

# Hypertension and Microalbuminuria 5 Years After Pregnancies Complicated by Pre-eclampsia

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**Introduction.** Pre-eclampsia is part of a spectrum of conditions known as the hypertensive disorders of pregnancy. It is claimed that pregnant women with pre-eclampsia or eclampsia are at increased risk of kidney disease and hypertension later in life. We investigated whether Iranian women with a history of pre-eclampsia had higher rates of hypertension and microalbuminuria compared with women with uneventful pregnancy.

**Materials and Methods.** Medical records of pregnancies delivered at two hospitals in Ahvaz, between March 2001 and February 2003 were reviewed. Thirty-five pre-eclamptic women were identified and contacted for assessment of hypertension and albuminuria. They were compared with 35 women matched for year of delivery and age who had a pregnancy uncomplicated by hypertension.

**Results.** The mean follow-up from the index pregnancy was 5.7 years (range, 5.2 to 7.3 years). While only 1 woman (2.9%) in the control group was currently hypertensive, 28.6% of those with a history of pre-eclampsia ( $n = 10$ ) were hypertensive ( $P = .003$ ; relative risk, 10.0; 95% confidence interval, 1.35 to 74.00), 7 of whom were receiving antihypertensive medication at the time of evaluation. Among the formerly pre-eclamptic women, 7 had albuminuria (20.0%), whereas none of the controls were albuminuric ( $P < .001$ ). Microalbuminuria was present in all hypertensive women in the pre-eclampsia group, but not in the only women in the control group with hypertension.

**Conclusions.** We showed that in patients with a history of pre-eclampsia, there are increased risks of hypertension and microalbuminuria in the long term after pregnancy.

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## INTRODUCTION

Pre-eclampsia is part of a spectrum of conditions known as the hypertensive disorders of pregnancy, affecting up to 5% of gestations.<sup>1</sup> A worldwide incidence of 8 370 000 cases per year has been estimated.<sup>2,3</sup> Pre-eclampsia is a syndrome that is usually defined as the onset of hypertension and proteinuria after 20 weeks of gestation in previously normotensive nonproteinuric pregnant women.<sup>4</sup> It is claimed that pregnant women with pre-eclampsia or eclampsia are at increased risk of kidney disease and hypertension later in life.<sup>5-15</sup>

Despite its frequent occurrence, relatively little research has been conducted into the long-term effects of pre-eclampsia in Iranian women. In view of its association with kidney disease, we investigated whether Iranian women with a history of pre-eclampsia have a higher rate of hypertension or microalbuminuria compared with those without pre-eclampsia during their pregnancy.

## MATERIALS AND METHODS

### Patients

Between March 2001 and February 2003, a total

of 47 primiparous women were diagnosed with pre-eclampsia or eclampsia at Razi Hospital and Emam Khomeini Hospital, in Ahvaz, Iran. Pre-eclampsia was defined as a blood pressure of 140/90 mm Hg and higher and urinary protein excretion of 300 mg/24 h and greater after 20 weeks of gestation. None of the women had a definite diagnosis of chronic hypertension. Eight women were excluded because no maternity data were available. Therefore, 39 patients were invited to participate in historical cohort study and 35 provided consent (participation rate, 83%). In addition, 35 volunteer women attending the same facilities were examined as a control group. They were women selected from the same database, matched for year of delivery and age, who had a pregnancy uncomplicated by hypertension during the same period.

#### Data Collection and Procedures

Data of blood pressure evaluations in the first trimester of pregnancy was obtained from medical records. Interviews with the participants were held by a medical research assistant. All participants were given a full explanation of the study and signed an informed consent form. Laboratory studies consisted of plasma concentrations of fasting blood glucose, blood urea nitrogen, serum creatinine, serum uric acid, and urinary creatinine clearance with the hydroxylamine method (SMA 12/60, Technicon, Tarrytown, PA, USA). A morning midstream urine sample was taken for microscopy, culture, microalbuminuria, and creatinine measurement. Microalbuminuria was defined as an albumin-creatinine ratio of 30 mg/mmol and higher.

The examination included measurement of systolic and diastolic blood pressure. Blood pressure was measured by a specially trained nurse using a standard sphygmomanometer. Arm circumference was measured and a cuff with a larger bladder was used for arms larger than 32 cm. The recorded value was the mean of 3 measurements made on the right arm after a participant's 15-minute rest. The fifth Korotkoff sound was used as the diastolic blood pressure. Hypertension was diagnosed if the systolic blood pressure was equal or greater than 140 mm Hg and/or the diastolic blood pressure was equal or greater than 90 mm Hg or if the participant was taking antihypertensive medication.

#### Statistical Analyses

Values are expressed as mean  $\pm$  standard

deviation for normally distributed continuous variables and median for nonparametric data. Comparisons of continuous variables between the two groups were undertaken using the 1-way analysis of variance (for normal distributions) or Mann-Whitney *U* test (for duration of follow-up and urinary albumin-creatinine ratio). Discrete variables were compared using the chi-square test with continuity correction or the Fisher exact test. A *P* value less than .05 was considered significant.

#### RESULTS

Table 1 shows the maternal characteristics of the participants during pregnancy. Characteristics of the women at follow-up are shown in Table 2. Both groups were comparable with respect to age, body mass index, and follow-up time. The mean age was  $25.8 \pm 2.3$  years for the women in the control group and  $25.0 \pm 2.1$  years for those in the pre-eclampsia group. The mean time from the index pregnancy to the scheduled visit was 5.7 years. None of the women used oral contraceptive pill. Body mass index had not changed significantly at follow up in either of the groups. None of the women were smoking at baseline or follow-up. None of the patients had urinary tract infection or hematuria at the time of sampling for microalbuminuria.

The mean follow-up was 5.7 years (range, 5.2 to 7.3 years). The women with a history of pre-eclampsia had higher blood pressures at follow-up

**Table 1.** Baseline Characteristics of Women During First Trimester of Pregnancy

Characteristics	Participants		<i>P</i>
	Pre-eclampsia	Control	
Age, y	$25.8 \pm 2.3$	$25.0 \pm 2.1$	.13
Body mass index, kg/m <sup>2</sup>	$21.4 \pm 1.2$	$20.9 \pm 1.1$	.07
Blood pressure			
Systolic, mm Hg	$105.0 \pm 8.0$	$104.0 \pm 10.0$	.65
Diastolic, mm Hg	$67.0 \pm 6.0$	$70.0 \pm 5.0$	.05

**Table 2.** Characteristics of Women at Follow-up\*

Characteristics	Participants		<i>P</i>
	Pre-eclampsia	Control	
Blood pressure			
Systolic, mm Hg	$138.0 \pm 10.0$	$127.0 \pm 8.0$	< .001
Diastolic, mm Hg	$84.0 \pm 9.0$	$73.0 \pm 10.0$	< .001
> 140/90 mm Hg	10 (28.6)	1 (2.9)	.003
Microalbuminuria	7 (20.0)	0	.01
Glomerular filtration rate, mL/min	$108 \pm 14$	$110 \pm 17$	.59

\*Values in parentheses are percents.

than the controls (Table 2). While only 1 woman (2.9%) from among the controls was currently hypertensive, 28.6% ( $n = 10$ ) of formerly pre-eclamptic women were hypertensive ( $P = .003$ ; relative risk, 10; 95% confidence interval, 1.35 to 74.00; attributable risk, 89.9%), 7 of whom were receiving antihypertensive medication at the time of recruitment. All formerly pre-eclamptic women with hypertension had a high systolic blood pressure and 9 had a high diastolic blood pressure (25.7%). Both the age at pre-eclamptic onset and the parity were comparable in formerly pre-eclamptic women with and without hypertension (mean age, 25.7 years for hypertensive versus 24.8 years; mean parity, 1.8 for hypertensive versus 2, respectively).

The frequency of microalbuminuria was higher in women who had pre-eclampsia compared with the controls (Table 2). Among the formerly pre-eclamptic women, 7 had albuminuria (20.0%), whereas none of the 35 controls had albuminuria ( $P < .001$ ). All of the formerly pre-eclamptic women with hypertension had microalbuminuria, whereas the only women in the control group with hypertension did not have albuminuria. Glomerular filtration rate was comparable between the two groups (Table 2).

## DISCUSSION

Several decades ago, Sibai and colleagues suggested that pregnancy is a risk factor for later hypertension and diabetes mellitus.<sup>12</sup> In order to evaluate the effects of pre-eclampsia on blood pressure and kidney disease in later life of women, we examined the association between changes in blood pressure and occurrence of albuminuria in women with a previous experience of pre-eclampsia. In our study, 28.6% of the women with pre-eclampsia were hypertensive and 20.0% had albuminuria at a follow-up of 5.7 years (range, 5.2 to 7.3 years). Compared to women with uncomplicated pregnancies, women with a history of pre-eclampsia had an increased risk of subsequent hypertension. Similar rates of new-onset hypertension following pre-eclampsia have been previously reported, but they are higher than that found in other study. This variation may be due to population differences and the use of different definitions of hypertension.

Hannaford and coworkers demonstrated an increased relative risk of hypertension (2.35) following pre-eclampsia.<sup>16</sup> Wilson and colleagues demonstrated significant positive associations between both

gestational hypertension and pre-eclampsia/eclampsia disorders and subsequent diagnosed and treated hypertension.<sup>17</sup> They found that the odds ratio of medicated hypertension (2.77) was greater in pre-eclampsia/eclampsia group. Forest and colleagues reported that the prevalence of hypertension was 13% in women with prior pregnancy-induced hypertension (11% for gestational hypertension and 16% for pre-eclampsia) compared with only 1% in controls.<sup>18</sup> Bar and coworkers demonstrated that women who had a pregnancy complicated by pre-eclampsia 3 to 5 years earlier had a higher rate of hypertension (29%) than women with uncomplicated pregnancies.<sup>19</sup> Recently, Spaan and associates reported that the prevalence of hypertension was 55% in formerly pre-eclamptic women compared to 7% in the control group (relative risk, 7.9).<sup>20</sup> More recently, Magnussen and colleagues reported that women with 2 episodes of pre-eclampsia were approximately 10 times more likely to use blood pressure medication at follow-up (adjusted odds ratio, 11.6, 95% confidence interval, 7.1 to 26.3).<sup>21</sup>

Nisell and colleagues found that microalbuminuria is significantly increased in women with a history of pre-eclampsia.<sup>22</sup> A 20% incidence of microalbuminuria compared with 2% in controls was found within 7 years of delivery. However, they used a semiquantitative method to detect microalbuminuria, which is known to be less sensitive than the radioimmunoassay technique applied in our study. Bar and colleagues demonstrated that women who had a pregnancy complicated by pre-eclampsia 3 to 5 years earlier had a higher rate of microalbuminuria (42%) than women with uncomplicated pregnancies (0%).<sup>19</sup> A study by Shammas and Maayah identified significant microalbuminuria in 23% of women with a history of pre-eclampsia compared to only 3% in women with normal blood pressures during pregnancy.<sup>23</sup> In contrast, another study by Jacquemyn and colleagues found no difference in abnormal kidney function between women with a history of the HELLP syndrome followed for 5 years or more compared to women with no evidence of hypertension during pregnancy.<sup>24</sup> Similarly, Spaan and coworkers found no difference in microalbuminuria between women with a history of pre-eclampsia (2%) followed for 23 years (range, 20 to 28 years) compared to women with no evidence of pre-eclampsia (3%) during pregnancy.<sup>20</sup>

## CONCLUSIONS

We found that a history of pre-eclampsia is associated with subsequent hypertension and microalbuminuria. Since there was not enough data about the history of patient, we cannot conclude that pre-eclampsia is a risk factor of chronic kidney disease or hypertension. We showed that in patients with a history of pre-eclampsia, there is increased rate of hypertension and microalbuminuria after pregnancy. It means that pre-eclampsia on the basis of our study is an alarming sign of hypertension and chronic kidney disease in long term.

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## CONFLICT OF INTEREST

None declared

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