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EDITORIAL

Reducing mid-life cardiovascular disease by improving reproductive health

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Worldwide more than 8 million women die as a consequence of cardiovascular disease (CVD), including heart disease and stroke[1]. Aging and the inexorable decrease of ovarian estrogenic secretion are two relevant factors. It is well known that body composition changes as women grow older. In particular, there is an increase in the percentage of total body fat and a shift in fat distribution from gynecoid to android. Whether or not this is due entirely to age, to menopause, or to a combination of both remains to be determined. In developed and developing countries, obesity has become an increasing social problem. Data from the World Health Organization indicate that more than 1.9 billion adults are currently overweight, with a third of these being obese. Interestingly in developing countries, obesity rates have increased as a direct consequence of changes in dietary and lifestyle habits: increased consumption of carbohydrates in regions living in extreme poverty; and a trend for adopting the lifestyles observed in developed countries.

An increase in body composition is directly related to a higher risk of suffering CVD, mainly heart disease and stroke, as well as other conditions such as diabetes, musculoskeletal disorders, and several cancers[1]. Recent research suggests that women who have had hypertensive states during their pregnancy, in particular preeclampsia of early onset, are at a higher risk of developing CVD later in life as well as a two-fold higher mortality risk. Hence, pregnancy may be seen as a 'stress test' for future female cardiovascular health[2]. Of interest is the fact that the majority of studies have focused on the identification of risk factors shortly after pregnancy; however, little is known about the prevalence of these risk factors or overt CVD 5–20 years later.

In a prospective observational study, Bokslag et al.[3] assessed cardiovascular risk in women who had preeclampsia of early onset (<34 weeks' gestation) and normotensive controls (≥37 weeks' gestation) 9–16 years after their index pregnancy. Evaluation of cardiovascular risk consisted of recording blood pressure and anthropometrics, and also performing blood and urine tests. It was found that women with a history of early-onset preeclampsia presented in their fifth decade of life with higher blood pressure readings, greater body mass index, higher lipid levels, greater glycated hemoglobin, and greater levels of albuminuria as compared to controls. Although these women are currently outside the scope of most preventive programs due to their relatively young age, they do present with modifiable CVD risk factors which can be subject to intervention.

The occurrence of the metabolic syndrome (METS) after suffering preeclampsia and the eventual culmination in CVD seems to suggest that this syndrome per se contributes to the pathophysiologic mechanism linking preeclampsia to future female CVD. Hence, the presence of hypertension or the METS may represent an opportunity for the implementation of preventive interventions that may reduce the risk of developing future mid-life myocardial infarctions or stroke. Pathophysiological mechanisms underlying preeclampsia include generalized endothelial dysfunction and hypertension, as well as metabolic abnormalities such as insulin resistance, dyslipidemia, obesity, and a chronic inflammatory state[4]. These derangements are exactly those that define the METS. These facts seem to point out that preeclampsia is the presentation of the METS during pregnancy[5]. On the other hand, current reports indicate that high pregestational body mass index as well as excessive gestational weight gain predispose women to preeclampsia and related adverse maternal fetal outcomes in the indexed pregnancy, and also give rise to a higher rate of obesity, insulin resistance, hypertension, diabetes, dyslipidemia, and cardiovascular events in later stages of life of both mother and the newborn. Thus, pregnancy and the lead up to pregnancy are a critical time to implement recommendations regarding appropriate gestational weight gain and lifestyle modifications, which will have a positive impact on the index pregnancy, the mid-life health of the mother, and the future health of the newborn.

Anatomic, physiologic, and metabolic adaptations occur in the mother as part of a normal pregnancy. In terms of metabolic changes, there is an increase in insulin resistance, lipids, and amino acid, mainly aimed at providing adequate nutrition to the growing fetus[6]. Preeclampsia appears to be an exaggeration of these biological changes and/or adaptations. Gestations complicated with preeclampsia present with increased insulin resistance and abnormal lipid profiles[6]. A study carried out as early as 15 weeks after having a pregnancy complicated by preeclampsia[7] found a higher prevalence of the METS in these women as compared to controls, suggesting that the metabolic perturbations that initiated during pregnancy seem to persist after delivery, marking the onset of the METS, and its components, as clusters of future female cardiovascular risk. The good news is that the components of the METS are modifiable. In this sense, novel strategies for the management of the METS have been

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proposed[8], but currently lifestyle modification strategies including increased physical activity, diet therapy, reduced alcohol intake, and cessation of smoking have successfully been used and are cost-effective[9,10]. In the sequence of events from preeclampsia to CVD, the METS seems to play an important role as a mediator or indicator of susceptibility. Some studies report that the presence of METS before pregnancy may predispose women to preeclampsia.

As mentioned, the risk of developing the METS after suffering preeclampsia is high, suggesting that this syndrome may be involved in the pathogenesis of CVD following preeclampsia. Hence, interventions for these modifiable cardiovascular risk factors will have an impact on future CVD. There is a need to prioritize the establishment of modifiable CVD risk screening programs for women with a history of preeclampsia to avoid the progression to CVD. On the other hand, research should not only be focused on finding a predictive model for the development of preeclampsia in a given pregnancy, but also determining which of these women will develop the METS after their pregnancy and/or during mid-life.

As health-care providers interested in women's health, we should support initiatives, in developed and also developing countries, aimed at aiding and promoting changes in lifestyles, with a special focus on limiting weight gain not only during the reproductive years (before, during, and after pregnancy) but also in the menopausal transition and beyond, in order to have an important impact on future female cardiovascular risk.

Conflict of interest The author reports no conflicts of interest.

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