Risk Estimation of Metabolic Syndrome at One and Three Years After a Pregnancy Complicated by Preeclampsia

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Abstract

Background: Our goal was to determine the prevalence of metabolic syndrome in women following a pregnancy complicated by preeclampsia and to determine whether this changes between one- and three-years postpartum.

Methods: We recruited women into a longitudinal prospective cohort following a pregnancy with or without preeclampsia. The prevalence of cardiometabolic factors were assessed at one- and three-years postpartum. A total of 217 women completed a visit at one year postpartum (n = 99 preeclampsia, n = 118 control subjects) and 120 completed a visit at three-years (n = 73 preeclampsia, n = 47 control subjects).

Results: The prevalence of metabolic syndrome at one- and three-years postpartum was significantly greater in women who had preeclampsia (18.18% at one year, 21.92% at three-years) than in control subjects (6.78%, 6.38%) ($P < 0.05$), but did not change over time.

Conclusions: Given the difficulty in following women long-term, either clinically or as part of study, and because cardiometabolic factors do not change significantly between one- and three-years postpartum, strategies for health preservation and disease prevention should be adopted in the first-year postpartum.

Résumé

Contexte : Notre objectif était de déterminer la prévalence du syndrome métabolique chez les femmes à la suite d'une grossesse compliquée par la présence d'une prééclampsie, ainsi que de déterminer si cette situation évoluait entre la première année et la troisième année suivant l'accouchement.

Méthodes : Nous avons sollicité la participation de femmes à une cohorte prospective longitudinale à la suite d'une grossesse s'étant accompagnée ou non d'une prééclampsie. La prévalence des facteurs cardiométaboliques a été évaluée à un an et à trois ans postpartum. Au total, 217 femmes ont fait l'objet d'une consultation à un an postpartum (n = 99 cas de prééclampsie, n = 118 témoins) et 120 en ont fait l'objet d'une à trois ans postpartum (n = 73 cas de prééclampsie, n = 47 témoins).

Résultats : Bien que la prévalence du syndrome métabolique à un an et à trois ans postpartum ait été considérablement plus élevée chez les femmes qui avaient connu une prééclampsie (18,18 % à un an, 21,92 % à trois ans) que chez les témoins (6,78 %, 6,38 %) ($P < 0,05$), cette situation n'a pas connu d'évolution avec le temps.

Conclusions : Compte tenu de la difficulté d'effectuer le suivi des femmes à long terme, que ce soit en clinique ou dans le cadre d'une étude, et puisque les facteurs cardiométaboliques ne connaissent pas une évolution significative entre la première et la troisième année suivant l'accouchement, des stratégies visant le maintien de la santé et la prévention de la maladie devraient être adoptées au cours de la première année postpartum.

Key Words: pregnancy, primary prevention, screening, metabolic syndrome

Competing Interests: None declared.

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INTRODUCTION

It is well established that the development of preeclampsia,[1,2] gestational hypertension, gestational diabetes,[3–5] placental abruption,[6] preterm birth,[7] and delivery of a growth-restricted baby[1] are clinically identifiable markers for a woman's increased risk of premature cardiovascular disease and cardiovascular death.[8] We have previously shown that many women who develop preeclampsia either already have underlying cardiovascular risks or are prone to developing them.[8] The American Heart Association now identifies these pregnancy complications as important components in

the assessment of a woman's risk for developing future cardiovascular disease.[9]

We hypothesize that pregnancy and the postpartum period provides a window of opportunity for screening and management of cardiovascular risks to prevent premature cardiovascular morbidity and mortality. Specifically, the identification of these pregnancy-related complications allows for the early detection of cardiovascular risk. Furthermore, the changes surrounding pregnancy provide an opportunity to implement lifestyle modifications and/or pharmacotherapy. For the purpose of this study, we hypothesized that an increasing number of women who had pregnancies complicated by preeclampsia would demonstrate cardiovascular risks, specifically the cluster referred to as the metabolic syndrome (three or more of elevated blood pressure, abdominal obesity, elevated serum triglycerides, decreased serum HDL cholesterol, or elevated fasting plasma glucose),[10] beyond the first-year postpartum. Clustering of risk factors that are independent and interrelated predicts a significant increase in cardiovascular disease risk, with the risk for cardiovascular events (i.e., myocardial infarction, stroke, coronary revascularization, cardiovascular death) increasing with the number of underlying risk factors. Our goal was to carry out a secondary analysis of the Pre-Eclampsia New Emerging Team (PE-NET) longitudinal prospective cohort[2] data to determine the prevalence of metabolic syndrome at one- and three-years after a pregnancy complicated by PE, and to determine whether the prevalence changes over this time period.

METHODS

The recruitment criteria and process have previously been described.[2] In brief, women were recruited at the Kingston General Hospital or the Ottawa General Hospital between September 2003 and October 2009 following either a pregnancy complicated by preeclampsia or an uncomplicated pregnancy (with no prior history of preeclampsia). Women with known chronic hypertension or diabetes were excluded from the study. A study reminder was mailed every six months and at the baby's birthday. Women were asked to return at one- and three-years postpartum for a clinical assessment and reminded by telephone or email one week prior to a scheduled visit. Every effort was made to accommodate women's schedules, and home visits were made if requested. If subjects missed their appointment, we attempted to contact them weekly for the following month before considering them lost to follow-up.

For statistical analysis, the mid-*P* exact chi-square test and the *t* test were used to compare physical and biochemical cardiovascular risk markers for women in the control group with women in the preeclampsia group at one- and three-years postpartum. The mid-*P* exact chi-square test was used to compare the prevalence of metabolic syndrome between the groups at each interval; these data are also presented as Taylor series risk ratios. The mid-*P* exact chi-square test was also used to compare the prevalence of metabolic syndrome within the groups at each time interval to determine whether there were any changes over time. The McNemar test was used to compare the movement of individuals into or out of the metabolic syndrome disease state from one- to three-years postpartum; thus, only individuals with complete data for both follow-up visits were included. When appropriate the Fisher exact test was used in place of the mid-*P* exact chi-square test. $P < 0.05$ was considered statistically significant. Statistical analysis was completed using R version 2.10.1 (R Foundation for Statistical Computing, Vienna, Austria) and OpenEpi version 2.3.1.

RESULTS

Of the 217 women who had a complete visit at one-year postpartum (n = 99 preeclampsia, n = 118 control subjects), 120 had a complete visit at three-years postpartum (n = 73 preeclampsia, n = 47 control subjects); a follow-up visit was considered complete when a participant's BMI, blood pressure, and fasting blood investigations were recorded. At the three-years postpartum visit, 29 participants (n = 11 preeclampsia, n = 18 control subjects) were excluded because of a new active pregnancy, failure to provide a fasting blood specimen, or inability to schedule an appointment. A further 68 women (n = 15 preeclamptic, n = 53 control subjects) were lost to follow-up because the study at the Ottawa site shut down before the follow-up at three-years postpartum. The baseline characteristics at recruitment for those women who were lost to follow-up were not different ($P > 0.05$) from those who did have a follow-up at three-years, as previously reported.[11] We have previously reported on the first 140 women (n = 70 preeclampsia, n = 70 control subjects) who had a visit at one year,[2] as well as on further cardiovascular risk scoring on the 217 women who had a complete visit at one year.[11]

The baseline characteristics of the preeclamptic and control women at the time of recruitment who were seen at one- and three-years are presented in Table 1. At the follow-up visits, baseline characteristics of the women in the preeclampsia group differed significantly from the

Table 1. Comparison of baseline characteristics at recruitment

	Participants followed at one-year postpartum		Participants followed at three-years postpartum	
	Preeclampsia (n = 99)	Control subjects (n = 118)	Preeclampsia (n = 73)	Control subjects (n = 47)
Maternal age, years, mean (SD)	30.3 (5.7)	30.3 (4.1)	30.5 (5.4)	30.1 (4.5)
Maternal race, n (%)				
White	95 (96.0)	118 (100.0)	70 (95.9)	47 (100.0)
Other	4 (4.0)	0 (0.0)	3 (4.1)	0 (0.0)
Maternal education level, n (%)				
High school or less	16 (16.1)	5 (4.2)	13 (17.8)	5 (10.6)
Post secondary not complete	9 (9.1)	17 (14.4)	5 (6.9)	6 (12.8)
Post secondary complete	74 (74.8)	96 (81.4)	55 (75.3)	36 (76.6)
Household income ($), n (%)				
≤ 29 999	8 (8.3)	8 (7.0)	6 (8.5)	4 (8.5)
30 000 to 59 999	21 (21.9)	17 (14.9)	16 (22.5)	10 (21.3)
60 000 to 89 999	29 (30.2)	30 (26.3)	31 (43.7)	14 (29.8)
≥ 90 000	38 (39.6)	59 (51.8)	18 (25.3)	19 (40.4)
Did not respond	3 (3.0)	4 (3.9)	2 (2.7)	0 (0.0)
Maternal smoking, n (%)				
Yes	9 (9.1)	5 (4.2)	5 (6.8)	1 (2.1)
No	90 (90.9)	113 (95.8)	68 (93.2)	46 (97.9)
Parity, n (%)				
Nulliparous	64 (64.6)	73 (61.9)	49 (67.1)	27 (57.4)
Multiparous	35 (35.4)	45 (38.1)	24 (32.9)	20 (42.6)
Previous pregnancy with PE, n (%)				
Yes	8 (8.1)	0 (0.0)	6 (8.2)	0 (0.0)
No	91 (91.9)	118 (100.0)	67 (91.8)	47 (100.0)
Maternal weight, kg, mean (SD)	71.3 (15.7)	70.1 (14.8)	70.6 (14.9)	71.5 (14.6)
Maternal BMI, kg/m^2, mean (SD)	26.7 (5.7)	25.5 (5.1)	26.5 (5.7)	26.1 (5.5)

PE: preeclampsia

control group only in maternal educational level achieved for those followed-up at one year; there were no significant differences in baseline characteristics at the three-year visit. Nor did the baseline characteristics of each group (preeclamptic or control) followed up at one year differ from those followed up at three years. The physical and biochemical cardiovascular risk variables at follow-up that make up the metabolic syndrome are shown in Table 2. Compared with control subjects, significantly more women ($P < 0.05$) in the preeclampsia group at one year were obese, had elevated systolic and diastolic blood pressures, and were using antihypertensive medication. After three years, only the mean systolic and diastolic blood pressures and the number of women with elevated diastolic pressures in the preeclampsia group were different ($P < 0.05$) from the control group. The scoring method used to determine the presence of the metabolic syndrome is shown in Table 3[10,12,13] and the prevalence of metabolic syndrome in the preeclampsia and control groups is shown in Table 4. The prevalence of metabolic syndrome was significantly greater ($P < 0.05$) in women who had preeclampsia (18.18%, 21.92%) than in control subjects (6.78%, 6.38%) at one and three years, respectively. There were also higher risk ratios for metabolic syndrome in preeclamptic women than in control subjects at one year (RR 2.68; 95% CI 1.22 to 5.90) and three years (RR 3.43; 95% CI 1.06 to 11.14). However, the prevalence of metabolic syndrome did not differ significantly within either the preeclampsia or the control group throughout the years of follow-up ($P > 0.05$). The results of the McNemar test showed no significant difference ($P > 0.05$); individuals with metabolic syndrome at one year postpartum were likely also to have metabolic syndrome at three years, while individuals who were disease-free tended to remain disease-free at each year of follow-up. There was no difference in the prevalence of metabolic syndrome between the different subgroups of

Table 2. Physical and biochemical cardiovascular risk variables measured at each year of follow-up

	Year 1			Year 3		
	Preeclampsia (n = 99)	Control subjects (n = 118)	*P*	Preeclampsia (n = 73)	Control subjects (n = 47)	*P*
BMI, kg/m^2, mean (SD)	28.7 (6.7)	26.3 (5.8)	< 0.05	28.2 (6.8)	28.2 (6.8)	NS
BMI ≥ 30, n (%)	34 (34.3)	25 (21.2)	< 0.05	24 (32.9)	17 (36.2)	NS
BMI < 30, n (%)	65 (65.6)	93 (78.8)		49 (67.1)	30 (63.8)	
SBP, mmHg, mean (SD)	118.3 (10.9)	109.2 (9.4)	< 0.05	116.2 (13.7)	109.6 (11.6)	< 0.05
SBP ≥ 125, n (%)	30 (30.3)	6 (5.1%)	< 0.05	15 (20.5)	4 (8.5)	NS*
SBP < 125, n (%)	69 (69.7)	112 (94.9)		58 (79.5)	43 (91.5)	
DBP, mmHg, mean (SD)	81.2 (9.4)	72.9 (7.9)	< 0.05	80.5 (10.0)	74.9 (8.7)	< 0.05
DBP ≥ 80, n (%)	53 (53.5)	26 (22.0)	< 0.05	37 (50.7)	10 (21.3)	< 0.05
DBP < 80, n (%)	46 (46.5)	92 (78.0)		36 (49.3)	37 (78.7)	
Using antihypertensive medication, n (%)	6 (33.3)	0 (0.0)	< 0.05*	6 (8.2)	0 (0.0)	NS*
Serum triglycerides, mmol/L, mean (SD)	1.32 (1.07)	0.95 (0.73)	NS	1.15 (0.86)	0.91 (0.43)	NS
≥ 1.7, n (%)	20 (20.2)	14 (11.9)	NS	7 (9.6)	3 (6.4)	NS*
< 1.7, n (%)	79 (79.7)	104 (88.1)		66 (90.4)	44 (93.6)	
Serum HDL cholesterol, mmol/L, mean (SD)	1.41 (0.37)	1.42 (0.31)	NS	1.36 (0.34)	1.32 (0.30)	NS
< 1.29, n (%)	44 (44.4)	39 (33.1)	NS	38 (52.1)	24 (51.1)	NS
≥ 1.29, n (%)	55 (55.6)	79 (66.9)		35 (47.9)	23 (48.9)	
Fasting plasma glucose, mmol/L, mean (SD)	4.94 (0.55)	4.85 (0.49)	NS	4.93 (0.45)	4.87 (0.40)	NS
≥ 5.6, n (%)	10 (10.1)	8 (6.8)	NS	6 (8.2)	3 (6.4)	NS*
< 5.6, n (%)	89 (89.9)	110 (93.2)		67 (91.8)	44 (93.6)	

SBP: systolic blood pressure; DBP: diastolic blood pressure; NS: not significant.

*Fisher exact test.

women who developed preeclampsia, including preterm delivery (< 34 or < 37 weeks' gestation) or delivery of a growth-restricted baby (data not shown).

DISCUSSION

We have known for more than a decade that the development of preeclampsia is associated with an increased risk of cardiovascular disease and cardiovascular death.[1,6,7,14,15] What is not understood is the evolution of risk factors in young women following a pregnancy complicated by preeclampsia or one of the other pregnancy-related cardiovascular risk indicators.[8] What is even less defined is the type and frequency of screening that should be undertaken. It appears that initiation of cardiometabolic screening, at either one- or three-years postpartum, specifically for women who have developed preeclampsia will identify the majority of those with underlying risk factors; a significant difference between control women and women who had preeclampsia was seen in systolic and diastolic blood pressures and in the prevalence of the metabolic syndrome at one year (6% vs. 18%) and at three years (6% vs. 22%), with no progressive change over time. However, later screening (i.e., at three-years postpartum or beyond) would potentially result in the identification and treatment of older adults with risk factors present for a longer time and potentially with a greater burden of established atherosclerosis; treatment introduced at this point would not reduce risk to the same extent as maintaining favourable risk factor levels throughout adulthood.[16] Furthermore, there was no significant trend in women who did or did not have preeclampsia either recovering from or developing metabolic syndrome over the study period. Given the difficulty in following women long term (either clinically or within the context of a prospective study), we would suggest that one year postpartum is the optimal time for initiating cardiometabolic screening in order to implement early lifestyle modification and pharmacotherapy with the best chance to prevent future cardiovascular disease.

Our conclusions are limited by the fact that individuals were excluded from the analysis if they were pregnant at the time of planned visits, missed planned visits, or did

Table 3. Metabolic syndrome scoring method[10]

Variable	Scoring method (variable score)	
BMI, kg/m^2	≥ 30 (1)	
	< 30 (0)	
Blood pressure, mmHg	If using antihypertensive medication (1)	
	If not using antihypertensive medication	SBP < 125 and DBP < 80 (0)
		SBP ≥ 125 and DBP < 80 (0.5)
		SBP < 125 and DBP ≥ 80 (0.5)
		SBP ≥ 125 and DBP ≥ 80 (1)
Serum triglycerides, mmol/L*	≥ 1.70 (1)	
	< 1.70 (0)	
Serum HDL cholesterol, mmol/L*	< 1.29 (1)	
	≥ 1.29 (0)	
Plasma glucose, mmol/L*	≥ 5.60 (1)	
	< 5.60 (0)	
The participant has metabolic syndrome if the sum of the variable score is ≥ 3.0.		

SBP: systolic blood pressure; DBP: diastolic blood pressure.

*Scoring method is valid only when blood is drawn after a minimum 12-hour fast.

Table 4. Prevalence of metabolic syndrome in the preeclampsia and control groups at one and three years of follow-up

				Chi-square test (PE vs. control)		
		Preeclampsia	Control	Risk ratio	95% CI	*P*
After one year	Number (sample size)	18 (18.18%) (n = 99)	8 (6.78%) (n = 118)	2.68	1.22, 5.90	0.01
After three years	Number (sample size)	16 (21.92%) (n = 73)	3 (6.38%) (n = 47)	3.43	1.06, 11.14	0.02
Chi-square test (PE vs. PE, control vs. control)	Year 1 vs. 3	*P* = 0.55	*P* > 0.99			
McNemar test (PE vs. PE, control vs. control)	Year 1 vs. 3	*P* = 0.22	*P* > 0.99			

PE: preeclampsia

not complete the requested investigations. Furthermore, there were declining numbers of subjects because of loss to follow-up resulting from the premature closure of the Ottawa site because of staffing and a lack of resources; recruitment in Ottawa stopped in December 2006, and follow-up concluded in September 2008. Potential bias could have occurred in the population followed beyond the first year, although the baseline characteristics of groups and the prevalence of cardiometabolic factors did not change across time. Additionally, this was a secondary analysis of the PE-NET data, so that its statistical power was limited by the sample size of the study.

Recent studies,[17,18] public opinion polls,[19] the *Canadian Heart Health Strategy and Action Plan*,[20] and the American Heart Association's *Effectiveness-based Guidelines for the Prevention of Cardiovascular Disease in Women–2011 Update*[9] state that women's cardiovascular health is a key national and international priority; it should be addressed through improving cardiovascular disease awareness and prevention, and reducing care inequities for women in general and younger women in particular. Given the costs of screening for and treating cardiovascular disease, novel and innovative methods for the early identification of women who should undergo cardiometabolic screening, including biochemical testing, are critical to achieving this goal.[20] Pregnancy and the postpartum period provide us with two of the earliest windows of opportunity to introduce strategies for maternal health preservation and cardiovascular disease prevention.

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