PREECLAMPSIA
foundation

Preeclampsia Identifies Women at Risk for Cardiovascular Disease

Preeclampsia Foundation
Position Statement

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INTRODUCTION

Preeclampsia is one of the most common and potentially life-threatening complications of pregnancy. It affects five to eight percent of all pregnancies and is one of the leading causes of maternal mortality and preterm delivery. But while preeclampsia itself may have devastating consequences, information on long-term effects of this disorder has been limited.

Heart disease is the leading cause of death for women in the United States. One in 2.5 women dies of cardiovascular causes. Heart disease kills more women that next five causes of death combined, including breast cancer. Despite advances in diagnosis and treatment of cardiovascular disease, decrease in rates of cardiovascular disease morbidity and mortality has not been observed in women. The traditional risk factor scoring system used to identify women who are at high risk for heart disease may underestimate the risk for up to one-third of women (1). Early identification of women at high risk for cardiovascular disease may lead to aggressive primary prevention, earlier diagnosis, more aggressive treatment, and improvement in survival.

According to the National High Blood Pressure Education Program (NHBPEP), preeclampsia does not in general increase a woman's risk for developing chronic hypertension, or other heart-related problems. However, while preeclampsia may not cause future cardiovascular disease, this population is substantially enriched with women destined to have these problems, while normotensive pregnancy suggests a better remote prognosis. Thus, the presence of preeclampsia affords a screening opportunity to detect women at risk for future heart disease, and to institute lifestyle changes that may help to avoid such consequences.

The link between heart disease and preeclampsia will be discussed in this Position Statement.

BACKGROUND

Preeclampsia is a disorder unique to human pregnancy. It is characterized by new onset hypertension in a previously normotensive woman and proteinuria after 20 weeks of pregnancy. The disease may also complicate other preexisting maternal disorders such as chronic hypertension, in which case it is termed "superimposed preeclampsia".

The etiology of preeclampsia remains unknown and several theories have been proposed to explain the pathophysiology. A current hypothesis implicates the placenta as the source for maternal pathology. Most prevalent are theories where trophoblastic invasion of the uterine spiral arteries is incomplete, resulting in relative placental ischemia, followed by release of antiangiogenic proteins from the placenta that lead to endothelial dysfunction. This final common pathway, systemic maternal endothelial dysfunction, results in hypertension, increased vascular permeability, and the activation of the coagulation cascade, while the effects of antiangiogenic proteins also affect the filtering mechanism of the kidney and are responsible for the new onset proteinuria. Changes in the levels of circulating angiogenic proteins, implicated in pathogenesis of preeclampsia, have been detected in the mother's blood, prior to onset of clinical disease. This latter observation is important in terms of developing preventive or therapeutic interventions. However, as appealing as this hypothesis is, it remains unproven.

While the above formulation represents that best documented through 2006, there are advocates for other theories. These include aberrant blood volume regulation during pregnancy, exaggerated increments in cardiac output, auto-antibodies to the angiotensin receptor, nutritional deficiencies, abnormal changes in circulating hormones and/or pressor protein, aberrations in both pro- and antioxidant balance, and enhanced systemic inflammatory state are all under investigation.

Several risk factors have been identified in women who developed preeclampsia. They include nulliparity, history of preeclampsia in previous pregnancy, extremes of maternal age, multifetal gestation, several preexisting maternal diseases (chronic hypertension, diabetes mellitus, chronic kidney disease, vascular or connective tissue disease, thrombophilia, high body mass index (BMI)), and possibly, long interval between pregnancies. Of these, obesity (where the risk of preeclampsia increases three-fold), is the most common. As over 30% of women of reproductive age are obese, increased BMI may be responsible for 30-40% of all cases of preeclampsia. Despite known risk factors, it is not possible to predict which woman will develop preeclampsia during pregnancy. Reproductive implications of pregnancy complicated by hypertensive disorder are well known, and women are advised regarding risk of preeclampsia in subsequent pregnancies. Until recently, the long-term risks for maternal health were regarded as low.

Cardiovascular disease in women has emerged as the leading cause of death for women over age 50. Risk factors for cardiovascular disease in women are similar to those in men, and include age, smoking, hypertension, diabetes, and dyslipidemia. Some risk factors are unique to women, such as estrogen exposure and postmenopausal state. Traditional Framingham risk scoring relies on shared risk factors, and may underestimate the risk for cardiovascular events in some women.

The pathophysiology of coronary artery disease may differ in women. Traditional methods of detection of obstructive atherosclerotic disease frequently miss concentric lesions common in women, leading to diagnosis of atypical chest pain in a female patient with acute coronary syndrome (2,3).

Mortality rates following acute myocardial infarction or coronary intervention are higher in women compared to men. Women appear to be under-screened and under-treated, sometimes despite falling into a high-risk category by traditional scoring. The National Heart, Lung, and Blood Institute (NHLBI)'s "The Heart Truth" campaign to direct attention to heart disease in women is designed to change that approach, and women with non-traditional risk factors such as preeclampsia may need a more aggressive approach than that suggested by current guidelines.

CARDIOVASCULAR MORBIDITY AND MORTALITY OF PREECLAMPSIA SURVIVORS

Survival of women with history of hypertensive disorders of pregnancy has been of interest to several authors. One of the best known studies is the long-term follow up of women with eclampsia by Chesley et al (4, 5). In this study mortality of eclampsia survivors was compared to that of women in general population. Increased mortality from cardiovascular disease was seen in Caucasian women who had eclampsia as multiparas, as well as African American women who had eclampsia as nulliparas or multiparas. Eclampsia was not associated with increased mortality

in general or mortality due to cardiovascular disease in women who survived eclampsia in the first pregnancy. The findings of this study were later challenged by several publications.

It should be noted that the sample size was relatively small and follow up for most women less than 30 years, making application of the statistics true for the population in general somewhat difficult, and difference in mortality less likely to be seen due to inclusion of women with history of preeclampsia and eclampsia in the control group.

Parity emerged as a risk factor for several disorders in a study by Beral (6). Based on analysis of the death registry in England and Wales between 1938 and 1960, parity was linked to increased risk for gallbladder disease, cervical cancer, coronary artery disease, stroke, hypertension, and diabetes mellitus. Based on this information, medical complications of pregnancy were warranted a closer investigation.

Several studies have been published in recent years regarding the cardiovascular outcomes of women with history of preeclampsia. The results of selected studies can be seen in Table 1. The results of these studies are different from Chelsey's eclampsia follow up study, mostly due to the difference in selection of the control cohort. In most studies women with a history of normotensive pregnancies were selected as control population, where Chesley considered general population statistics as more appropriate control cohort.

Table 1. Cardiovascular outcomes of preeclampsia survivors

STUDY				RESULTS		
Authors	Year Published	Population Studied	Outcomes Studied	Groups Compared	Outcome	OR/RR/HR (CI 95)
Jonsdottir, Armgrimsson, Geirsson, Sigvaldson, Sigfusson (7)	1995	Iceland	Death from IHD	1.HTN in pregnancy vs. general population 2.Eclampsia vs. general population 3.Preeclampsia vs. general population	Death from IHD Death from IHD Death from IHD	1.47 (1.95-2.02) 2.61 (1.11-6.12) 1.90 (1.02-3.52)
Hannaford, Terry, Hirsch (8)	1997	UK	HTN Acute MI, Chronic IHD All IHD	Toxemia vs. normotensive	HTN Acute MI Chronic IHD All IHD	2.35 (2.08-2.65) 2.24 (1.42-3.53) 1.74 (1.06-2.86) 1.65 (1.26-2.16)
Irgens, Reisaeter, Irgens, Lie (9)	2001	Norway	All Cause Death CV Causes	Preeclampsia vs. normotensive PG delivery >37 w PG delivery 16-36 w	Death CV death CV death	1.3 (1.02-1.57) 1.65 (1.01-2.07) 8.12 (4.31-15.33)
Smith, Pell, Walsh (10)	2002	Scotland	IHD	Preeclampsia vs. normotensive	IHD	2.0 (1.5-2.5)
Kestenbaum, Seliger,	2003	Women of Wash. State	Acute Cardiovascular	1. Gestational HTN vs. normotensive	Acute CV event	2.8 (1.6-4.8)

Easterling, Gillen, Critchlow (11)			Events 1st Thromboembolic Event	2. Mild preeclampsia vs. normotensive 3. Severe preeclampsia vs. normotensive	Acute CV event Acute CV event	2.2 (1.3-3.6) 3.3 (1.7-6.5)
Wilson, Watson, Prescott (12)	2003	Grampian Scotland	HTN CVA	Preeclampsia/ecl vs. normotensive	CVA	3.59 (1.04-12.04)
Arnadottir, Geirsson, Arngrimsson, Jonsdottir (13)	2005	Iceland	IHD, Cerebrovascular Disease	HTN in Pregnancy vs. normotensive	Death due to IHD	1.66 (1.27-2.17)
Funai, Friedlander, Paltiel, Tiram, Xue (14)	2005	Israel	Death (any cause) Cardiovascular disease	1.Preeclampsia vs. normotensive 2. Preeclampsia vs. normotensive	Death Death, IHD	2.0 (1.63-2.46) 3.07 (2.18-4.34)
Wikstrom, Haglund, Olovsson, Lindeberg (15)	2005	Sweden	Fatal and Non fatal IHD	1. Gestational HTN vs. normotensive 2. Mild preeclampsia vs. normotensive 3. Severe preeclampsia vs. normotensive	IHD IHD IHD	1.6 (1.3-2.0) 1.9 (1.6-2.2) 2.8 (2.2-3.7)
Ray, Vermeulen, Schull, RedelmeierKay (16)	2005	Ontario, Canada	Composite CAD CV, PAD	Maternal placental syndrome (PE, gest HTN, placental abruption & infarction) vs. normal Preeclampsia vs. normotensive	CVD CV	2.0 (1.7-2.2) 2.1 (1.8-2.4)
Brown, Dueker, Jamieson (17)	2006	Baltimore - Washington, DC	CVA	Preeclampsia vs. normotensive	CVA	1.63 (1.02-2.62)

Legend:
IHD – ischemic heart disease ▪ HTN – hypertension ▪ CVD – cardiovascular disease ▪ CAD – coronary artery disease ▪ PAD – peripheral artery disease ▪ CVA – cerebrovasacular accident ▪ MI – myocardial infarction

Population-based studies demonstrate an increased risk of cardiovascular disease in preeclampsia survivors as compared to women with a history of normotensive pregnancy. Women with early severe preeclampsia, preeclampsia as multiparas, and especially women with recurrent preeclampsia are at much greater risk and appear to present with cardiovascular disease earlier, whereas women with preeclampsia at term and only as primiparas are more likely to experience increased risk during postmenopausal years (10,14).

These findings do not mean that every preeclampsia survivor is destined to develop heart disease, but rather, that a history of preeclampsia may identify a population at significantly increased risk for cardiovascular events compared to women with a history of healthy pregnancies. A study by Kestenbaum at al demonstrated that over the course of an average follow-up of 10 years women with history of preeclampsia experienced an increase in hazard equivalent to smoking (11). Further studies comparing the risk of cardiovascular disease in patients with hypertensive disorders of pregnancy to the general population should be conducted.

Furthermore, the studies do not answer if the propensity to higher risk for cardiovascular disease in this group is due to underlying conditions that predispose women to both conditions, or due to long-term vascular damage from preeclamptic episodes, the latter being less likely. It is not known if preeclampsia is an independent risk factor and conveys increased risk beyond traditional risk factors for cardiovascular disease, such as obesity, tobacco use, hypertension, diabetes, and hyperlipidemia. Additional research is indicated to evaluate the reason for the association of preeclampsia and increased cardiovascular morbidity.

HEART DISEASE AND PREECLAMPSIA: SHARED RISK FACTORS

Cardiovascular sequellae of preeclampsia prompted a search for a common mechanism or predisposing factors. Several common risk factors have emerged in women with a history of preeclampsia that can explain increased heart disease susceptibility.

One strong predictor of early cardiovascular disease is family history. It is also known that a family history of preeclampsia increases a woman's risk of developing preeclampsia herself. Family history of cardiovascular risk factors in preeclampsia was studied by Ness et al (18). Data analysis demonstrated increased prevalence of coronary artery disease and stroke in families of women who developed preeclampsia. Having two or more relatives with cardiovascular risk increased the risk of preeclampsia by 1.9 (CI95% 1.1 – 3.2), and having two or more relatives with coronary artery disease or cerebrovascular accident increased the risk to 3.2 (CI95% 1.4 – 7.7). Specific mechanisms of disease were not studied in this epidemiologic study.

A connection between certain thrombophilias and preeclampsia has been demonstrated in several studies (19, 20, 21, 22, 23, 24). The strength of association has been variable in different studies and populations, suggesting that while thrombophilia may play a role in pathophysiology of preeclampsia, it does not explain all cases of the disease. Thrombophilia has also been implicated in cardiovascular disease, particularly in younger patients (25). Association between Factor V Leiden, prothrombin gene mutation, and coronary artery disease is stronger in women. Hereditary thrombophilias has been shown to have stronger association with more severe forms of preeclampsia. Both Factor V Leiden and prothrombin gene mutations are common in both populations and interpretation of the studies may be difficult to apply to individual patients.

Microvascular dysfunction has been implicated in pathophysiology of both preeclampsia and cardiovascular disease in women. It has been demonstrated that endothelial dysfunction persists following preeclamptic pregnancy as evident by endothelial-mediated brachial artery dilation and stress-induced forearm blood flow (26, 27). Specific mechanisms of the endothelial dysfunction are not clear. Several systems have been studied as possible candidates, including nitric oxide/ L-arginine (nitric oxide synthase, asymmetric dimethylarginine, dimethylarginine dimethylaminohydrolase gene polymorphism) (28, 29,30,31), renin-angiotensin (angiotensin II receptor gene, ACE insertion/deletion gene polymorphism, angiotensinogen, angiotensin II receptor antibodies) (32 -38), and sympathetic nervous system tone dysregulation (39). The results of the studies are not consistent and are often conflicting in different populations, suggesting that more that one mechanism may be simultaneously involved.

PREECLAMPSIA AND METABOLIC SYNDROME

In recent years increasing attention has been focused on weight as a risk factor for cardiovascular disease. With 60% of the population in the United States being obese or overweight, the prevalence of metabolic syndrome is expected to increase. Criteria for metabolic syndrome in women include abdominal adiposity (abdominal circumference >35 inches), elevated blood pressure (above 130/85 mmHg), elevated fasting glucose (above 100 mg/dL), and dyslipidemia (HDL-cholesterol below 50 mg/dL and triglycerides above 150 mg/dL). Metabolic syndrome has been implicated in pathogenesis of cardiovascular disease, diabetes, non-alcoholic fatty liver disease, kidney disease, and sleep-disordered breathing (40, 41, 42, 43, 44). There is currently no consensus on whether or not metabolic syndrome is a stronger predictor of cardiovascular disease than the sum of its components, but recognition of this condition may facilitate implementation of lifestyle interventions that may prevent progression of the syndrome.

Another feature of preeclamptic pregnancy is insulin resistance. Normal pregnancy is associated with increased insulin levels; however, fasting insulin is higher in preeclamptic pregnancy, even prior to the onset of clinical disease (45, 46). More importantly, this feature does not reverse in the postpartum period. Women with a history of preeclampsia have insulin resistance up to 20 years after the index pregnancy (47, 48). Insulin resistance is a cardinal feature of metabolic syndrome, an important risk factor for cardiovascular disease in women (49). Increased prevalence of diabetes in eclampsia survivors had been noted by Chesley (4). Development of diabetes was preceded by eclampsia by an average of 25 years. This finding may confirm increased incidence of insulin resistance in women with history of hypertensive disorders of pregnancy. Further studies are currently in progress to confirm that finding. Preeclampsia may emerge as a risk marker for diabetes later in life in women who had no gestational diabetes in pregnancy.

High body mass index (BMI) is not always a feature of metabolic syndrome; however, obesity is more common in metabolic syndrome patients. High maternal BMI is a strong predictor of several adverse pregnancy outcomes, including preeclampsia. A large meta-analysis by O'Brien et al demonstrated doubling of the risk for preeclampsia with each BMI increase by 5-7 kg/m2 (50). Limited data is available to confirm that weight loss prior to pregnancy could decrease the risk of preeclampsia, but the results of follow up studies of women with weight loss following bariatric surgery are encouraging. More studies are needed to confirm the findings (51).

Women with a history of preeclamptic pregnancy frequently exhibit features of metabolic syndrome (52, 53, 54). It is unlikely that metabolic syndrome is a late complication of preeclampsia; rather it is likely a condition that would develop in these women even without pregnancy. Women with a history of preeclampsia need to be closely monitored for the development of metabolic syndrome. Counseling about appropriate lifestyle modifications may prevent onset of the syndrome as well as its complications.

PREECLAMPSIA SURVIVORS: RECOMMENDATIONS FOR FOLLOW UP

Preeclampsia survivors frequently receive information about the recurrence of preeclampsia. But they are rarely advised on their increased cardiovascular risk and available interventions for risk reduction. Evidence on appropriate interventions for these women is limited, however, we will review applicability of known evidence-based national guidelines such as Seventh Report of Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) (55) and Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) (56, 57).

Preeclampsia is associated with cardiovascular risk later in life; however, the risk appears to be very different for women who had mild preeclampsia at term versus women who developed severe preeclampsia remote from term. Women with preeclampsia and preterm delivery (prior to 36 weeks) face significantly increased risk for cardiovascular events and thus constitute the highest risk group (10). Until further information on further risk stratification and management is available, the following recommendations are advised:

1. **An accurate history of pregnancy complications should be obtained for every woman.** When possible, actual prenatal and delivery records should be obtained and entered into a woman's medical record. If records are not available, a history may be sufficient for further risk stratification. Women often have excellent recall of their pregnancies, babies' birth weights, and of any complications of these pregnancies (58). Women with severe preeclampsia, preterm delivery, and low birth weight neonates constitute the highest risk group and need the closest monitoring.

2. **A complete assessment of a woman's past medical as well as family history should be performed.** Women with chronic hypertension, diabetes, and other comorbid conditions that may have contributed to the development of preeclampsia are often at increased cardiovascular risk due to the nature of the comorbidities, which should be managed in accordance with national guidelines. A family history of premature cardiovascular disease may identify women who need early aggressive risk factor modifications.

3. **Physical examination and laboratory assessment of preeclampsia survivors should focus on features of metabolic syndrome, which is more prevalent in this population.** Women with a history of hypertensive disorders of pregnancy need to be assessed for obesity, hypertension, and dyslipidemia, as well as abnormal glucose metabolism (impaired fasting glucose, impaired glucose tolerance or diabetes), as these disorders are risk factors for cardiovascular disease, as well as preeclampsia.

4. **Counseling and treatment goals should focus on primary prevention of cardiovascular disease:**

    ☑ **Lifestyle modifications**

    One of the most important steps in cardiovascular disease prevention is the improvement of lifestyle choices. One of the cornerstones of the healthy lifestyle is smoking cessation. Any patient who smokes tobacco should be routinely

advised to quit given significantly increased cardiovascular risk associated with tobacco use. This may be particularly important for preeclampsia survivors, based on one study that found a 40-fold increase in risk for a cardiovascular event if the preeclampsia survivor was a smoker (59). Other healthy lifestyle features include a healthy diet and regular exercise, according to several observational studies (62, 63). Current recommendations call for a diet low in saturated and trans fat, high in fiber and marine omega-3 fatty acids, and calorically appropriate in order to maintain healthy weight (61). Current national guidelines call for 30-60 minutes of exercise daily. While these changes should be recommended to all women, preeclampsia survivors may obtain additional benefits, such as decreased incidence of type 2 diabetes mellitus given improved insulin sensitivity with regular exercise.

☑ Antihypertensive medications

Hypertensive disorders are common in general population and may be more prevalent in preeclampsia survivors. Blood pressure should be monitored on a regular basis, and annual screening can be recommended. Women should be advised on blood pressure levels that are considered normal, and prehypertension as well as hypertension should be treated according to JNC 7 recommendations. Current JNC guidelines define normal blood pressure to be less than 120/80 mm Hg, and levels between 120-139/80-89 are considered prehypertensive. Hypertension is a sustained blood pressure elevation above 140/90, or 130/80 for patients with such comorbidities as diabetes mellitus or chronic kidney disease. Given the possible increased risk of kidney disease in preeclampsia survivors (60), screening for proteinuria and microalbuminuria should be considered standard of care for these patients.

Prehypertension should be treated with aggressive lifestyle modifications, and hypertension with lifestyle modifications as well as pharmacological agents appropriate for individual patient's comorbid conditions. Due to potential metabolic effects of thiazide diuretics as well as beta-blockers (64, 65,66) and recently reported favorable effects of angiotensin receptor blockers on insulin sensitivity, the preference should be given to angiotensin converting enzyme inhibitors (ACE inhibitors), as well as angiotensin receptor blockers (ARBs) (67,68).

While current guidelines do not recommend pharmacologic therapy, a recent clinical trial suggested that there might be benefit in using ARBs in prehypertensive patients to deter progression to hypertension (69). At this point the decision to treat prehypertension with medications may be left to be determined on an individual basis. Women with a history of severe early onset disease may be candidates for early pharmacologic intervention due to significantly increased risk of cardiovascular disease and chronic kidney disease. Further research in formerly preeclamptic patients is needed.

☑ Management of lipid disorders

Disorders of lipid metabolism often occur in conjunction with hypertension as well as impaired insulin sensitivity. Fasting lipid panel should be periodically

checked in preeclampsia survivors due to an increased incidence of abnormal cholesterol levels in this population (70). Recent national guidelines define optimal LDL-C level as under 100, low HDL-C as under 50 for a woman, and recommends intensive lifestyle changes for people with multiple cardiovascular risk factors (metabolic syndrome). ATP III guidelines should be followed, and the appropriate agent discussed with the patients and prescribed in addition to implementing aggressive lifestyle modifications.

HMG-CoA reductase inhibitors (statins) should not be avoided altogether in women of reproductive age due to fear of potential exposure in pregnancy. Instead, benefits and risks of therapy should be discussed, and plans for future pregnancy should be addressed. Women of reproductive age requiring aggressive lipid-lowering therapy, including statins, need to use effective contraception to avoid exposure to such agents during pregnancy. Individual counseling on potential risks and benefits of pharmacological therapy, as well as the decision to use specific drugs should be determined between physician and patient.

Specific goals of therapy as well as threshold for initiation of pharmacologic therapy will depend on the presence of several cardiovascular risk factors and may be guided by available ATP III calculator. Once medications are deemed necessary, it may be considered to lower LDL-C levels to normal (below 100) as lower levels are associated with decrease in cardiovascular events. As was demonstrated by Heart Protection Study, people with several cardiovascular risk factors may benefit from statin therapy even if the pretreatment cholesterol levels were normal (71).

☑ Impaired insulin sensitivity

Women with a history of preeclampsia were identified in several studies as a population with a higher incidence of insulin resistance. Given that finding, it would be considered prudent to screen patients with a history of preeclampsia for diabetes or impaired fasting glucose with periodic fasting glucose measurements. Measurement of plasma glucose should be performed as recommended by the American Diabetes Association. The glucose tolerance test is currently not routinely recommended, however, it may be considered for diagnosis of diabetes. Intensive lifestyle modifications have been demonstrated to be an effective tool in prevention of progression of impaired glucose tolerance to diabetes, and should be routinely recommended to patients with insulin resistance (72).

Fasting insulin measurements are not recommended due to limited experience in clinical practice as well as significant variability of the insulin levels as well as insulin assays. Insulin sensitizers such as metformin or thiazolidinediones are not recommended for routine use in euglycemic patients even though experimental data demonstrate their efficacy in prevention of diabetes (72, 73). Use of medications in patients without diabetes would result in significant expense and exposure of large number of patients to potential side effects, whereas lifestyle modifications are inexpensive and do not carry the risk of adverse reaction.

☑ **Aspirin therapy**

Antiplatelet therapy is one of the cornerstones of both primary and secondary prevention of cardiovascular disease. Current guidelines call for use of aspirin for primary prevention in women in high-risk category (calculated Framingham 10 year risk score above 20%) (74-76). Women in lower risk categories should not be routinely started on antiplatelet therapy due to the risk of adverse events potentially overweighing the cardiovascular benefits in this group of patients. At this time, the risk of women with history of preeclampsia cannot be accurately estimated or calculated based on Framingham data.

Decision on aspirin use may need to be determined based on the severity of the preeclampsia as women with early severe disease have significantly increased risk (up to an eight-fold increase compared to women with normotensive pregnancies) (10). Additional research is clearly needed; meanwhile, adherence to the current guidelines is advised.

CONCLUSIONS

1. In several large studies, women with a history of preeclampsia have been found to develop heart disease at an increased rate compared to women with a history of normal pregnancies.
2. Preeclampsia and heart disease share several risk factors, including family history, thrombophilia, insulin resistance, microvascular dysfunction, and metabolic syndrome.
3. Women with a history of preeclampsia – particularly early morbid preeclampsia – may especially benefit from careful monitoring for conventional cardiovascular risk factors, aggressive lifestyle modifications aimed at prevention of cardiovascular disease, and counseling about implications of pregnancy complications for future pregnancies and future cardiovascular health.
4. Future studies should be focused on further elucidation of the link between preeclampsia and heart disease, screening for early cardiovascular disease in preeclampsia survivors, as well as preventive strategies to improve maternal health following adverse pregnancy outcome.

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