Can J Diabetes 36 (2012) 133–141

Contents lists available at SciVerse ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

Review

Pregnancy is a Critical Period for Prevention of Obesity and Cardiometabolic Risk

Kristi B. Adamo PhD [a,b,c,*], Zachary M. Ferraro PhD [a,c], Kendra E. Brett MSc [a,c]

[a] Healthy Active Living and Obesity Research Group, Children's Hospital of Eastern Ontario Research Institute, Ottawa, ON
[b] Faculty of Medicine, Pediatrics, University of Ottawa, Ottawa, ON
[c] Faculty of Health Sciences, School of Human Kinetics, University of Ottawa, Ottawa, ON

ARTICLE INFO

Article history:
Received 9 March 2012
Received in revised form
4 May 2012
Accepted 22 May 2012

Keywords:
cardiometabolic risk
child obesity
gestational diabetes
gestational weight gain
lifestyle change
pregnancy

ABSTRACT

Obesity is a global epidemic whose development is rooted in complex and multi-factorial interactions. Excessive weight gain throughout the lifecourse is tightly linked to, and generally precedes, the emergence of impaired glycemic control. As such, a parallel increase in the incidence of type 2 diabetes has emerged resulting in a dual epidemic. Once established, obesity is difficult to reverse and epidemiological, animal model and experimental studies have provided strong evidence implicating the intrauterine environment in downstream obesity. This review focuses on the gestational period, a crucial time of growth, development and physiological change in mother and child. It describes the interplay between maternal obesity, gestational weight gain and lifestyle behaviours, which may act independently or in combination, to perpetuate the intergenerational cycle of obesity and cardiometabolic risk. Pregnancy represents a window of opportunity for intervention via maternal nutrition and/or physical activity that may induce beneficial physiological alternations in the fetus that are mediated through favourable adaptations to in utero environmental stimuli. Many avenues of research are merging to identify the predisposing factors for positive energy balance, insulin resistance and cardiometabolic risk throughout the lifecourse and evidence in the emerging field of epigenetics suggests that chronic, sub-clinical perturbations during pregnancy may affect fetal phenotype and long-term health.

Mots clés:
risque cardiométabolique
obésité infantile
diabète gestationnel
prise de poids gestationnelle
modification du style de vie
grossesse

RÉSUMÉ

L'obésité est une épidémie mondiale dont le développement prend racine dans des interactions complexes et multifactorielles. La prise de poids excessive tout au long de la vie est bien liée à l'émergence de l'altération de la régulation glycémique, et généralement la précède. À ce titre, une augmentation parallèle de l'incidence du diabète de type 2 est apparue, entraînant ainsi une double épidémie. Une fois établie, l'obésité est difficilement réversible, et le modèle animal épidémiologique et les études expérimentales ont fourni des éléments probants importants impliquant l'environnement intra-utérin de l'obésité associée. Cette revue porte sur la période gestationnelle, un moment crucial de la croissance, le développement et le changement physiologiques chez la mère et l'enfant. Il décrit le rapport entre l'obésité maternelle, la prise de poids gestationnelle et les comportements liés au style de vie, qui peuvent agir indépendamment ou de manière combinée pour perpétuer le cycle intergénérationnel de l'obésité et le risque cardiométabolique. La grossesse constitue une circonstance opportune d'intervention par la nutrition maternelle ou l'activité physique qui peuvent induire des permutations physiologiques chez le fœtus qui sont médiés par des adaptations favorables aux stimuli environnementaux in utero. Plusieurs avenues de recherche s'associent pour identifier les facteurs prédisposants à un bilan énergétique positif, à l'insulinorésistance et au risque cardiométabolique tout au long de la vie, et des données probantes dans le domaine émergent de l'épigénétique suggèrent que des perturbations sous-cliniques chroniques durant la grossesse peuvent nuire au phénotype fœtal et à la santé à long terme.

Introduction

Not only are the rates of obesity and its related co-morbidities (e.g. diabetes) at an all time high, they are manifesting earlier in life (1). Much time and effort are spent trying to identify efficacious interventions and prevention programs to halt the growing

* Address for correspondence: Kristi B. Adamo, PhD, Healthy Active Living and Obesity Research Group, Children's Hospital of Eastern Ontario Research Institute, 401 Smyth Rd. Ottawa, Canada ON K1H 8L1.
E-mail address: kadamo@cheo.on.ca (K.B. Adamo).

1499-2671/$ – see front matter © 2012 Canadian Diabetes Association
http://dx.doi.org/10.1016/j.jcjd.2012.05.004

trajectory of these dual epidemics. Accordingly, our group is interested in early prevention of obesity and downstream health threats, recognizing that obesity and related conditions track very closely from childhood to adolescence to adulthood (2). The untoward medical and psychosocial effects of obesity underscore the importance of early intervention to optimize prevention. This is especially important given the economic burden that obesity related diseases have on the health care system, which is estimated to cost Canada $4.3 billion annually (3). Obesity during pregnancy can lead to considerable downstream metabolic complications in mothers and their offspring. Recognizing that early intervention is vital, pregnancy may also be the most opportune time for primary prevention. Thus, if obesity prevention prior to conception is not feasible, gestation appears to be the ideal period for preventive efforts, as it is the most critical phase of growth and development experienced throughout the lifespan. It is possible that lifestyle modifications during gestation may promote an optimal intrauterine environment and produce beneficial changes in health outcomes of both mother and baby.

The Threat of Maternal Obesity to Cardiometabolic Health

Maternal health

More than two-thirds of North American women of childbearing age are overweight or obese (4), a prevalence comparable to other developed nations. This is concerning because of the myriad of adverse outcomes associated with a pregnancy complicated by obesity (Fig. 1). While these various complications are reviewed elsewhere (5), it is notable that the risk of any form of obstetrical complication is about 3-fold greater in obese versus non-obese mothers (6).

Insulin resistance and gestational diabetes

Obesity is the most common risk factor for insulin resistance (IR). Knowing that peripheral insulin sensitivity is reduced by 50% to 60% over the course of gestation in all women to preferentially shuttle fuel to the fetal-placental unit (7), it is not surprising that overweight or obese women, who are prone to beta-cell dysfunction and compromised glucose tolerance pre-pregnancy, are at increased risk of metabolic dysregulation. Thus gestational diabetes mellitus (GDM) prevalence rates are much higher in overweight and obese women than the general obstetric population (8). For example, in comparison to women with a normal body mass index (BMI), the risk of developing GDM rises exponentially with increasing BMI, with odds ratios (OR) of 1.97 (95% CI 1.77-2.19), 3.01 (95% CI 2.34 to 3.87) and 5.55 (95% CI 4.27-7.21) for those who are overweight, obese and morbidly obese, respectively (9). In fact, women with a BMI in the referenced 'normal' range (i.e. 22-25 kg/m^2) are at greater risk for development of glucose intolerance and GDM than leaner women (10). While increased adiposity is clearly a contributor, it seems that the location of the adipose tissue is also important, with accumulation in the visceral depots being disadvantageous from a cardiometabolic standpoint. Consequently, those with greater proportions of visceral to subcutaneous adipose tissue in the first trimester (12 weeks) of pregnancy, as measured by ultrasonography, had significantly greater likelihood (OR 16.9, CI 1.5-195) of having a positive glucose challenge test in later pregnancy (24-28 weeks) (11). Furthermore, waist-to-hip ratio and waist circumference (surrogate markers of visceral adiposity) are independently associated with higher 2-h glycemia following glucose tolerance test, suggesting that central fat distribution is an independent predictor of gestational glucose intolerance (12). Of great concern is that those who develop GDM during one pregnancy are at increased risk for GDM in subsequent pregnancies (13),

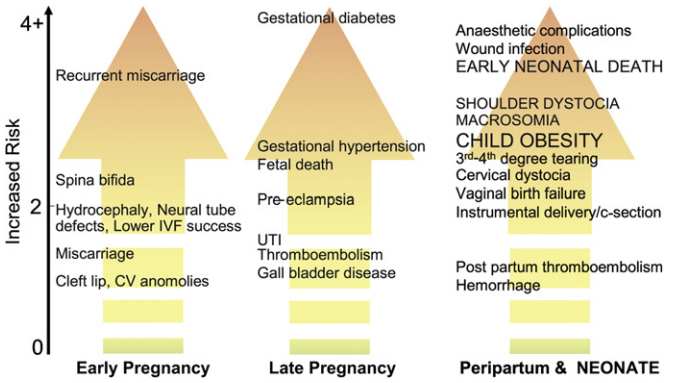

Figure 1. Risks associated with pregnancies complicated by overweight or obesity. The *x*-axis shows the time course and the *y*-axis illustrates the degree of elevated risk for each outcome based on published literature (*IVF*, in vitro fertilization; *CV*, cardiovascular; *UTI*, urinary tract infection).

and that the majority of GDM patients (50%-60%) will develop type 2 diabetes in the years following delivery (14).

Hypertensive disorders and pre-eclampsia

The risk of pregnancy-induced hypertension and pre-eclampsia is also greater in obese women. The risk of gestational hypertension in nulliparous women is estimated to be 2.5 to 3.2 times greater for obese and severely obese women, respectively. Similarly, pre-eclampsia risk is 1.6 and 3.3 times greater for obese and severely obese women, respectively (15), with both groups being at risk for recurrent pre-eclampsia (16). Findings from a recent meta-analysis indicate that pre-eclampsia risk seems to double with each 5 to 7 kg/m^2 increase in weight over normal (17) and weight loss or gain between pregnancies can decrease or increase the risk, respectively (16). While the mechanisms are not yet fully characterized, several lines of evidence suggest a link between reduced insulin sensitivity, endothelial dysfunction, cytokines, and pregnancy-related hypertensive disorders. For instance, women with pre-eclampsia have been shown to have decreased concentrations of the insulin sensitizing high molecular weight adiponectin (18), decreased insulin sensitivity in late gestation, elevated non-esterified fatty acids (NEFAs), triglycerides, and C-peptide concentrations (19), as well as higher levels of pro-inflammatory cytokines. Studies have shown that compared to BMI matched controls, women with a history of pre-eclampsia exhibit higher levels of fasting insulin, lipid, and coagulation profiles postpartum and show signs of deficiencies in endothelial-dependent vascular function (20). These characteristics may help explain the epidemiological reports showing a strong relationship between pre-eclampsia and future risk of coronary artery disease with a 2-fold greater relative risk of death from ischemic heart disease in pre-eclampsia complicated pregnancies (21).

Dyslipidemia

Although we often focus on the role of insulin in glucose metabolism, insulin also plays an instrumental role in lipid metabolism. As pregnancy progresses, there is a marked increase in plasma lipid concentrations, and these increases are more pronounced in pregnancies complicated by obesity and/or GDM (22). The elevated NEFA level is related to the reduced ability of insulin to suppress lipolysis as gestation progresses and subsequently these NEFAs are available to support maternal needs in late gestation when energy requirements are highest. However, the obesity-associated disturbances in adipocyte metabolism resulting