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The mother – The long-term implications on metabolic and cardiovascular complications

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There is cumulating evidence linking the occurrence of pregnancy complications, including miscarriage, stillbirth, hypertensive disorders of pregnancy, gestational diabetes mellitus, preterm birth, and fetal growth restriction, with increased future risk of type 2 diabetes mellitus, and hospitalization and death due to cardiovascular and cerebrovascular diseases. Such association is largely related to genetic predisposition and shared pathophysiological mechanisms and changes, which may precede the index pregnancy. Awareness of this association would allow identification of the at-risk women for implementation of preventive measures to reduce the recurrence risk of these complications and mitigate the future development of metabolic and cardiovascular diseases worldwide.

Introduction

Cardiovascular diseases (CVDs) and type 2 diabetes (T2D) mellitus are major noncommunicable diseases (NCDs) recognized by the World Health Organization (WHO), to which are attributed more than 9 million deaths [1]. There is now evidence that a history of pregnancy complications, such as hypertensive disorders of pregnancy (HDP) and gestational diabetes mellitus (GDM), increased the future risk of CVD and T2D in women (Table 1). As pregnancy complications occur in 29–36% of pregnancies in the US [2] and UK [3], obstetric history could help predicting future CVD risk in 20–30%

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Table 1
Association between obstetric factors and complications with future metabolic and cardiovascular complications in the mother.

Obstetric factors	*Cardiac Complications*[a]	*Vascular complications*[b]	*Metabolic Disturbances*[c]	*Diabetes mellitus*[d]
Parity = 1	√	√	–	–
Parity ≥5	√	√	–	–
TA	√	√	–	√
Pregnancy loss	√	√	√	–
Stillbirth	√	√	–	–
Abruption	√	√	–	–
GH	√	√	√	–
PE/eclampsia	√	√	√	√
GDM	√	√	√	√
PTB	√	√	√	√
LBW/FGR	√	√	–	√
LGA	–	–	√	√

TA = threatened abortion, GH = gestational hypertension, PE = preeclampsia, GDM = gestational diabetes mellitus, PTB = preterm birth (<37 weeks), LBW = low birth weight (<2500 g), FGR = fetal growth restriction including small-for-gestational age, LGA = large-for-gestational age.

[a] Include coronary artery/ischemic heart disease, myocardial infarction, congestive heart failure, and related deaths.

[b] Include atherosclerosis, increased intima-media thickness, endothelial dysfunction, increased vascular resistance, hypertension, cerebrovascular diseases and stroke, thromboembolic complications, and related deaths.

[c] Include dyslipidaemia, metabolic syndrome, and obesity.

[d] Include abnormal glucose tolerance and frank type 2 diabetes mellitus.

of the estimated 80% parous women worldwide [2]. Therefore, it is possible to identify these high-risk women for preventive measures that impact on future pregnancies and long-term health.

Obstetric conditions and future maternal metabolic complications

There is consensus that GDM is associated with future T2D in the mother [2]. However, other pregnancy conditions can also increase the risk of T2D and the metabolic syndrome (MS).

Hypertensive pregnancy disorders

This category includes gestational hypertension (GH), preeclampsia (PE), and eclampsia. In the limited literature on this association, the hazard ratio (HR) for subsequent T2D was 3.12, 3.53, and 3.68 after GH, mild PE, and severe PE, respectively [4]. Another study found the adjusted HR (aHR) for T2D was significant at 1.52 and 2.22 for GH and superimposed PE, but not for PE/eclampsia (aHR 1.42) [5]. Five years after a pregnancy complicated by the hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, there was 4% increase in new-onset diabetes [6]. Thus, the risk of future T2D is influenced by the severity of HPD.

Gestational diabetes mellitus

The risk of future T2D is associated with GDM diagnosed in the first half of pregnancy, obesity, and need for insulin treatment [7]. Nevertheless, even among women tested normal or with impaired glucose tolerance at the postnatal assessment, 10.6% became diabetic 4 years later, which was associated with higher glucose at diagnosis and homocysteine levels at the postnatal assessment [8]. Chinese women with prior GDM converted to T2D at 1.6% per year, resulting in significantly increased T2D (24.4% vs. 5.3%) and impaired glucose regulation (26.6% vs. 14.9%) compared to women with normal glucose tolerance, 15 years after the index pregnancy [9]. Overall, GDM is associated with a sevenfold increased risk of later T2D [10]. Of note, the study on the Northern Finland Birth Cohort of 1986 revealed that while the cumulative incidence of diabetes in the whole study population was 1.3%, concomitant overweight and GDM greatly increased the risk (HR 47.24) [11]. Furthermore, prepregnancy overweight without GDM had a greater effect (HR 12.63) than GDM in normal-weight women (HR 10.61) on future risk of T2D. Similarly, women with previous diet-treated GDM, compared with