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Review

Gestational diabetes mellitus: Taking it to heart

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ABSTRACT

Globally, cardiovascular disease (CVD) accounts for 1/3 of all deaths to women. While much research identifies the increased risk in CVD associated with pre-diabetes measurements, there is growing interest in the role of gestational diabetes mellitus (GDM)–a condition of glucose intolerance diagnosed during pregnancy–as a potential CVD risk factor. This article reviews existing evidence supporting this association, particularly regarding GDM and type 2 diabetes, hypertension, atherogenic dyslipedmia, and CVD events. Finally, it discusses the research and clinical ramifications of identifying GDM as a CVD risk factor, highlighting the need for more rigorous research on this topic.

Contents

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1. Introduction

Cardiovascular disease (CVD), the largest single cause of mortality worldwide, accounts for 1/3 of all deaths among women [1]. In Europe, 54% of female deaths are attributable to CVD [2], while one in three adult American women has some form of CVD [3]. It is not a disease of the wealthy; in low and middle-income countries, more women die from CVD than from pregnancy-related complications [4]. Risk also increases with age. Although men in their 40 s have higher coronary heart disease (CHD) risk than women of the same age, as women reach menopause, their risk increases to almost that of men [3].

Type 2 diabetes mellitus (T2DM) has long been associated with increased CVD risk. Research supports that pre-diabetes measurements – namely, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) – are also associated with increased CVD risk [5,6], and IGT has specifically been labeled by the World Health Organization and American Diabetes Association a major risk factor for CVD [7]. Several studies assessing the possibility of delaying progression to diabetes in IGT individuals show success from both pharmaceutical and lifestyle interventions [8], and some studies show a positive impact on CVD risk factors [9].

Current literature on gestational diabetes mellitus (GDM) parallels early literature on IGT identifying IGT as a CVD risk factor. Once thought a transient condition, GDM proves to be of greater concern for both mother and child for adverse effects not only during pregnancy but also in the postpartum period. This article discusses the potential increased risk of CVD among women with previous GDM (pGDM). We highlight existing evidence supporting this association, and the research and clinical ramifications of identifying GDM as a CVD risk factor.

2. Definition and classification

GDM is defined as a degree of glucose intolerance with onset or first recognition during pregnancy [10]. Changes in such hormones as human placental lactogen, progesterone, prolactin, cortisol, and TNF-alpha – particularly during late pregnancy – antagonize the effects of insulin, triggering a state of insulin resistance, thereby increasing insulin requirements (Fig. 1). These changes in the hormonal milieu, along with the manifestation of subclinical inflammation [11,12], create a 'diabetogenic' environment in which insulin resistance can – and does – naturally result. When a woman's body is exacerbated by this environment, glucose intolerance increases and manifests as a positive GDM diagnosis. GDM is thus a result of both pancreatic beta-cell insufficiency and increased insulin resistance, though genetic factors and other processes might also be involved. Since the majority of cases return back to normoglycemic levels postpartum, GDM has been considered a 'transient condition'. However, mounting evidence suggests that GDM should be viewed more as a marker for chronic disease.

3. Epidemiology

GDM affects ~7% of all pregnancies in the US [13], and 2–6% of pregnancies in Europe [14]. Globally, prevalence estimates

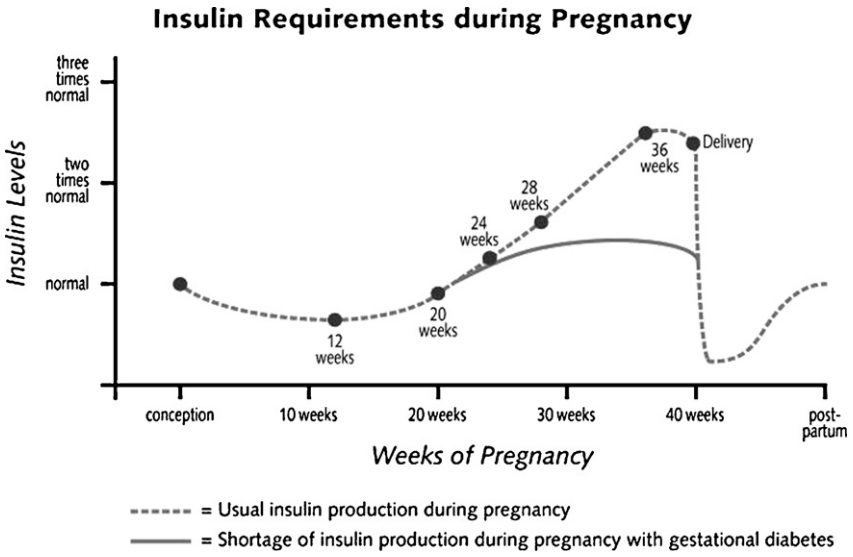

Fig. 1 – Insulin requirements vs. production in normal pregnancy and pregnancy with gestational diabetes. Source: Gestational Diabetes BASICS (c) 2010 International Diabetes Center at Park Nicollet.