Cardio-metabolic Risk Profile in Women with Previous History of Pre-Eclampsia

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Abstract

Introduction: Preeclampsia is one of the leading causes of maternal and neonatal morbidity and mortality. However there is growing evidence that there are differences during the post partum period between subjects with prior preeclampsia and prior uncomplicated pregnancy and women with a history of preeclampsia are more likely to develop cardiovascular disease later in life. The aim of our study was to assess the cardio-metabolic risk profile in women with previous history of pre-eclampsia and to their counterparts who had normal pregnancy.

Material and Methods: In a hospital based case-control study, 50 women aged 20-45 years who had history of preeclampsia and equal numbers of age matched women who had normal pregnancy were included. Apart from routine anthropometric and biochemical parameters, they were assessed for insulin resistance, Hs CRP (High sensitive C reactive protein) and flow mediated vasodilatation (FMD).

Results: Significant difference was noted with regard to BMI and waist circumference, systolic and diastolic blood pressures, and HOMA-IR which were higher and HDL and FMD were lower in women the previous preeclampsia than women with normal pregnancy. The prevalence of various cardio-metabolic risk factors increased in with increase in duration from index pregnancy.

Conclusion: Women with previous history of preeclampsia had adverse cardio-metabolic profile than those who had normal pregnancy. They had higher insulin resistance and endothelial dysfunction. They also have high prevalence of chronic metabolic disorders with increased duration since index pregnancy.

Introduction

Preeclampsia is a pregnancy disorder, characterized by new onset hypertension and proteinuria that occurs after 20 weeks of pregnancy and complicates 5–8% of pregnancies.¹ Preeclampsia is one of the leading causes of maternal and neonatal morbidity and mortality causing high rates of preterm delivery and intra-uterine growth restriction.² The prevalence of preeclampsia in developing countries ranges from 1.8% to 16.7%.³ Most of the pathological conditions associated with preeclampsia seem to resolve after delivery. However there is growing evidence that there are differences during the post partum period between subjects with prior preeclampsia and prior uncomplicated pregnancy and women with a history of preeclampsia are more likely to develop cardiovascular disease later in life.⁴ ⁵ ⁶

There has been a rise in cardiovascular disease death rates in women aged 35–54, which has been postulated to be secondary to the obesity epidemic.⁷ Cardiovascular disease (CVD) has gained interest in obstetrics in recent years because large observational studies revealed a remarkable increase in the long-term risk of CVD in women who experienced different types of gestational hypertensive disorders. Pre-eclampsia in pregnancy is associated with characteristic cardiovascular and biochemical alterations including vasomotor dysfunction, hypertension, endothelial damage, inflammation, and metabolic disturbances (oxidative stress, dyslipidemia, dysglycaemia).

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and insulin resistance). These alterations are known predictors of future cardiovascular risk in life.8-10

Efforts focusing on improving awareness and preventive strategies particularly in high risk population are needed that can result in an overall decline in the number of cardiovascular deaths. Insulin resistance, and endothelial dysfunction in women with previous preeclampsia have been indicated to contribute to their increased risk of cardiovascular disease.11-13 Furthermore, given that endothelial dysfunction represents an early indicator of cardiovascular risk,14 Assessment of endothelial dysfunction by measuring flow mediated dilatation (FMD) of the brachial artery is considered as potential tool for predicting coronary atherosclerosis.15 Highly sensitive C-reactive protein (hsCRP) is also a well known surrogate marker and good predictors of subclinical atherosclerosis and future cardiovascular events.16

The aim of our study was to assess the cardio-metabolic risk profile in women with previous history of pre eclampsia and in their counterparts who had normal pregnancy.

Material and Methods

We studied 50 women aged 20-45 years who had history of preeclampsia which was identified from medical records at the Department of Obstetrics and Gynecology from the Era’s Lucknow Medical College, Lucknow between January 2014 to July 2016. The diagnosis of preeclampsia was based on criteria of the International Society for the Study of Hypertension in Pregnancy (ISSHP) defined as diastolic blood pressure of 90 mm Hg or more at two consecutive measurements 6 h apart with the patient resting in the semirecumbent position, with or without proteinuria greater than 0.3 g/24 h or more than 1 g/liter (or 2+ with dipstick) in a random sample. The elevation in blood pressure was diagnosed after 20 wk gestation in a previously normotensive woman.17

They were firstly interviewed by phone. Then, they were invited to visit the endocrine clinic during the same phase of their menstrual cycles for sample collection. Exclusion criteria comprised of Diabetes mellitus, Hypertension or chronic kidney disease diagnosed before index pregnancy. Women with malignancy, end stage diseases, chronic inflammatory diseases or autoimmune disorders were also excluded.

Blood pressure in mmHg (BP) was measured by a Mercury sphygmomanometer. Anthropometric parameters such as BMI (body mass index, Kg/m²) and hip (cm) and waist circumference (WC, in cm) were recorded in all subjects and Laboratory investigations, including lipid profile, fasting blood glucose, fasting insulin, uric acid were done. Homeostasis model assessment (HOMA) index was calculated as the product of fasting glucose and insulin values divided by 22.5.18 The hsCRP concentration was determined using an immunoturbidimetric method (Randox, Mauguio, France) in mg/dl.

FMD was performed using a linear 7 MHz transducer (Vivid 7, GE Healthcare), and both groups were directed to abstain from Tea/caffeine 12 hours prior to the study. A longitudinal image was used to measure brachial artery diameter (1st baseline image), and a blood-pressure cuff was inflated on the upper arm (2–5 cm above the cubital fossa) to 50 mmHg above systolic pressure for 5 minutes and then deflated after 1 minute. A second longitudinal scan was obtained (from the same position) to calculate the brachial artery diameter (post-occlusion value). Flow-mediated dilation (FMD) was calculated as: maximum diameter during reactive hyperemia–diameter at baseline)×100/(diameter at baseline). All measurements of the brachial artery lumen diameter were assessed at end diastole.

Fifty women of the control group of the same hospital were matched for age. All the study participants provided written informed consent and study was approved by Institutional Ethics Commitee.

Statistical Analysis

The Statistical Package for the Social Sciences Version SPSS version17 (SPSS, Inc., Chicago, IL) was used for data analysis. To ensure the normal distribution of variables, Kolmogorov-Smirnov test was applied. Comparison between groups was performed using Student’s unpaired t test. Comparisons between frequencies were assessed by chi square analysis. We used Pearson’s correlation coefficient to assess the relationships. P < 0.05 was considered statistically significant.

Results

We included 100 women aged 20-45 years having singleton pregnancy in our study. Out of which 50 women had history of preeclampsia defined as cases and 50 who had normal pregnancy were defined as controls. Baseline characteristics of two groups have been shown in Table 1. Women in the cases group were of similar age compared with the control but significant difference was noted with regard to body mass index and waist circumference. Systolic and diastolic blood pressures in women with the previous preeclampsia pregnancy were higher in women than with normal pregnancy.

Metabolic Characteristics

Fasting glucose levels were higher in cases but not significantly different from controls.

Fasting insulin levels and HOMA were significantly higher in women with history of preeclampsia than in control subjects (P=0.002 and...
CVD is a disease of preventable and treatable risk factors, and evidence shows that when guidelines are followed and risk factors appropriately addressed and treated, CVD outcomes improve.20

Previous history of preeclampsia presents as an opportunity which should be used appropriately to assess for and treat CVD risk factors early to improve a women’s cardiovascular risk profile earlier in their health care trajectory. This study was aimed to detect presence of atherosclerotic markers in this high risk cohort.

Women diagnosed with preeclampsia are at increased risk of future cardiovascular or cerebrovascular events, with an estimated doubling of odds compared to unaffected women.20 This has implications for the follow-up of all women who experience pre-eclampsia, not just those who deliver pre-term. The theory to explain enhanced cardiovascular risk in women with a history of pre-eclampsia is that pregnancy is a ‘stress test’ and the development of hypertensive disorders during pregnancy identifies a woman destined to develop cardiovascular disease. This association may reflect shared common risk factors for both pre-eclampsia and cardiovascular and cerebrovascular disease. This is based on ample data revealing overlapping risk factors for pre-eclampsia and cardiovascular disease.21

The underlying pathophysiology of preeclampsia (PE) is not completely understood, but it is currently believed that the initiating event in PE is reduced placental perfusion, which develops from shallow cytotrophoblast migration toward the uterine spiral arteries which leads to inappropriate vascular remodeling and a hypoperfused placenta.1 This placenta becomes ischemic as the pregnancy continues which leads to the release of factors that cause maternal vascular endothelial dysfunction.22,23

Endothelial dysfunction appears to be a central component of the pathophysiology of preeclampsia.24 In our study, endothelial function was significantly lower in women with a history of preeclampsia. This is consistent with previous reports and indicates that preeclampsia-associated endothelial dysfunction persists in later life too.25-27

Increased resistance to insulin and metabolic markers in women with a history of preeclampsia was also found.28-30

Table 1: Baseline clinical characteristics and biochemical parameters in women with h/o previous preeclampsia and control subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>H/o previous preeclampsia (N=50)</th>
<th>Controls (N=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.82 ± 3.26</td>
<td>35.7 ± 4.6</td>
<td>0.54</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 ± 4.8</td>
<td>24.7 ± 4.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>90.2 ± 6.8</td>
<td>86.3 ± 6.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>136 ± 20</td>
<td>118 ± 16</td>
<td>0.04</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>86.4 ± 7.2</td>
<td>70 ± 7.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>86 ± 7.6</td>
<td>82.2 ± 6.0</td>
<td>0.08</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>122 ± 54</td>
<td>119 ± 32</td>
<td>0.12</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>102 ± 39.2</td>
<td>96 ± 27</td>
<td>0.6</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>40.8 ± 7.6</td>
<td>48 ± 9.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Uric acid</td>
<td>4.5 ± 1.8</td>
<td>3.8 ± 1.2</td>
<td>0.05</td>
</tr>
<tr>
<td>Insulin (mu/ml)</td>
<td>10.2 ± 3.4</td>
<td>6.1 ± 1.8</td>
<td>0.002</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.2 ± 0.22</td>
<td>1.12 ± 0.18</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Data is expressed in mean ± SD

P=0.01, Table 1). Lipid profile was normal in all study subjects except that HDL was significantly lower in cases than controls.

Hs CRP levels were also higher in cases as compared to controls as shown in Table 2. Baseline brachial artery diameter (vessel size) was similar in the two groups and FMD was significantly reduced in women with previous preeclampsia.

Correlation analysis between FMD and the various parameters examined that showed strong negative association of Hs CRP with FMD (r =-0.600; P=0.001). Negative significant correlations were also found between FMD and HOMA as well as between FMD and fasting insulin (r=0.45; P=0.014 and r=0.38; P =0.03 respectively. Conversely, FMD exhibited positive relations with HDL cholesterol (r = 0.48; P= 0.002). A significant correlation was also found between FMD and body mass index and waist circumference (r =0.36; P = 0.046, r=0.42, P=0.01).

We studied prevalence of various comorbidities in women with previous preeclampsia with increasing duration from index pregnancy that revealed increased number in all diseases in women who had preeclamptic pregnancy more than 10 years (Table 3).

Discussion

CVD is a disease of preventable and treatable risk factors, and evidence shows that when guidelines are followed and risk factors appropriately addressed and treated, CVD outcomes improve.19

Previous history of preeclampsia presents as an opportunity which should be used appropriately to assess for and treat CVD risk factors early to improve a women’s cardiovascular risk profile earlier in their health care trajectory. This study was aimed to detect presence of atherosclerotic markers in this high risk cohort.

Women diagnosed with preeclampsia are at increased risk of future cardiovascular or cerebrovascular events, with an estimated doubling of odds compared to unaffected women.20 This has implications for the follow-up of all women who experience pre-eclampsia, not just those who deliver pre-term. The theory to explain enhanced cardiovascular risk in women with a history of pre-eclampsia is that pregnancy is a ‘stress test’ and the development of hypertensive disorders during pregnancy identifies a woman destined to develop cardiovascular disease. This association may reflect shared common risk factors for both pre-eclampsia and cardiovascular and cerebrovascular disease. This is based on ample data revealing overlapping risk factors for pre-eclampsia and cardiovascular disease.21
action is a well-established cardiovascular risk factor. The exact mechanism by which insulin resistance impairs endothelial function are not known, however, oxidative stress and inflammation may act synergistically, leading to a reduced expression of endothelial nitric oxide synthase. As previously observed, we also found increased insulin resistance in women with previous preeclampsia as both fasting insulin and HOMA-IR were significantly higher in cases along with hsCRP, though rise in hs CRP could not achieve statistical significance.

Romundstad et al. noted that women with a history of pre-eclampsia or gestational hypertension also had substantially higher body mass index and systolic and diastolic blood pressures and unfavourable lipids compared with those with normotensive pregnancies. In our study systolic and diastolic blood pressures were higher, waist circumference was greater and HDL was lower in women with previous preeclampsia than controls who had normal pregnancy.

There is not much literature addressing cardiovascular risk markers in our population so our study is unique in this respect. We tried to study prevalence of various cardio-metabolic co morbidities in our study group with increasing duration from the index pregnancy that revealed increase in all diseases with increase in duration.

Our study had certain limitations including small sample size and cross-sectional design. More prospective studies which are appropriately designed with large sample size that include follow up are needed in our population.

Conclusion

Women with previous history of preeclampsia had adverse cardio-metabolic profile than those who had normal pregnancy. They had higher insulin resistance and endothelial dysfunction. They also have high prevalence of chronic metabolic disorders with increased duration since index pregnancy. Primary prevention of cardiovascular disease in this group of women should be undertaken, and reProductive history needs to be considered when dealing with cardiovascular risk assessment.

References


