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Obesity in Pregnancy: Maternal and neonatal effects

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ABSTRACT

In the 21st Century, obesity has become a world-wide epidemic. In Mexico, about 75% of non-pregnant women of reproductive age (between 20-49 years of age) are overweight or obese (body mass index > 25). In the USA, over 60% are overweight or obese. Overweight and obese women are more likely to gain excessively during pregnancy, and they are more likely to maintain excess weight after delivery. This weight gain also has implications for the child's future risk of being overweight. In this paper, we will review the impact of maternal adiposity on reproduction, the effect of obesity on maternal metabolism and complications in pregnancy, the short and long-term effects on the infant, and potential interventions for alleviating poor outcomes.

KEY WORDS: *Overweight, obesity, pregnancy, adiposity.*

INTRODUCTION

Overweight and obese women are more likely to gain excessively during pregnancy, and they are more likely to maintain excess weight after delivery.[1] This weight gain also has implications for the child's future risk of being overweight.[2]

IMPORTANCE OF MATERNAL BODY FAT FOR REPRODUCTION

In 1980, Rose Frisch hypothesized that a minimum amount of body fat is necessary for the appearance of menarche. This hypothesis was confirmed by Ahima less than ten years ago after performing a series of elegant studies showing that the plasma leptin (hormone excreted by the adipose tissue, responsible of some of the mechanisms involved in regulating the appetite and whose name is derived from the Greek word *leptos*, meaning thin) concentration diminishes in animals receiving an hypoenergetic diet. This decrease induces neuroendocrine changes that affect reproductive performance. When leptin is injected into these animals and they recover their fat depots, neuronedocrine and reproductive changes are quickly reverted.[3] Actually, body fat is an important modulator of reproductive performance. It has been reported that after stratifying women by Body Mass Index (BMI), the highest reproductive efficiency is found in those with a BMI between 20 and 25 while women with extreme values of BMI (< 20 and > 25) diminish their reproductive performance.

In normal conditions, water explains 53% of women's body weight and fat represents between 26 and 28% of their weight; almost twice as high as the percentage of men who have 14% of fat and 61% of water. Due to the above-mentioned differences females have a higher tendency to accumulate body fat. This predisposition is the result of a metabolic adaptation directed towards ensuring first hominids' survival even in conditions of food shortage.[4]

In this context, it is convenient to remember that the most efficient way of storing energy is through the fat deposition; due to its hydrophobic characteristics,

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one kilogram of fat cells contain around 800 mg of triacyl glycerides that provide around 72000 kcal.

Therefore, in normal conditions, women's fat stores are more than enough to cover gestational energy needs, breastfeeding and newborn's fat deposition. Actually, human newborns have higher fat storage (around 14% of their body weight) than the rest of the primates, who are born with 3% of fat.

As mentioned before, fat reserves gave females an evolutionary advantage very useful under food deprivation conditions, like those occurred several millions of years ago, when the climatic changes forced hominids to adapt in order to live in the savanna where food was hardly available. As a matter of fact, several Paleolithic figurines of fertility goddess, dated 35 millions of years old, show silhouettes of women with evident obesity. However, currently we are living in an environment with an overabundance of energy dense foods that together with a sedentary lifestyle, are leading to an excessive fat storage and, consequently, the increasing of chronic diseases.[5]

Maternal obesity, infertility, and early pregnancy loss

Menstrual disorders and infertility are common problems of obese women.[6] It is estimated that 25 percent of ovulatory infertility in the United States is attributable to overweight and obesity.[7] Because adipose tissue synthesizes estrogen, obese women have higher levels of endogenous estrogen compared to non-obese women, which increases the risk for irregular menstrual cycles and infertility.[8] It is not uncommon for infertility specialists to advise morbidly obese women to lose weight before beginning with fertility treatments.

Obese pregnant women also experience higher rates of spontaneous abortions or early pregnancy losses,[3,9-11] The risk of spontaneous abortion is about 20% higher in obese than in normal BMI women.[12] Spontaneous abortion rates are also higher in overweight women after in vitro fertilization than in lean women (22% *versus* 12%).[13] The risk of infertility and early pregnancy loss can be reduced if obese women lose weight prior to conception.[14]

Maternal obesity and metabolic complications during pregnancy

In non-pregnant adults, obesity is associated with the metabolic syndrome, characterized by hypertension, glucose intolerance, and dyslipidemia.[15] The normal metabolic adjustments of pregnancy make the obese woman especially prone to develop hypertension and its related metabolic disorder, preeclampsia, and glucose intolerance and its related metabolic disorder, gestational diabetes mellitus. The degree of maternal adiposity and risk for these metabolic complications are related; the higher body weight, the greater the risk.[16] The risk for gestational diabetes ranges from 2 to 8-fold higher than that of normal weight women as the body weight of the woman increases from overweight to severely obese.[17] A similar trend exists for preeclampsia; the risk is about 2-fold higher in overweight women and 3-fold higher in obese women compared to normal weight women.[11,17] Preeclampsia is more common in women with gestational diabetes than in non-diabetic women suggesting related underlying biological aberrations. Tight blood glucose control during pregnancy lowers the risk for preeclampsia in women with gestational diabetes.[11]

The risk for gestational diabetes rises during pregnancy because the peripheral tissue sensitivity to insulin declines by about 50 to 60 percent in late pregnancy presumably to limit maternal glucose use and to conserve it for fetal growth and development. Since insulin also inhibits lipolysis, when insulin sensitivity declines in pregnancy, the breakdown of stored triglycerides occurs and fatty acids are released into circulation. It is thought that the insulin resistance of pregnancy is mediated by placental hormones and cytokines.[18,19] The decline in insulin sensitivity during gestation is greater in obese than in normal weight women. Possibly, an increased level of proinflammatory cytokines produced by the excess adipose tissue in obese women contributes to their increased risk for glucose intolerance. Serum C-reactive protein levels, a marker of inflammation, have been correlated with the body mass index of women in late pregnancy.[20]

In the past, women with gestational diabetes were prescribed diets providing about 1200 to 1800 kcal/d.[21] These low calorie diet improved maternal glucose tolerance and reduced fetal overgrowth. However, a concern about maternal ketosis with the severe energy restriction and potential impaired fetal neurodevelopment caused a shift from severe energy restriction to carbohydrate restriction.[22] In 2004, the amount of carbohydrate recommended for pregnant

women with gestational diabetes has been increased from 45 to 65% of the energy, with an emphasis on whole grains and high fiber foods.[23] Studies by Fraser et al.,[24,25] Clapp et al.,[26,27] and Zhang et al.,[28] have all shown that lowering the glycemic load while increasing cereal fiber is an efficacious way to reduce the risk of gestational diabetes or glucose intolerance in women during pregnancy. The type of dietary fat consumed may also influence the risk of developing glucose intolerance during pregnancy. Diets low in polyunsaturated fatty acids and high in saturated fat appear to increase the rise of hyperglycemia of pregnancy.[29,30] Research has also shown that moderate, consistent physical activity throughout gestation reduces subclinical inflammation and insulin resistance.[31] In fact, maintaining physically active throughout pregnancy reduced the risk of gestational diabetes by nearly one-half.[32] Most of these studies were done in normal weight women, but there is no reason to believe that a high fiber, low glycemic, low saturated fat diet along with moderate physical activity will reduce insulin resistance and glucose intolerance in obese as well as lean women.

Gestational hypertension or preeclampsia occur more frequently in obese women as well as glucose intolerance.[33] It has been proposed that preeclampsia is related to an inadequate placental blood supply, which causes oxidative stress and an increased release of placental factors into maternal circulating that trigger an inflammatory response. Thus, preeclampsia, like gestational diabetes, is linked to a subclinical inflammatory state. Because preeclampsia is associated with inflammation and oxidative stress, antioxidant supplementation trials have been done to prevent this disorder. However, the two recent randomized controlled trials of vitamin C (1000 mg) and vitamin E (400 IU) given daily from the first or second trimesters of pregnancy to delivery failed to show a beneficial effect.[34,35] Since the placenta is fully established by the second trimester, failure to administer the antioxidants during the first trimester when the placenta is developing may interfere with their effectiveness at preventing preeclampsia.

Other dietary treatments used to prevent preeclampsia include calcium supplementation, sodium restriction, and calorie restriction. An inverse relationship between calcium intake and preeclampsia was first described in 1980.[36] It is thought that a low calcium intake causes vasoconstriction and reduces placenta blood supply leading to preeclampsia. A Cochrane Review of 12 high-quality calcium supplementation trials showed that providing calcium supplements to women with *low* intakes reduced the incidence of preeclampsia by about one-half, and no adverse effects were observed. However, there is no evidence that calcium supplementation reduces the risk of preeclampsia in women with adequate calcium intakes. Sodium restriction and calorie restricted diets have also been used to treat preeclampsia, but there is little evidence that those treatments are effective.[33,37]

Other complications that occur more frequently in obese pregnant women include insufficient or excessively high gestational weight gains, and increased rate of cesarean sections and prolonged labors. Unlike underweight and normal weight women, the relationship between maternal weight gain and birth weight is attenuated in overweight or obese women[38] suggesting that the metabolic adjustments required to support fetal growth are less dependent on weight gain in obese women than in normal weight women. In general, gestational weight gain is more variable among obese women (BMI > 29) than any other weight group.[39] The risk of gaining either above or below the Institute of Medicine standards for gestational weight gain was high –a 19-fold risk of gaining above and nearly a 7-fold risk of gaining below. Obese women are also more likely to have cesarean sections; in the U.S. about 50% of obese women with BMIs between 35 and 40 have cesarean sections whereas it is only about 30% among normal weight women.[40] Labors also tend to be longer in overweight and obese women.[41]

In the postpartum period, the risk infections is increased among overweight and obese women, especially if they had a cesarean section.[11] Venous thromboembolisms occur more frequently among obese than normal-weight women in the early postpartum months.[42] Anemia is another problem is twice as high among overweight women and three times as high among obese women compared to normal-weight women in the postpartum period.[43] Since cesarean sections are performed more frequently in overweight and obese women, the higher risk of anemia is probably associated with excessive blood loss following a c-section. Furthermore, obese women are less likely to breast-feed, which speeds uterine healing and increases the duration of postpartum amenorrehea.

Finally, gestational hypertension, dyslipidemia, glucose intolerance, and gestational diabetes are associated with an increased risk of type 2 diabetes, hypertension, and cardiovascular disease later in life.[44]

SHORT AND LONG-TERM OUTCOMES ON INFANT AND CHILD HEALTH

Congenital anomalies are more common among infants born to obese women than that occurring in infants of normal-weight women.[21] Neural tube defects are about twice as high among obese compared to non-obese women.[8] Other birth defects include oral clefts, heart anomalies, hydrocephaly, and abdominal wall abnormalities. The underlying cause of the increased risk of congenital anomalies is unknown, but accumulating evidence suggests that poor glycemic control plays a role.[21]

Maternal obesity is also a risk factor for intrauterine fetal death and stillbirth.[11] On the other hand, maternal obesity tends to protect against preterm birth and small-for-gestational age infants. Instead, maternal obesity increases the risk of having a large-for-gestational age (LGA) infant.[45] The prevalence of LGA babies is about 60% higher among obese women than normal-weight women. The higher prevalence of LGA babies born to obese mothers may reflect the higher rates of hyperglycemia leading to an increase fetal fuel supply and fetal overgrowth. Studies of the body composition of newborns show that infants born to obese mothers with gestational diabetes tend to have 60% more body fat at birth than do appropriate for gestational age infants born to normal weight, glucose tolerant women.[46] No consistent effect of maternal BMI on birth length has been reported.

Table 1
Nutritional and metabolic indicators in overweight and obese pregnant women

Indicator	Type of evaluation	Objective
Clinical	Family and personal history of overweight and obesity.	To identify genetic and lifestyle risk patterns.
	Dietary assessment (food frequency, 24hrs recall survey).	To evaluate: Glycemic and glucose load index in the regular diet. Food patterns consumption Energy intake and antioxidant consumption.
	Blood pressure	Gestational hypertension or preeclampsia.
Anthropometrical	Weight, body composition (Air displacement pletismography (ADP), skin folds (triceps, biceps, sub scapular and thigh)), monthly.	To evaluate: Weight gain Fat % and fat distribution.
	Symphysis-fundus height and Fetal ultrasound, monthly.	Fetal growth (small-for-gestational age infants and large-for-gestational age (LGA) infants).
Biochemical	Glucose Challenge Test at 20 weeks of pregnancy. Glucose tolerance test at 28 weeks of pregnancy.	To diagnose gestational diabetes mellitus
	Lipids profile, each trimester.	Dyslipidemia.
	Hemoglobin, each trimester.	Anemia.

Later on in life, infants born to obese women are more likely to develop obesity and associated comorbidities.[47] Most studies that have examined maternal pregravid BMI and childhood weight status have found positive associations with adjusted odds ratios ranging from 2 to 4.[47-48] This tracking of weight status from birth to adolescence and young adulthood begs for identifying maternal interventions that reduce fetal overgrowth and fat gain in order to break this vicious cycle. Also the risk of having the metabolic syndrome at 6, 7, 9 and 11 years of age was increased by 81% if the mother was obese prior to pregnancy.[51]

As mentioned above, overweight and obese women have lower rates of breastfeeding. Breastfeeding has been demonstrated to reduce the risk of later obesity.[52] Using data from the National Longitudinal Survey of Youth, Li, et al.[48] showed that children whose mothers were obese prior to pregnancy and who never breast-fed were at six times greater risk of being overweight compared to children whose mothers were normal weight and breast-fed for at least four months. Reduced rates of breastfeeding among obese women are related to mechanical difficulties associated with latching on and proper positioning of the infant, the high c-section rates that delays the first suckling, and a lower prolactin response to suckling at greater than 48 hours after delivery that could compromise milk production.[53] Finally, there is a growing body of evidence that maternal obesity influences infant and child feeding styles. In a highly controlled metabolic study of obese and normal-weight non-breast feeding mothers of infants five months of age, it was found that obese mothers fed their infants less frequently and spent less time feeding them or interacting with them.[54]

Thus, the cost of maternal obesity is very high with detrimental effects on both maternal and infant health. The effects of maternal obesity on long-term risk of obesity and chronic disease in the child have grave implications for perpetuating the vicious cycle of this public health problem.

ASSESSING OVERWEIGHT AND OBESE MEXICAN WOMEN DURING PREGNANCY TO REDUCE SHORT- AND LONG-TERM HEALTH PROBLEMS IN THE MOTHER AND CHILD

Table 1 list the principal clinical, authropometrical and biochemical indicators for evaluating over weight and obese pregnant women.

RESUMEN

En el siglo XXI la obesidad se ha convertido en una epidemia en todo el mundo. En México cerca de 75% de las mujeres en edad reproductiva (entre 20-49 años) presentan obesidad o sobrepeso (índice de masa corporal > 25); mientras que en Estados Unidos más de 60% presentan esta condición. La obesidad y el sobrepeso se suelen asociar con una ganancia excesiva de peso en la gestación, además de una retención del sobrepeso meses después de haber resuelto el embarazo. Este exceso de peso tiene efecto sobre la evolución del recién nacido e incrementa su riesgo a desarrollar sobrepeso. En este artículo se revisan las principales implicaciones metabólicas de la adiposidad materna en la reproducción y los efectos tanto a corto como largo plazo de esta condición sobre el neonato. Por último se presentan algunas guías prácticas para el manejo de este problema de salud.

PALABRAS GUÍA: *Sobrepeso, obesidad, embarazo, adiposidad.*

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