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Incidence and Risk Factors That Predict Chronic Hypertension after Delivery in Women with Hypertensive Disorders of Pregnancy

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ABSTRACT

Background: hypertensive disorders of pregnancy (HDP) are important disorders complicating 5% to 10% of all pregnancies and they are a leading cause of maternal and fetal morbidity and mortality and associated with subsequent development of chronic hypertension. **Aim of the work:** this study aimed to determine the incidence and risk factors that predict chronic hypertension after delivery in women with hypertensive disorders of pregnancy. **Patients and Methods:** this cohort prospective study was conducted at Ain Shams University, Maternity Hospital. This study included a sample of 207 pregnant women with hypertensive disorders of pregnancy, followed up for persistence of hypertension after 3 months postpartum. **Results:** the subjects were categorized into case group (n=25, 12.1%) included patients diagnosed as chronic hypertension at the postpartum period and the control group (n =182, 87.9%) included the rest of the study subjects. Clinical and demographic factors were evaluated. By multivariate regression analysis, age, gestational age at diagnosis, parity, preeclampsia and early onset hypertension with end-organ dysfunction were predictors of progression to chronic hypertension. **Conclusion**: 12.1% of women diagnosed with HDP continued with persistent hypertension after delivery and some clinical and demographic risk factors such as old maternal age at HDP, lower gestational age at diagnosis, multiparous women, preeclampsia and hypertension with end-organ dysfunction were predictors of progression to chronic hypertension. **Recommendations**: further studies on a larger scale of patients are needed to confirm the current results.

Keywords: risk factor, chronic hypertension, delivery, hypertensive disorders of pregnancy.

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) are important disorders with lethal effects on mothers and children (1). They complicate 6–8% of pregnancies and usually resolve postpartum (2) and associated with pulmonary edema, stroke, acute kidney injury, disseminated intravascular coagulopathy, and death in the antepartum period (3). Clinical monitoring, risk factor evaluation, and early intervention could benefit women with hypertension in pregnancy (4). HDP is strongly and associated with future hypertension and women who experience this condition should be counseled regarding lifestyle modification and careful ongoing blood pressure monitoring, this might be provided to all pregnant and postpartum women with identifiable risk factors for future hypertension (5). Greater awareness of this association may lead to earlier diagnosis and improved management, thus reducing a proportion of the morbidity and mortality from such diseases (6). Postpartum hypertension can be related to persistence of gestational hypertension, preeclampsia, or preexisting chronic hypertension, or it could develop de novo postpartum secondary to other causes. The differential diagnosis is extensive, and varies from benign (mild gestational or essential hypertension) to life-threatening such as severe preeclampsia, eclampsia and cerebrovascular accidents (7).

Several metabolic and obstetric risk factors (eg. obesity) related to hypertension postpartum in the short term and predisposed to the subsequent development of chronic hypertension after preeclampsia in initially normotensive women (8).

Preeclampsia may be the better predictor of future cardiovascular diseases since it was associated with a wider range of cardiovascular risk factors (9). Proteinuria in hypertensive pregnancy diseases is associated with a longer persistence of hypertension postpartum (10).

A recent study showed that some clinical and demographic risk factors such as early onset hypertension with end-organ dysfunction, higher pre-pregnancy BMI and smoking were reliable predictors of progression to chronic hypertension in the postpartum period (11).

Postpartum hypertension can threaten well-being and longevity in life. Controlling the high BP during antepartum and postpartum periods is related to reduce maternal morbidity and mortality (12).

Stepwise approach toward the diagnosis and management of women with persistent hypertension postpartum should be provided (7).

Currently, there is very little information on the clinical risk factors of chronic hypertension at the postpartum period. This study aimed to determine the incidence and risk factors that predict chronic

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hypertension after delivery in women with hypertensive disorders of pregnancy.

PATIENTS AND METHODS

This was a cohort prospective study conducted at Ain Shams University, Maternity Hospital. This study included a sample of 207 pregnant women with hypertensive disorders of pregnancy.

Sample size justification

Sample size would be calculated using PASS® [13]. version11 program, setting the type-1 error (α) at 0.05 and the power (1-β) at 0.95. The primary outcome measure would be incidence of women with persistent hypertension after 3 months postpartum among women with hypertensive disorders of pregnancy. Results from a previous study [11] showed that the incidence of chronic HTN was 6.8% among females with Hypertensive disorders of pregnancy (HDP). So, calculation according to these values produced a minimal sample size of 207 cases.

Inclusion criteria

This study included all pregnant women who were developed either gestational hypertension or preeclampsia.

Gestational hypertension [14]: new onset of hypertension after 20 weeks of gestation. The diagnosis requires that the patients have elevated blood pressure (systolic ≥ 140 or diastolic ≥ 90 mm Hg), previously normal blood pressure, no proteinuria and no manifestations of preeclampsia or eclampsia.

Preeclampsia [14]: is defined as elevated blood pressure after 20 weeks of gestation (≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic measured 6 hours apart) plus proteinuria (> 0.3 g/24 hours). In the absence of proteinuria, new-onset hypertension with platelet count below 100000/μL, serum creatinine concentration of 1.1 mg/dL, doubling of the serum creatinine concentration in the absence of other renal disease, levels of liver transaminases elevated to twice the normal concentration, pulmonary edema or cerebral or visual symptoms defines preeclampsia.

Preeclampsia with severe features, formerly (severe preeclampsia) [14]: in a patient with preeclampsia, the presence of systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on two occasions at least four hours apart while the patient is on bed rest, platelet count below 100000/μL, serum creatinine concentration of 1.1 mg/dL, doubling of the serum creatinine concentration in the absence of other renal disease, levels of liver transaminases elevated to twice the normal concentration, pulmonary edema or cerebral or visual symptoms indicates a diagnosis of preeclampsia with severe features.

Exclusion criteria

1- Chronic hypertension prior to pregnancy.

2- Comorbidities such as renal disease (including the glomerulonephritis, polycystic kidney disease and chronic kidney diseases), heart disease (including angina pectoris with medication, valvular heart disease and atrial septal defect), diabetes mellitus (DM) and vascular diseases.

All included women were subjected to the following:

1. History

Detailed personal, present, menstrual, obstetric, past and family histories were included.

2. Clinical examination including:

● **General examination**:

a. Assessment of vital data (blood pressure, heart rate, respiratory rate and body temperature).
b. Assessment of general condition (pallor of mucous membranes, yellowish discoloration of the sclera (in day light), lower limb edema, visual symptoms, severe headache, altered mental status or pulmonary edema.
c. Measurement of body mass index (BMI) = weight (kg) / (height m)² where the height is the distance from the bottom of the feet to the top of the head while standing erect in meters.

● **Abdominal examination:**

a. Inspection for shape, contour, pigmentation and scars.
b. Fundal level, fundal grip, umbilical grip, first pelvic grip and second pelvic grip.
c. Auscultation of fetal heart sounds by pinard's stethoscope or by sonicaid.

3. Investigations

● **Laboratory**

- Complete blood picture.
- Urine analysis for proteinuria.
- ALT, AST.
- Serum creatinine.

● **Ultrasonography:**

- Fetal biometry for fetal dating, fetal viability and fetal number.

4. Informed consent was obtained from each subject following a detailed explanation of the objective of this study.

5. The following risk factors were included [11]: maternal age at diagnosis with HDP, gestational age at diagnosis of HDP,body mass index (BMI),

smoking, end organ dysfunction, presence of proteinuria and parity (primi or multipara).

6. The primary outcome measure was incidence of women with persistent hypertension (continued elevation of blood pressure ≥ 140 / 90 mm Hg or blood pressure controlled < 140/90 only by medication) after 3 months postpartum among women with hypertensive disorders of pregnancy.

The secondary outcome measure was presence of possible risk factors that predict chronic hypertension; all patients were divided into two groups according to persistence of hypertension after 3 months postpartum or not.

a) **Case group:** patients with persistent hypertension after 3 months postpartum.
b) **Control group:** patients who became normotensive within 3 months postpartum.

Both groups were compared according to the risk factors included in the analysis and according to the standard statistical methods.

The study was done after approval of ethical board of Ain Shams university and an informed written consent was taken from each participant in the study.

Statistical analysis

Analysis of data was done using SPSS (Statistical Package for Social Sciences) program version 18.

To describe the studied sample, quantitative data were presented as minimum, maximum, mean and standard deviation. Qualitative data were presented as count and percentage.

An independent sample t test was used to compare quantitative data between cases and controls groups and Chi-Square test was used to compare qualitative data between them.

Multiple logistic regression analysis with the significant variables (P<0.05) on univariate analysis was conducted to choose the independent clinical predictors of persistent hypertension. Receiver-operating characteristic (ROC) analysis was conducted and the area under the curves (AUCs) was used to compare predictive ability of different regression models. P value < 0.05 was considered statistically significant.

- **P- value: level of significance**

-P>0.05: Non significant (NS).
-P< 0.05: Significant (S).
-P<0.01: Highly significant (HS).

RESULTS

Baseline Characteristics

Finally, 207 enrolled patients were included in the 2 groups. The included subjects were further divided into case and control groups. The case group (n=25, 12.1%) included patients diagnosed as chronic hypertension at the postpartum period. The control group (n =182, 87.9%) included the rest of the study subjects.

A total of 207 patients in this study were characterized with established risk factors with subsequent chronic hypertension in the postpartum period. There were statistically significant differences in pre-eclampsia (P<0.001) and hypertension with end-organ dysfunction (P<0.001). The women in the case group were older (26.24 ± 2.30 vs 24.77 ± 2.25, P=0.01) and had higher BMI (32.80 ± 1.73vs 31.90 ± 1.60, *P*=0.003) compared to the control group. There was the significant difference in the number of the delivery (primi vs multipara) (P=0.01) at HDP. Gestational age of fetus in weeks was statistically different between the case vs control groups (33.64 ± 1.75vs 34.58± 1.39, P=0.02). Also percent of smokers was significantly higher among cases than controls (P=0.04).

Predictors of Progression of the Chronic Hypertension

In multivariate regression analysis, age, gestational age at diagnosis, parity, preeclampsia and early onset hypertension with end-organ dysfunction were predictors of progression to chronic hypertension. We used a series of multiple logistic regression models to estimate the adjusted odds ratio of chronic hypertension in the postpartum period.

In model 1, we adjusted for maternal age at HDP and.

In model 2, we included gestational age at diagnosis and parity.

In model 3, we included maternal age at HDP and preeclampsia.

In model 4, we included gestational age at diagnosis and hypertension with end-organ dysfunction.

The value of AUCs was used to check the incremental effect of predictors of progression to chronic hypertension in the respective models. These results show that model I (age and GA at diagnosis) has the higher predictive ability for prediction of persistent hypertension after delivery, while model III (age and preeclampsia) has the lower predictive ability.

Table 1: comparison between cases and controls regarding personal data

		Persistent hypertension				t*	P value
		Yes (N=25)		No (N=182)			
		Mean	SD	Mean	SD		
Age at diagnosis		26.24	2.30	24.77	2.25	3.05	0.003
Body mass index		32.80	1.73	31.90	1.60	2.61	0.01
		N	%	N	%	X^{2**}	P value
Smoking	No	23	92.0%	181	99.5%	8.54	0.04
	Yes	2	8.0%	1	0.5%	FE	

*Independent samples t test **Chi square test

Table 1 showed that mean age of cases was significantly higher than controls (p value < 0.05). Cases have higher BMI (p value <0.05) and percent of smokers was significantly higher among cases than controls.

Table 2: comparison between cases and controls regarding obstetric history

		Persistent hypertension				t*	P value
		Yes (N=25)		No (N=182)			
		Mean	SD	Mean	SD		
Gestational age at diagnosis		33.64	1.75	34.58	1.39	2.56	0.02
		N	%	N	%	X^{2**}	P value
Parity	Primi	7	28.0%	101	55.5%	6.66	0.01
	Multipara	18	72.0%	81	44.5%		

*Independent samples t test **Chi square test

Table 2 showed that gestational age at diagnosis was significantly lower than controls (p value < 0.05). Parity was statistically significant (p value < 0.05).

Table 3: comparison between cases and controls regarding clinical data

		Persistent hypertension				X^{2*}	P value
		Yes (N=25)		No (N=182)			
		N	%	N	%		
Proteinuria	No	8	32.0%	42	23.1%	0.96	0.33
	Yes	17	68.0%	140	76.9%		
gestational HTN	No	17	68.0%	140	76.9%	0.96	0.33
	Yes	8	32.0%	42	23.1%		
Preeclampsia	No	15	60.0%	47	25.8%	12.24	<0.001
	Yes	10	40.0%	135	74.2%		
End organ disease	No	18	72.0%	177	97.3%	25.67	<0.001
	Yes	7	28.0%	5	2.7%		

*Chi square test

Table 3 showed that presence of preeclampsia and end organ disease symptoms were statistically significant (p value < 0.05). Proteinuria and gestational HTN were not significant different (p value >0.05).

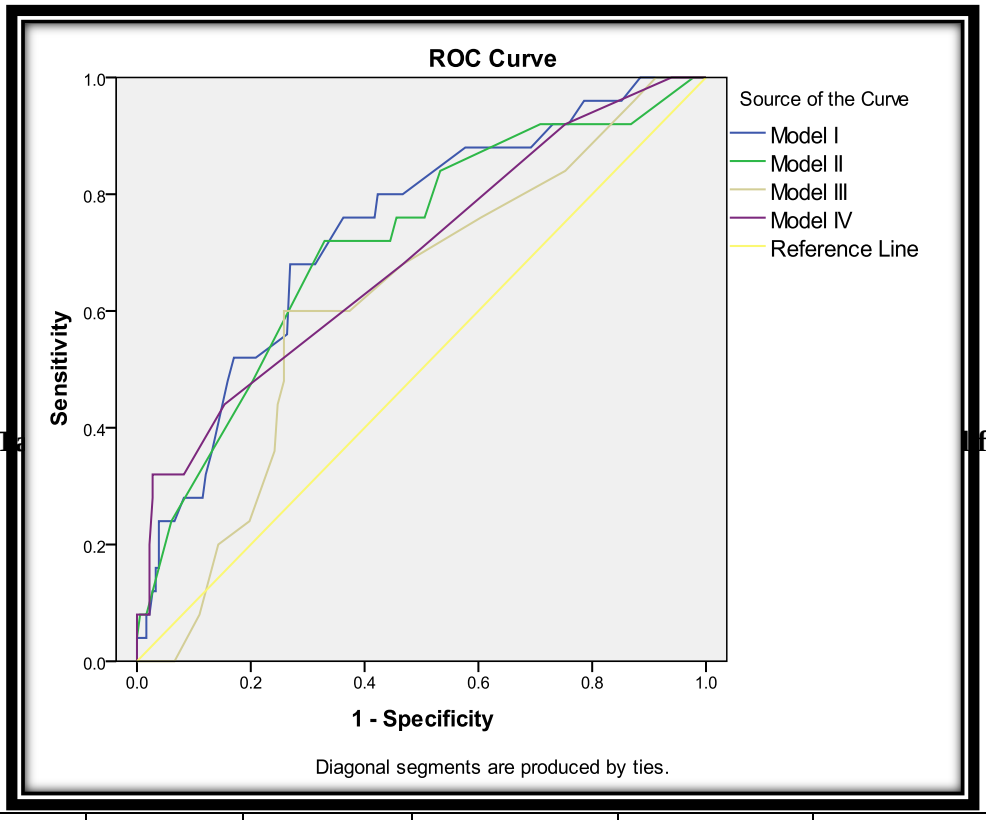
Table 4: logistic regression analysis for risk factors of chronic hypertension

	B	Sig.	Odds ratio	95% C.I. for odds ratio	
				Lower	Upper
Model I:					
Age	0.322	<0.001	1.380	1.159	1.644
GA	-0.299	<0.001	0.742	0.648	0.849
Model II:					
GA	-0.080	<0.001	0.923	0.902	0.945
Parity	1.252	0.009	3.497	1.360	8.990
Model III:					
Age	-0.041	<0.001	0.960	0.939	0.982
Preeclampsia	-1.595	<0.001	0.203	0.087	0.472
Model IV:					
GA	-0.066	<0.001	0.936	0.923	0.949
EOD	2.493	<0.001	12.094	3.512	41.650

GA: gestational age, EOD: end organ dysfunction

Table 4 showed four different models for prediction of persistent hypertension using different predictors.

Fig.1: comparison of receiver-operating characteristic (ROC) analysis for different logistic regression models



Ta **fferent logistic regression**

	AUC	SE	Sensitivity	Specificity	95% CI	
					Lower Bound	Upper Bound
Model I	0.736	0.052	76%	63.7%	0.634	0.838
Model II	0.715	0.056	72%	67%	0.605	0.825
Model III	0.620	0.056	74.2%	60%	0.509	0.730
Model IV	0.692	0.059	68%	53.3%	0.575	0.808

AUC (Area under the curve)

The above fig. showed that model I (age and GA at diagnosis) has the higher predictive ability for prediction of persistent hypertension after delivery. While, model III (age and preeclampsia) had the lower predictive ability.

DISCUSSION

Hypertensive disorders of pregnancy (HDP) had lethal effects on mothers and their children [(1)]. They complicated 6–8% of pregnancies and usually resolve postpartum [(2)] and they are associated with pulmonary edema, stroke, acute kidney injury, disseminated intravascular coagulopathy and death in the antepartum period [(3)].

Clinical monitoring, risk factor evaluation and early intervention could benefit women with hypertension in pregnancy [(4)]. HDP is strongly associated with future hypertension, and women who experience this condition should be counseled regarding lifestyle modification and careful ongoing blood pressure monitoring, this might be provided to all pregnant and postpartum women with identifiable risk factors for future hypertension [(5)]. Greater awareness of this association may lead to earlier diagnosis and improved management, thus reducing a proportion of the morbidity and mortality from such diseases [(6)].

Currently, there are little informations on the clinical risk factors of chronic hypertension at the postpartum period. So, this study tried to determine the incidence and risk factors that predict chronic hypertension after delivery in women with hypertensive disorders of pregnancy.

Our study was a cohort prospective study aiming to determine the incidence and risk factors that predict chronic hypertension after delivery in women with hypertensive disorders of pregnancy,

conducted at Ain Shams University Maternity Hospital for a period of six months from February 2017 to August 2017.

Our study involved 207 pregnant women diagnosed with new onset hypertension with pregnancy in the absence of any comorbidity. Hypertension with pregnancy is diagnosed by S ystolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient [(14)].

Patients were investigated for the presence of established potential risk factors that might predict persistent hypertension after delivery and they are maternal age at diagnosis with HDP, gestational age at diagnosis of HDP Body mass index (BMI), smoking, presence of proteinuria and parity.

IN the present study patients were followed up for 3 months after delivery for the persistence of hypertension or not. Accordingly they had been divided into case and control groups and were compared as regard the established risk factors. In this study, the main finding was that, of the 207 patients with diagnosis of new onset hypertension with pregnancy, 25 (12.1%) patients had persistent hypertension after 3 months postpartum. Old maternal age, high BMI, preeclampsia, early onset hypertension with end-organ dysfunction, early gestational age at diagnosis, high parity and smoking were statistically significant risk factors. Among them maternal age, gestational age at diagnosis, parity, preeclampsia and hypertension with end-organ dysfunction were predictors of progression to chronic hypertension.

A study done by **Hwang *et al.*** [(11)] showed that the incidence of patients with persistent hypertension after 6 months postpartum was 6.8% and significant risk factors were lower in gestational age, older maternal age, high pre-pregnancy BMI, number of the pregnancy (primi vs multigravida),preeclampsia, early onset hypertension with end-organ dysfunction and smoking [(11)]. Our results agree with those in this study as regard risk factors and predictors of chronic hypertension after delivery in women with HDP except for the incidence which was 12.1% in ours; this may be related to the shorter duration of postpartum follow up for persistence of hypertension in our study (3 months) after which some of the hypertensive patients would regain normal blood pressure, higher BMI in our studied patients or different race (Caucasian and Asian).

Another study done by **Spaan *et al.*** [(8)] concluded that hypertension at postpartum screening (17% of all cases) was related to obesity , elevated fasting levels of insulin, low-density lipoprotein, microalbuminuria, family history of hypertension, and delivery before 34 weeks of gestation [(8)]. Our results came in accordance with this as regard obesity, proteinuria and early onset hypertension as risk factors for chronic hypertension.

Also **Nakimuli *et al.*** [(15)] performed a prospective cohort study of hypertension persisting after preeclampsia at Mulago Hospital, Uganda that involved 188 women with preeclampsia and they found that 64 (34%) had persistent hypertension at three months after delivery. Women who had persistent hypertension were older than those who became normotensive. The gestational age at delivery and birth weight were lower among women who had persistent hypertension. More women in this group were multiparous. None of the women reported ever smoking and all women had conceived naturally. The women's age, parity, gestational age at delivery, and severity of preeclampsia had significant risk of persistent hypertension, among them women's age (especially among those aged 35 years or more) and multiparity were statistically significant in predicting persistent hypertension [(15)]. Our result came in accordance with those in this study except for the incidence which was 12.1% in ours, this may be due to inclusion of gestational hypertension in our study and may be related to the different race (Caucasian and Negro).

Our findings suggested that clinicians should determine the occurrence of risk factors in all pregnant women and accordingly guide lifestyle modification such as weight reduction, and regularly BP monitoring, with continued care through the postpartum period, and future by their other medical providers.

The medical providers have a role providing timely patient education, continuous monitoring of signs and symptoms, and prompt and appropriate case management. Our results also indicate that the patients would need ongoing hypertension management provided by cardiologists or nephrologists in the associated divisions as well as possible long-term antihypertensive medications.

The risk factors we identified were easy to assess and handle in the clinical field. Furthermore, the prevalence of metabolic modifiable risk factors such as obesity and high BMI was high at postpartum screening. The results suggest that lifestyle intervention would be beneficial to the women with chronic hypertension after delivery.

CONCLUSION AND RECOMMENDATIONS

Hypertensive disorders of pregnancy (HDP) are strongly associated with future hypertension; identification of risk factors for subsequent hypertension may be beneficial in earlier diagnosis and improved management, thus reducing a proportion of the morbidity and mortality from such diseases.

We showed that 12.1% of women diagnosed with HDP continued with persistent hypertension after delivery and some clinical and demographic risk factors such as older maternal age at HDP, lower gestational age at diagnosis, multiparous women, preeclampsia and hypertension with end-organ dysfunction were predictors of progression to chronic hypertension.

Further large population-based studies, with long term follow up, are needed to determine the important risk for ischemic cardiovascular and cerebrovascular diseases among women who had new onset hypertensive disorders of pregnancy.

We concluded that 12.1% of women diagnosed with HDP continued with persistent hypertension after delivery and some clinical and demographic risk factors such as old maternal age at HDP, lower gestational age at diagnosis, multiparous women, preeclampsia and hypertension with end-organ dysfunction were predictors of progression to chronic hypertension.

Abbreviations: **ALT** = alanine aminotransferase, **AST** = aspartate aminotransferase, **AUCs** = area under the curves, **BMI** = body mass index, **BP** = blood pressure, **DM** = diabetes mellitus, **EOD** = end organ dysfunction , **GA** = gestational age, **HDP** = hypertensive disorders of pregnancy, **HTN**=hypertension , **OR** = odd ratios, **ROC** = receiver-operating characteristic, **SD** = standard deviation.

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