (0.6)	0.9 (0.2 – 3.7)	0.98
Parity				
1	150 (23.6)	116 (18.2)	Reference	Reference
2	54 (8.5)	93 (14.6)	0.4* (0.2 – 0.6)	<0.0001
3	40 (6.3)	58 (9.1)	0.5* (0.3 – 0.8)	0.009
≥4	74 (11.6)	51 (8)	1.1 (0.7 – 1.7)	0.60
Pre-existing diabetes				
No	309 (48.6)	312 (49.1)	Reference	Reference
Yes	9 (1.4)	6 (0.9)	1.5 (0.5 – 4.3)	0.43
Anemia				
No	235 (36.9)	216 (34)	Reference	Reference
Yes	83 (13.1)	102 (16)	0.7 (0.5 – 1.1)	0.09
Pre-existing eclampsia				
No	300 (47.2)	316 (49.7)	Reference	Reference
Yes	18 (2.8)	2 (0.3)	9.4* (2.1 – 41.2)	0.003
Pre-existing hypertension				
No	305 (48)	313 (49.2)	Reference	Reference
Yes	5 (2)	5 (0.8)	2.6 (0.9 – 7.5)	0.06
Mother's Rh				
Positive	277 (45.4)	277 (45.4)	Reference	Reference
Negative	30 (4.9)	26 (4.3)	1.1 (0.6 – 2)	0.61
Contraceptive				
No	252 (39.6)	234 (36.8)	Reference	Reference
OCP	11 (1.7)	22 (3.5)	0.4* (0.2 – 0.9)	0.04
WD	39 (6.1)	45 (7.1)	0.8 (0.5 – 1.2)	0.35
IUD	12 (1.9)	10 (1.6)	1.1 (0.4 – 1.6)	0.80
Barrier	4 (0.6)	7 (1.1)	0.5 (0.1 – 1.8)	0.312
Gestational age at first antenatal visit (weeks)				
≤20	1 (0.2)	2 (0.3)	Reference	Reference
21 – 35	86 (13.7)	62 (9.9)	2.7 (0.2 – 31)	0.40
≥36	227 (36.2)	249 (39.7)	1.8 (0.1 – 20)	0.62
Family history of pre-eclampsia				
No	313 (49.2)	317 (49.8)	Reference	Reference
Yes	5 (0.8)	1 (0.2)	5.0 (0.5 – 43.5)	0.14
UTI				
No	307 (48.3)	315 (49.5)	Reference	Reference
Yes	11 (1.7)	3 (0.5)	3.7* (1.1 – 13.6)	0.04
Consanguinity				
No	277 (43.6)	278 (43.7)	Reference	Reference
Yes	41 (6.3)	40 (6.4)	1.0 (0.6 – 1.6)	0.90
BMI				
18.5 – 24.9 (normal)	23 (6.7)	27 (7.9)	Reference	Reference
25 – 29.9 (overweight)	43 (12.6)	80 (23.5)	0.6 (0.3 – 1.2)	0.17
≥ 30 (obese)	97 (28.4)	71 (20.8)	1.6 (0.8 – 3.0)	0.14
Season				
Spring	87 (13.7)	100 (15.7)	Reference	
Summer	80 (12.6)	84 (13.2)	1.1 (0.7 – 1.6)	0.67
Autumn	68 (1.7)	90 (14.2)	0.8 (0.5 – 1.3)	0.51
Winter	83 (13.1)	44 (6.9)	2.1 (1.3 – 3.4)	0.001

Percentages (%) are of total sample. Reference groups are in bold. CI=confidence intervals; OR=odds ratio.

drome associated with an increase in risk by a factor of 3.1.

In conclusion, with regard to the complex process of pre-eclampsia that cannot be attributed to any one single cause,<sup>4</sup> additional research about its various risk factors, particularly in different races, might help to better understand its cause. At the same time, women at risk are identified on the basis of epidemiological and clinical risk factors<sup>2</sup> and awareness of pre-eclampsia risk factors can help to monitor patients, make earlier diagnoses and predict which patients are more likely to develop pre-eclampsia.

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**Table 3.** Crude and adjusted odds ratio (OR) of risk factors in pre-eclampsia.

Factors	With pre-eclampsia n (%)	Without pre-eclampsia n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Mother's age (years)				
15–20	59 (9.3)	44 (6.9)	Reference	Reference
21–30	151 (23.7)	187 (29.4)	0.6* (0.3 – 0.9)	0.5 (0.2 – 1.1)
≥31	108 (17)	87 (13.7)	0.9 (0.5 – 1.4)	0.8 (0.3 – 1.9)
Education level				
Illiterate	22 (6.1)	39 (3.5)	Reference	Reference
Elementary	129 (23)	146 (20.3)	0.6 (0.3 – 1.1)	0.6 (0.2 – 1.7)
Secondary	163 (19.8)	126 (25.6)	0.4* (0.2 – 0.7)	0.4 (0.1 – 1.2)
University	4 (1.1)	7 (0.6)	0.9 (0.2 – 3.7)	1.0 (0.1 – 8.6)
Parity				
1	150 (23.6)	116 (18.2)	Reference	Reference
2	54 (8.5)	93 (14.6)	0.4* (0.2 – 0.6)	0.7 (0.4 – 1.7)
3	40 (6.3)	58 (9.1)	0.5* (0.3 – 0.8)	0.4* (0.1 – 0.9)
≥4	74 (11.6)	51 (8)	1.1 (0.7 – 1.7)	1.1 (0.5 – 2.9)
Pre-existing diabetes				
No	309 (48.6)	312 (49.1)	Reference	Reference
Yes	9 (1.4)	6 (0.9)	1.5 (0.5 – 4.3)	2.0 (0.3 – 12.3)
Anemia				
No	235 (36.9)	216 (34)	Reference	Reference
Yes	83 (13.1)	102 (16)	0.7 (0.5 – 1.1)	0.5* (0.3 – 0.9)
Pre-existing eclampsia				
No	300 (47.2)	316 (49.7)	Reference	Reference
yes	18 (2.8)	2 (0.3)	9.4* (2.1 – 41.2)	5.7* (1.1 – 32.4)
Pre-existing hypertension				
No	305 (48)	313 (49.2)	Reference	Reference
Yes	5 (2)	5 (0.8)	2.6* (1.5 – 4.6)	1.6 (0.3 – 9.7)
Mother's Rh				
Positive	277 (45.4)	277 (45.4)	Reference	Reference
Negative	30 (4.9)	26 (4.3)	1.1 (0.6 – 2)	1.2 (0.5 – 1.7)
Contraceptive				
No	252 (39.6)	234 (36.8)	Reference	Reference
OCP	11 (1.7)	22 (3.5)	0.4* (0.2 – 0.9)	0.3 (0.1 – 1.1)
WD	39 (6.1)	45 (7.1)	0.8 (0.5 – 1.2)	0.8 (0.4 – 1.7)
IUD	12 (1.9)	10 (1.6)	1.1 (0.4 – 1.6)	1.5 (0.4 – 4.8)
Barrier	4 (0.6)	7 (1.1)	0.5 (0.1 – 1.8)	0.9 (0.1 – 4.2)
Gestational age at first antenatal visit (weeks)				
≤20	1 (0.2)	2 (0.3)	Reference	Reference
21–35	86 (13.7)	62 (9.9)	2.7 (0.2 – 31)	1.1 (0.5 – 20.1)
≥36	227 (36.2)	249 (39.7)	1.8 (0.1 – 2.0)	0.6 (0.03 – 12.8)
Family history of pre-eclampsia				
No	313 (49.2)	317 (49.8)	Reference	Reference
Yes	5 (0.8)	1 (0.2)	5.0 (0.5 – 43.5)	1.1 (0.7 – 16.1)
UTI				
No	307 (48.3)	315 (49.5)	Reference	Reference
Yes	11 (1.7)	3 (0.5)	3.7* (1.1 – 15.3)	2.2 (0.3 – 15.1)
Consanguinity				
No	277 (43.6)	278 (43.7)	Reference	Reference
Yes	41 (6.3)	40 (6.4)	1.0 (0.6 – 1.6)	0.6 (0.3 – 1.3)
BMI				
18.5 – 24.9 (normal)	23 (6.7)	27 (7.9)	Reference	Reference
25 – 29.9 (overweight)	43 (12.6)	80 (23.5)	0.6 (0.3 – 1.2)	0.6 (0.2 – 1.3)
≥ 30 (obese)	97 (28.4)	71 (20.8)	1.6 (0.8 – 3.0)	1.5 (0.7 – 3.1)

\*Statistically significant findings ( $P<0.05$ ), reference groups are in bold. CI= confidence intervals; OR= odds ratio. Percentages (%) are of total sample.

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