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The challenge of feeding the maternal-placental-fetal triad

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Abstract

The global epidemic of overweight and obesity in pre-pregnancy and excessive gestation weight gain are challenging the nutrition community to formulate a literacy platform with guidelines for pregnancy weight gain. Before developing a health literacy platform, understanding the central role of the placenta as a mediator of the mother and fetus is critical. In this brief, we present illustrative statistics about pre-pregnancy body mass and gestation weight gain; the role of specific hormones in pregnancy related to weight gain and adverse pregnancy outcomes like large-for-date newborns. Recent evidence demonstrates how placental function is essential to the maternal-fetal dyad contingent on its size, any pregnancy comorbidity like preeclampsia and the sex of the offspring. Threading the information about the maternal-placental-fetal triad in a sex-specific context offers new insights into future directions for nutrition science.

Short review

Gestational weight gain (GWG) is a multifaceted, complex phenomenon central to the viability of the maternal-placental-fetal triad. GWG has a bidirectional feedback loop with maternal hormones, body mass index (BMI), physiology, metabolism, physical activity and diet in pregnancy all playing a part. The systemic effects of GWG on the mother and placenta in turn influence fetal growth and sex-specific offspring health. Therefore, this review aims to briefly synopsize the maternal-placental-fetal triad, focus on sex-specific offspring outcomes, and identify gaps for future research on GWG in the maternal-placental-fetal triad.

The Maternal-gestation weight gain connection

National statistics reveal a relationship between maternal BMI and GWG. In 2014, 17 to 27% of U.S. women were obese in pre-pregnancy, with a higher percentage amongst Blacks and Hispanics (34.8 and 27.3%, respectively) than white women (22.7%) [1]. The state-specific prevalence of excessive GWG ranges from 38 to almost 55% across the U.S [2]. The connection is evident from a higher percent of moderate-to-high and high GWG in 63% and 28% of overweight and obese women in U.S. prenatal centers, respectively [3]. Importantly, women with moderate to high GWG are at a range of risk from 78% greater risk up to over 2.45-fold higher risk of a large-for-gestation age newborn [3]. These data present a perplexing challenge to formulate interventions for women with both high BMI and GWG to improve the health of the mother and newborn.

Most pregnant women gain approximately 22-33 lbs, predominantly in the last two trimesters of pregnancy [4-6].

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Weight gain is a natural result of the hormonal milieu influencing physiologic and metabolic changes in pregnancy. Hormones vary by parity, with higher levels in first than later pregnancies and co-vary by GWG. In 12 U.S. prenatal centers, 52%, 27% and 21% of women had high GWG in their 1st, 2nd and 3rd or more pregnancies, respectively [3]. Progesterone, a hormone vital for fetal growth and placentation, has pronounced effects on the mother. Notably, progesterone causes vasodilation and serves as a precursor to aldosterone [7]. Aldosterone increases circulating plasma as a result of the kidney's increased resorption of sodium and water [8]. The rise in intravascular volume with increasing gestation corresponds to an increase in maternal cardiac output necessary to meet the demand of the larger body mass in the mother, placenta and fetus [9].

Estrogens also influence GWG. The placenta produces about 30 times the mother's normal level of estrogens. These hormones contribute to reabsorption of sodium and water retention, and increase blood flow to the uterus, thus increasing uterine size and weight. Estrogen's role in fat deposition is augmented in pregnancy, as more fat is deposited in the buttocks, thighs, and breast tissue to ultimately enhance fetal growth and lactation [10]. With mounting estrogen levels, the body's metabolic rate rises to supply the nutritional demands of the mother and fetus [4].

Human placental lactogen (HPL) decreases sensitivity and utilization of glucose in the mother, leading to increased glucose levels supplied to the fetus. Consequently, there is an increase in use of free fatty acids from the mother's adipose tissue, providing an alternative nutritional support to the mother [4]. With the concurrent increased metabolic demand through estrogen, and the increased storage of excess energy as maternal fat, GWG may rise above average if not monitored.

A major contributor to GWG is the growing and developing fetus. A fetus at term weighs approximately 7.5 ± 1.1 lbs [11]. Another 3lbs of weight are attributable to the placenta and amniotic fluid [12]. Maternal appetite increases during the 2nd and 3rd trimesters of pregnancy and food intake rises [13]. Indeed, women delivering a son consume more energy than those delivering a daughter [14]. Thus sex of the fetus is a contributor to GWG.

High GWG has implications for the mother during pregnancy, delivery and postpartum. GWG above the recommended range is associated with abnormal glucose tolerance in some studies [15-17] while others report no association [18] or an association between low GWG and higher incidence of gestational diabetes [19,20]. Likewise, conflicting evidence has been found for the association between high GWG and pregnancy-induced hypertension and pre-eclampsia [21-23] in part due to gestation age at birth that varies by the severity of these conditions. At delivery, high GWG has been associated with failed labor induction and therefore higher risk of caesarian section [24,25]. Perhaps the most noteworthy effect of high GWG on maternal health occurs after pregnancy in the form of postpartum weight retention. Women who had high GWG are more likely to retain weight postpartum [26,27]. and develop obesity, [28,29] consequently increasing risk of diabetes, hypertension and cardiovascular disease [30,31]. Research on the effect of high GWG on mental health during and after pregnancy is lacking [32] additional research is needed in this area.

The central role of the placenta

The placenta is both a barrier and transporter of substances between the mother and fetus, and secretes hormones and other metabolites contributing to GWG through the aforementioned pathways [10]. The placenta may contribute to local and systemic inflammation through a cascade of syncytiotrophoblast microparticles binding to monocytes and producing inflammatory cytokines, and through macrophages infiltrating maternal adipose tissue for regulation. The placenta produces cytokines, including leptin for placentation, but also contributes to resistance to central satiety [33].

Placental size and weight covary in a sex-specific manner with pregnancy comorbidities. For example, in two studies of singleton and twin deliveries, sex-specific differences appeared with higher placental weights and fetal: placental weight ratios seen in male versus female offspring [34,35]. In comparison to male offspring of mothers with asthma, female offspring had lower birth weights. Further sexually dimorphic changes in peripheral microvascular blood flow were reported in response to maternal preeclampsia [37]. Male offspring of preeclamptic mothers had greater microvascular flow at 6 hours of age that did not change from 6 to 72 hours of age, whereas male offspring of normotensive mothers had an increasing blood flow from 6 to 72 hours of age. In contrast, female offspring of preeclamptic mothers had a similar microvascular blood flow to those of normotensive mothers at 6 hours of age that increased by 72 hours of age. High GWG is associated with higher risk of larger placental size and weight, [38] and alterations in genes associated with placental nutrient transport regulation [39]. However insufficient evidence exists describing placental dysregulation of metabolic and hormonal pathways in pregnancy co-morbidity like preeclampsia and by maternal BMI and GWG status.

Sex-specific outcomes

High GWG is associated with large-for-gestational age babies (weight, length or head circumference >90th percentile for gestational age) and high birth weight (>4 kilograms) [40] and infant body fat [41]. These infants may subsequently develop obesity, an adverse body composition and lipid profile, high blood pressure, and increased inflammatory markers in childhood and adulthood [42]. Sexual dimorphisms by intrauterine exposures are evident with faster and earlier growth of male than female fetuses [43].

Despite the plethora of research on maternal GWG, the sex-specific effects of maternal GWG have been reported in limited studies with suggestions of more adverse effects among boys than girls. High GWG in the first trimester was associated with reduced placental thickness and cord blood omega-3 polyunsaturated fatty acids in male offspring in a cross-sectional study [44]. In placentas collected from women with uncomplicated pregnancies, GWG was inversely correlated with glucose uptake in female placentas, suggesting a placental adaptation inherent to females [45]. In a prospective cohort study of mother-offspring dyads recruited at birth, high GWG was associated with higher levels of cardiometabolic risk factors such as insulin, homeostatic model assessment of insulin resistance (HOMA-IR), leptin, diastolic blood pressure and resting pulse in male offspring at 20 years of age, while female offspring showed decreases in total and LDL cholesterol [46]. The association between maternal GWG and offspring BMI was also stronger among boys than girls in early adulthood in one study [47].

Future directions

Paramount to understanding the connection between pre-pregnancy BMI-the placenta-fetal triad and GWG is the ability to disaggregate the effects of the pre-pregnant weight status from the GWG. Metabolic pathways including inflammation established prior to pregnancy may set the stage for a plethora of different effects of GWG from those in pregnancy. Preventive options to reduce excessive GWG may be tailored to pre-pregnancy BMI and monitored by different pathways prior to conception. We recommend research in women of varying BMI who want to get pregnant to assess hormonal and other metabolic pathways prior to pregnancy. They should then be examined for trajectory of changes in metabolic and other physiological compartments throughout pregnancy by sex of the offspring. Of importance would be an assessment of the body fat distribution in pre-pregnancy by maternal BMI to be able to compare metabolic and GWG differences in women with high visceral versus overall body fat.

Many women do not know what to eat, how much and when to gain the weight in pregnancy. The IOM guidelines do not offer a health literacy platform to inform women about the quality of and quantity of food by trimester of pregnancy with implications for GWG, the placenta and the health of the offspring. Repeated collections of diet and physical activity across pregnancy are essential to create dietary plans to achieve optimal GWG and pregnancy outcomes. Finally placenta work-ups by sex of the offspring using various 'omics' would then enliven the knowledge base of the transport of food across the mother-placenta-fetal triad.

Industry is changing the amount and composition of prenatal vitamin-mineral supplements. Women are taking prenatal supplements or individual supplements before pregnancy with limited data to assess the benefits or adverse effects of the supplements to the triad by sex of the offspring. Too little or too much folic acid in pregnancy is associated with risk of neural tube defects and obesity in the offspring [48]. The maternal-placenta-fetal triad is exposed to supplements without complete understanding how much gets through the placenta to the fetus, let alone the effects on the mother and offspring. The triad is the unit to study to address feeding the next birth cohorts in the U.S.

Figures

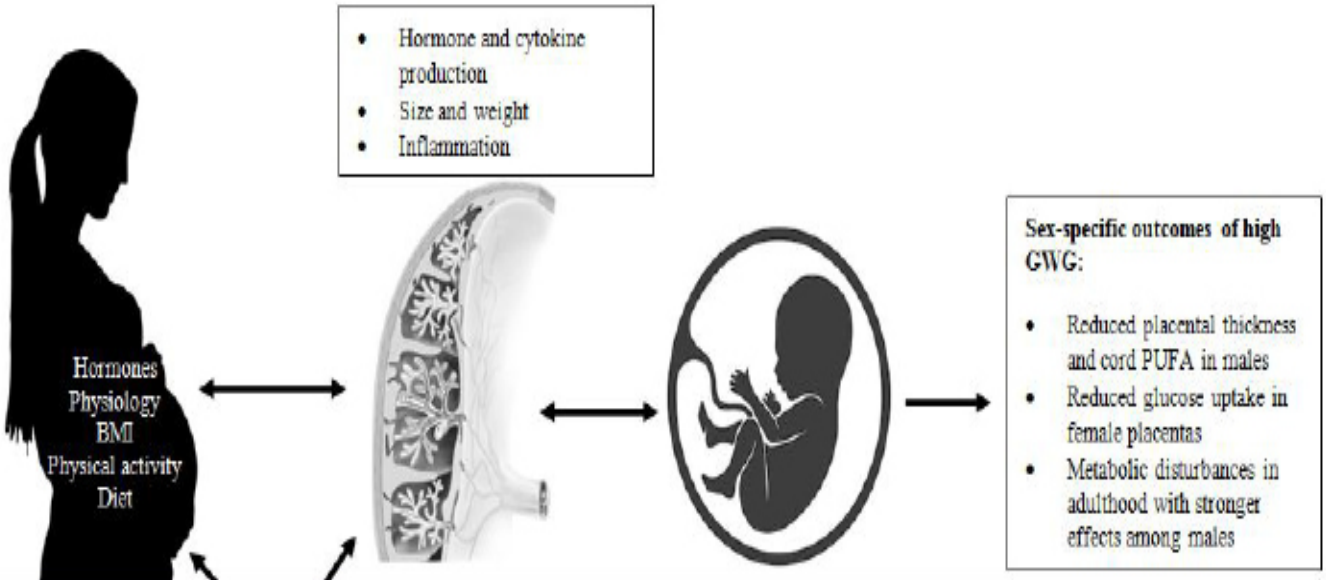

Figure 1: The maternal-placental-fetal triad

References

1. Branum AM, Kirmeyer SE, Gregory ECW. Pre-pregnancy body mass index by maternal characteristics and state: Data from the birth certificate, 2014. National vital statistics reports. Hyatsville MD. National Center for Health Statistics. 2016; 65.

2. Deputy NP, Sharma AJ, Kim SY. Gestational Weight Gain - United States, 2012 and 2013. MMWR Morb Mortal Wkly Rep. 2015; 64: 1215-1220.

3. Pugh SJ, Albert PS, Kim S, Grobman W, Hinkle SN, Newman RB, et al. Patterns of gestational weight gain and birthweight outcomes in the Eunice Kennedy Shriver National Institute of Child Health and Human Development Fetal Growth Studies-Singletons: a prospective study. Am J Obstet Gynecol. 2017; 341-346.

4. Institute of Medicine (US) Committee on Nutritional Status During Pregnancy and Lactation. Nutrition During Pregnancy: Part I Weight Gain: Part II Nutrient Supplements. In: Washington (DC): National Academies Press (US). 1990.

5. Hinkle SN, Mitchell EM, Grantz KL, Ye A, Schisterman EF. Maternal Weight Gain During Pregnancy: Comparing Methods to Address Bias Due to Length of Gestation in Epidemiological Studies. Paediatr Perinat Epidemiol. 2016; 30: 294-304.

6. Johnson JL, Farr SL, Dietz PM, Sharma AJ, Barfield WD, Robbins CL. Trends in gestational weight gain: the Pregnancy Risk Assessment Monitoring System, 2000-2009. Am J Obstet Gynecol. 2015; 212: 801-808.

7. Szmuilowicz ED, Adler GK, Williams JS, Green DE, Yao TM, Hopkins PN, et al. Relationship between aldosterone and

progesterone in the human menstrual cycle. J Clin Endocrinol Metab. 2006; 91: 3981-3987.

8. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc J Afr. 2016; 27: 89-94.

9. Hall ME, George EM, Granger JP. [The heart during pregnancy]. Rev Esp Cardiol. 2011; 64: 1045-1050.

10. Guyton AC, Hall JE. Textbook of medical physiology. 11 ed. Philadelphia: New Delhi: Elsevier Saunders. 2006.

11. Donahue SM, Kleinman KP, Gillman MW, Oken E. Trends in birth weight and gestational length among singleton term births in the United States: 1990-2005. Obstet Gynecol. 2010; 115: 357-364.

12. Barbour LA. Weight gain in pregnancy: is less truly more for mother and infant? Obstet Med. 2012; 5: 58-64.

13. Faas MM, Melgert BN, de Vos P. A Brief Review on How Pregnancy and Sex Hormones Interfere with Taste and Food Intake. Chemosens Percept. 2010; 3: 51-56.

14. Tamimi RM, Lagiou P, Mucci LA, Hsieh CC, Adami HO, Trichopoulos D. Average energy intake among pregnant women carrying a boy compared with a girl. BMJ. 2003; 326: 1245-1246.

15. Saldana TM, Siega-Riz AM, Adair LS, Suchindran C. The relationship between pregnancy weight gain and glucose tolerance status among black and white women in central North Carolina. Am J Obstet Gynecol. 2006; 195: 1629-1635.

16. Herring SJ, Oken E, Rifas-Shiman SL, Rich-Edwards JW, Stuebe AM, Kleinman KP, et al. Weight gain in pregnancy and risk of maternal hyperglycemia. Am J Obstet Gynecol. 2009; 201: e61-67.

17. Tovar A, Must A, Bermudez OI, Hyatt RR, Chasan-Taber L. The impact of gestational weight gain and diet on abnormal glucose tolerance during pregnancy in Hispanic women. Matern Child Health J. 2009; 13: 520-530.

18. Murakami M, Ohmichi M, Takahashi T, Shibata A, Fukao A, Morisaki N, et al. Pre-pregnancy body mass index as an important predictor of perinatal outcomes in Japanese. Arch Gynecol Obstet. 2005; 271: 311-315.

19. Yang W, Han F, Gao X, Chen Y, Ji L, Cai X. Relationship Between Gestational Weight Gain and Pregnancy Complications or Delivery Outcome. Sci Rep. 2017; 7: 12531.

20. Brennand EA, Dannenbaum D, Willows ND. Pregnancy outcomes of First Nations women in relation to pregravid weight and pregnancy weight gain. J Obstet Gynaecol Can. 2005; 27: 936-944.

21. Shao Y, Qiu J, Huang H, Mao B, Dai W, He X, et al. Pre-pregnancy BMI, gestational weight gain and risk of preeclampsia: a birth cohort study in Lanzhou, China. BMC Pregnancy Childbirth. 2017; 17: 400.

22. Macdonald-Wallis C, Tilling K, Fraser A, Nelson SM, Lawlor DA. Gestational weight gain as a risk factor for hypertensive disorders of pregnancy. Am J Obstet Gynecol. 2013; 209: e321-327.

23. Saftlas A, Wang W, Risch H, Woolson R, Hsu C, Bracken M. Pre-pregnancy body mass index and gestational weight gain as risk factors for preeclampsia and transient hypertension. Ann Epidemiol. 2000; 10: 475.

24. Xiong C, Zhou A, Cao Z, Zhang Y, Qiu L, Yao C, et al. Association of pre-pregnancy body mass index, gestational weight gain with cesarean section in term deliveries of China. Sci Rep. 2016; 6: 37168.

25. Kwon HY, Kwon JY, Park YW, Kim YH. The risk of emergency cesarean section after failure of vaginal delivery according to pre-pregnancy body mass index or gestational weight gain by the 2009 Institute of Medicine guidelines. Obstet Gynecol Sci. 2016; 59: 169-177.

26. Ashley-Martin J, Woolcott C. Gestational weight gain and postpartum weight retention in a cohort of Nova Scotian women. Matern Child Health J. 2014; 18: 1927-1935.

27. Vesco KK, Dietz PM, Rizzo J, Stevens VJ, Perrin NA, Bachman DJ, et al. Excessive gestational weight gain and postpartum weight retention among obese women. Obstet Gynecol. 2009; 114: 1069-1075.

28. Mamun AA, Kinarivala M, O'Callaghan MJ, Williams GM, Najman JM, Callaway LK. Associations of excess weight gain during pregnancy with long-term maternal overweight and obesity: evidence from 21 y postpartum follow-up. Am J Clin Nutr. 2010; 91: 1336-1341.

29. Amorim AR, Rössner S, Neovius M, Lourenço PM, Linné Y. Does excess pregnancy weight gain constitute a major risk for increasing long-term BMI? Obesity (Silver Spring). 2007; 15: 1278-1286.

30. McClure CK, Catov JM, Ness R, Bodnar LM. Associations between gestational weight gain and BMI, abdominal adiposity, and traditional measures of cardiometabolic risk in mothers 8 y postpartum. Am J Clin Nutr. 2013; 98: 1218-1225.

31. Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. Rev Obstet Gynecol. 2008; 1: 170-178.

32. Cunningham SD, Mokshagundam S, Chai H, Lewis JB, Levine J, Tobin JN, et al. Postpartum Depressive Symptoms: Gestational Weight Gain as a Risk Factor for Adolescents Who Are Overweight or Obese. J Midwifery Womens Health. 2018; 63: 178-184.

33. Rasmussen KM, Yaktine AL. Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. Washington (DC): National Academies Press (US). 2009.

34. Wallace JM, Bhattacharya S, Horgan GW. Gestational age, gender and parity specific centile charts for placental weight for singleton deliveries in Aberdeen, UK. Placenta. 2013; 34: 269-274.

35. Almog B, Shehata F, Aljabri S, Levin I, Shalom-Paz E, Shrim A. Placenta weight percentile curves for singleton and twins deliveries. Placenta. 2011; 32: 58-62.

36. Murphy VE, Gibson PG, Giles WB, Zakar T, Smith R, Bisits AM, et al. Maternal asthma is associated with reduced female fetal growth. Am J Respir Crit Care Med. 2003; 168:

1317-1323.

37. Stark MJ, Clifton VL, Wright IM. Neonates born to mothers with preeclampsia exhibit sex-specific alterations in microvascular function. Pediatr Res. 2009; 65: 292-295.

38. Ouyang F, Parker MG, Luo ZC, Wang X, Zhang HJ, Jiang F, et al. Maternal BMI, gestational diabetes, and weight gain in relation to childhood obesity: The mediation effect of placental weight. Obesity (Silver Spring). 2016; 24: 938-946.

39. Brett KE, Ferraro ZM, Holcik M, Adamo KB. Placenta nutrient transport-related gene expression: the impact of maternal obesity and excessive gestational weight gain. J Matern Fetal Neonatal Med. 2016; 29: 1399-1405.

40. Goldstein R, Teede H, Thangaratinam S, Boyle J. Excess Gestational Weight Gain in Pregnancy and the Role of Lifestyle Intervention. Semin Reprod Med. 2016; 34: e14-21.

41. Hull HR, Thornton JC, Ji Y, Paley C, Rosenn B, Mathews P, et al. Higher infant body fat with excessive gestational weight gain in overweight women. Am J Obstet Gynecol. 2011; 205: e211-217.

42. Fraser A, Tilling K, Macdonald-Wallis C, Sattar N, Brion MJ, Benfield L, et al. Association of maternal weight gain in pregnancy with offspring obesity and metabolic and vascular traits in childhood. Circulation. 2010; 121: 2557-2564.

43. Eriksson JG, Kajantie E, Osmond C, Thornburg K, Barker DJ. Boys live dangerously in the womb. Am J Hum Biol. 2010; 22: 330-335.

44. O'Tierney-Ginn PF, Gillingham M, Fowler J, Brass E, Marshall NE, Thornburg KL. Maternal Weight Gain Regulates Omega-3 Fatty Acids in Male, Not Female, Neonates. Reprod Sci. 2017; 24: 560-567.

45. Walker SP, Ugoni AM, Lim R, Lappas M. Inverse relationship between gestational weight gain and glucose uptake in human placenta from female foetuses. Pediatr Obes. 2014; 9: e73-76.

46. Hrolfsdottir L, Rytter D, Olsen SF, Bech BH, Maslova E, Henriksen TB, et al. Gestational weight gain in normal weight women and offspring cardio-metabolic risk factors at 20 years of age. Int J Obes (Lond). 2015; 39: 671-676.

47. Mamun AA, O'Callaghan M, Callaway L, Williams G, Najman J, Lawlor DA. Associations of gestational weight gain with offspring body mass index and blood pressure at 21 years of age: evidence from a birth cohort study. Circulation. 2009; 119: 1720-1727.

48. Perkins E, Murphy SK, Murtha AP, Schildkraut J, Jirtle RL, Demark-Wahnefried W, et al. Insulin-like growth factor 2/H19 methylation at birth and risk of overweight and obesity in children. J Pediatr. 2012; 161: 31-39.