

Bölüm 6

GEBELİK VE OBEZİTE



Aslı AKDÖNER¹

| GİRİŞ

Obezite, obstetride, anne ve yenidoğanı etkileyen en önemli sağlık problemidir (1). Obezite, Dünya Sağlık Örgütü ve Ulusal Sağlık Enstitüsü tarafından vücut kitle indeksinin $> 30 \text{ kg/m}^2$ olması olarak tanımlanmıştır. Obezite; dünya çapında, epidemi düzeyinde bir toplumsal sağlık problemidir ve gebelik sürecinde obezite, maternal ve neonatal morbidite ve mortalitede artış ile ilişkilidir (2). 2015 yılında FIGO, maternal ve neonatal risk artışı ile ilgili bir rapor yayınlamış ve obez kadınların; preterm doğum, makrozomi ve prenatal ölüm gibi riskleri azaltmak için gebelik öncesinde kilo vermeleri gerektiğini belirtmiştir (3). Ulusal Sağlık ve Beslenme Değerlendirme Araştırması (NHANES), 2012 yılında, Amerika'daki kadınların %58,5'nin fazla kilolu ya da obez olduğunu göstermiştir. Siyahi ve Meksikalı kadınlarda bu oran daha da artmaktadır (4,5). Fazla kiloluluk ve obezite insidansı, geçtiğimiz son 30 yılda, özellikle gelişmiş ülkelerde, erkeklerin %70'ini ve kadınların da %60'ını etkileyerek, küresel bir sağlık problemi oluşturmaktadır (6). Populasyon verileri, kadınların %50'sinin gebeliğin başında fazla kilolu ya da obez olduğunu göstermektedir. Bu durum hem anne hem de fetus için gebelik ve doğumla ilgili tüm risklerde artışla ilişkilidir (7,8). Gebelik sürecindeki obezite, spontan ve tekrarlayan abortlara neden olabilmektedir. Ayrıca, fetal anomali tespiti için ultrason görüntülemesinin suboptimal olmasına ve fetal kardiyak ve nö-

¹ Öğr. Gör. Dr., Dokuz Eylül Üniversitesi Kadın Hastalıkları ve Doğum AD.,
drasliakdoner@gmail.com

önerilere uymayan ve fazla kilo alan kadınlara göre, daha uygun düzeyde doğum ağırlığı ve daha az obstetrik komplikasyon ile ilişkilidir (98).

Obezite ile mücadele kapsamında en etkili yöntemin; diyet düzenlemesi, egzersiz planlanması ve davranış değişikliklerini temel alan yoğun programların planlanması olduğu bulunmuştur. Gebelik, bu uygulama için çok uygun bir dönemdir. Çünkü, pek çok kadın, gebeliklerini daha sağlıklı geçirmek ve bebeklerinin sağlığını korumak için, davranış şekillerini değiştirmeye oldukça isteklidir (99). Ancak, antenatal dönemde diyet ve hayat tarzı değişikliklerinin fazla kilolu ve obez kadınlardaki kilo alımına sınırlı etkisi olduğu LIMIT ve UPBEAT çalışmalarında gösterilmiştir. Bu çalışmaların sonuçları, daha kapsamlı bir sistematik derleme ile de uyumlu bulunmuştur (100-103). Bu derlemede, her ne kadar küçük çaplı olsa da pek çok çalışma diyet düzenlenmesi ve hayat tarzı değişikliklerinin gebelikte kilo alımı üzerine etkisini değerlendirmiştir (103). Bu çalışmalara göre bu değişikliklerin maternal gebelik ve doğum sonuçlarına etkisi azdır (100,101). Yine de gebelikle aşırı kilo ve obezite ile mücadele, diyet ve hayat tarzı değişikliklerine dayanmaktadır. Gebelik sürecinde hastaya diyet, hayat tarzı değişiklikleri ve fiziksel egzersiz önerilmesi sağ duyulu bir öneridir. Her ne kadar etkileri sınırlı da olsa, esas amaç, öncelikle, hastaya zarar vermemektir. Gebelik sonuçlarını iyileştirmek için kadınların gebelik öncesinde kilo vermesi daha etkin bir yaklaşımdır ve genelde göz ardı edilmektedir. Her ne kadar, yeterli düzey kanıt olmasa da prekonsepsiyonel danışmanlık olarak, uygun kilo aralığına ulaşan obez veya aşırı kilolu kadınların gebelik sonuçlarını iyileştirebileceği düşünülmektedir (104).

SONUÇ

Obezite, gebelik sonuçlarını etkileyen epidemik bir hastalıktır. Pregestasyonel obezitenin, gebelikte aşırı kilo alımına göre daha çok obstetrik probleme neden olduğu bilinmektedir (99). Obezite, hem anne hem de yenidoğan için kısa ve uzun dönemde risk oluşturmaktadır. Bu nedenlerle, obez kadınların gebelik öncesinde kilo vermesinin sağlanması, maternal ve neonatal sonuçları iyileştirecektir. Bunun sağlanması için, toplum sağlığı eğitim programlarının oluşturulması ve tüm kesimlerin bu eğitimlere ulaşabilmesi önemlidir (5).

KAYNAKLAR

1. Flegal KM, Carroll MD, Kit BK, Ogden CL, Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. *AMA* 2012; 307: 491-7. DOI:10.1001
2. American College of Obstetricians & Gynecologists. Practice bulletin # 156: obesity in pregnancy. *Obstet Gynecol* 2015; 126 (6): e112-e126.

3. International Federation of Gynecology and Obstetric (FIGO). New born health. London: FIGO, 2015.
4. Robker R and International Federation of Gynecology and Obstetrics (FIGO). Fertility. London: FIGO, 2015.
5. Federico G. Mariona, Perspectives in obesity and pregnancy, *Women's Health* 2016, 12 (6): 523– 532.
6. Ng, M. et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*, 2014; 384, 766–781.
7. Scheil W. et al. Pregnancy outcome in South Australia 2012. [online], (2014), <http://www.sahealth.sa.gov.au/wps/wcm/connect/4301aa8048429ccb831e9d5ae66e927/14134.1-Pregnancy+Outcomes+ Report-ONLINESecurev2.pdf?MOD=AJPERES& ACHEID=4301aa8048429ccb831e9d5ae 66e927>.
8. Dodd JM, Grivell RM, Nguyen AM, Chan A, Robinson JS, Maternal and perinatal health outcomes by body mass index category. *Aust. NZ J. Obstet. Gynaecol.*, 2011; 51, 136–140.
9. Lim CC, Mahmood T. Obesity in pregnancy. *Best Pract Res Clin Obstet Gynaecol.* 2015; 29(3): 309-319.
10. Catalano PM, Shankar K. Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child. *BMJ*, 2017; 356: j1.
11. Mission JF, Marshall NE, Caughey AB. Pregnancy risks associated with obesity. *Obstet Gynecol Clin North Am.* 2015; 42(2):335–53. DOI: 10.1016
12. Sohlberg S, Stephansson O, Cnattingius S, Wikstrom AK. Maternal body mass index, height, and risks of preeclampsia. *Am J Hypertens.* 2012; 25: 120–125. DOI: 10.1038
13. MacInnis N, Woolcott CG, McDonald S, Kuhle S, Population Attributable Risk Fractions of Maternal Overweight and Obesity for Adverse Perinatal Outcomes. *Sci Rep.* 2016; 6:22895. DOI: 10.1038
14. Lutsiv O, Mah J, Beyene J, McDonald SD, The effects of morbid obesity on maternal and neonatal health outcomes: a systematic review and meta-analyses. *Obes Rev.* 2015; 16(7):531–46. DOI: 10.1111
15. Marchi J, Berg M, Dencker A, Olander EK, Begley C, Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. *Obes Rev.* 2015; 16(8):621–38. DOI: 10.1111
16. Santangeli L, Sattar N, Huda SS, Impact of maternal obesity on perinatal and childhood outcomes. *Best Pract Res Clin Obstet Gynaecol.* 2015; 29(3):438–48. DOI: 10.1016
17. Stang J, Huffman LG, Position of the Academy of Nutrition and Dietetics: Obesity, Reproduction, and Pregnancy Outcomes. *J Acad Nutr Diet.* 2016; 116(4):677–91. DOI: 10.1016
18. Rivera HM, Christiansen KJ, Sullivan EL. The role of maternal obesity in the risk of neuropsychiatric disorders. *Front Neurosci.* 2015; 9:194. DOI: 10.3389
19. Nguyen MU, Wallace MJ, Pepe S, Menheniott TR, Moss TJ, Burgner D, Perinatal inflammation: a common factor in the early origins of cardiovascular disease? *Clin Sci (Lond).* 2015; 129(8):769–84. DOI: 10.1042
20. LaCoursiere DY, Barrett-Connor E, O'Hara MW, Hutton A, Varner MW, The association between prepregnancy obesity and screening positive for postpartum depression. *BJOG.* 2010; 117(8):1011–8. DOI: 10.1111
21. Dubova EA, Pavlov KA, Borovkova EI, Bayramova MA, Makarov IO, Shchegolev AI, Vascular endothelial growth factor and its receptors in the placenta of pregnant women with obesity. *Bull Exp Biol Med.* 2011; 151(2):253–8.
22. Moran MC, Mulcahy C, Zombori G, Ryan J, Downey P, McAuliffe FM, Placental volume, vasculature and calcification in pregnancies complicated by pre-eclampsia and intra-uterine

- growth restriction. *Eur J Obstet Gynecol Reprod Biol.* 2015; 195:12–7. DOI: 10.1016
23. Kristy R. Howell, PhD and Theresa L. Powell, PhD, Effects of maternal obesity on placental function and fetal development, *Reproduction.* 2017 March; 153(3): R97–R108. DOI:10.1530
 24. Ford SP, Zhang L, Zhu M, Miller MM, Smith DT, Hess BW, Moss GE, Nathanielsz PW, Nijland MJ. Maternal obesity accelerates fetal pancreatic beta-cell but not alpha-cell development in sheep: prenatal consequences. *Am J Physiol Regul Integr Comp Physiol.* 2009; 297(3): R835–43. DOI: 10.1152
 25. Bolton JL, Bilbo SD, Developmental programming of brain and behavior by perinatal diet: focus on inflammatory mechanisms. *Dialogues Clin Neurosci.* 2014; 16(3):307–20.
 26. Hinkle SN, Schieve LA, Stein AD, Swan DW, Ramakrishnan U, Sharma AJ, Associations between maternal prepregnancy bodymass index and child neurodevelopment at 2 years of age. *Int J Obes.* 2012; 36:1312–1319. DOI: 10.1038
 27. Hinkle SN, Sharma AJ, Kim SY, Schieve LA. Maternal prepregnancy weight status and associations with children’s development and disabilities at kindergarten. *Int J Obes.* 2013; 37:1344–1351. DOI: 10.1038
 28. Adane AA, Mishra GD, Tooth LR. Maternal pre-pregnancy obesity and childhood physical and cognitive development of children: a systematic review. *Int J Obes (Lond).* 2016; 40, 1608–1618. DOI: 10.1038
 29. Tanda R, Salsberry PJ, Reagan PB, Fang MZ, The impact of prepregnancy obesity on children’s cognitive test scores. *Matern Child Health J.* 2013; 17:222–229. DOI: 10.1007
 30. Hytten F, Blood volume changes in normal pregnancy. *Clin Haematol* 1985;14(3):601–612.
 31. Duvekot JJ, Peeters LL, Maternal cardiovascular hemodynamic adaptation to pregnancy. *Obstet Gynecol Surv* 1994;49(12, Suppl): S1–S14.
 32. Clark SL, Cotton DB, LeeW, et al., Central hemodynamic assessment of normal term pregnancy. *Am J Obstet Gynecol* 1989;161(6 Pt 1): 1439–1442.
 33. Marshall NE, Spong CY, Obesity, Pregnancy Complications, and Birth Outcomes, *Semin Reprod Med* 2012; 30: 465–471.
 34. Heit JA, Kobbervig CE, James AH, PettersonTM, Bailey KR, Melton LJ III. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. *Ann Intern Med* 2005; 143 (10): 697–706.
 35. Brenner B. Haemostatic changes in pregnancy. *Thromb Res* 2004; 114(5-6): 409–414.
 36. Doyle NM, Monga M. Thromboembolic disease in pregnancy. *Obstet Gynecol Clin North Am*, 2004; 31 (2): 319–344.
 37. Allman-Farinelli MA, Obesity and venous thrombosis: a review. *Semin Thromb Hemost* 2011;37(8):903–907.
 38. Larsen TB, Sørensen HT, Gislum M, Johnsen SP, Maternal smoking, obesity, and risk of venous thromboembolism during pregnancy and the puerperium: a population-based nested case-control study. *Thromb Res* 2007; 120 (4): 505–509.
 39. Robinson HE, O’Connell CM, Joseph KS, McLeod NL. Maternal outcomes in pregnancies complicated by obesity. *Obstet Gynecol* 2005; 106 (6): 1357–1364.
 40. Abbasi F, Brown BW Jr, Lamendola C, McLaughlin T, Reaven GM. Relationship between obesity, insulin resistance, and coronary heart disease risk. *J Am Coll Cardiol* 2002; 40 (5): 937–943.
 41. McLaughlin T, Allison G, Abbasi F, Lamendola C, Reaven G. Prevalence of insulin resistance and associated cardiovascular disease risk factors among normal weight, overweight, and obese individuals. *Metabolism* 2004; 53 (4): 495–499.
 42. Catalano PM, Tyzbir ED, Roman NM, Amini SB, Sims EA. Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women. *Am J Obstet Gynecol* 1991;165(6 Pt 1): 1667–1672.

43. Catalano PM, Huston L, Amini SB, Kalhan SC. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. *Am J Obstet Gynecol* 1999; 180 (4): 903–916.
44. Hauth JC, Clifton RG, Roberts JM, et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Maternal insulin resistance and preeclampsia. *Am J Obstet Gynecol* 2011; 204 (4): 327, e1–e6.
45. Mangge H, Almer G, Truschig-Wilders M, Schmidt A, Gasser R, Fuchs D. Inflammation, adiponectin, obesity and cardiovascular risk. *Curr Med Chem* 2010; 17 (36): 4511–4520.
46. Ramsay JE, Ferrell WR, Crawford L, Wallace AM, Greer IA, Sattar N. Maternal obesity is associated with dysregulation of metabolic, vascular, and inflammatory pathways. *J Clin Endocrinol Metab* 2002; 87 (9): 4231–4237.
47. Roberts JM, Bodnar LM, Patrick TE, Powers RW. The role of obesity in preeclampsia. *Pregnancy Hypertens* 2011; 1 (1): 6–16.
48. Segovia SA, Vickers MH, Gray C, Reynolds CM. Maternal obesity, inflammation, and developmental programming. *Biomed Res Int*. 2014; 2014:418975. DOI: 10.1155
49. Wedekind L, Belkacemi L. Altered cytokine network in gestational diabetes mellitus affects maternal insulin and placental-fetal development. *J Diabetes Complications*. 2016; 30 (7): 1393–400. DOI: 10.1016
50. Hauguel-de Mouzon S, Guerre-Millo M. The placenta cytokine network and inflammatory signals. *Placenta*. 2006; 27 (8): 794–8.
51. Pavlov OV, Niauri DA, Selutin AV, Selkov SA. Coordinated expression of TNF α - and VEGF-mediated signaling components by placental macrophages in early and late pregnancy. *Placenta*. 2016; 42: 28–36. DOI: 10.1016
52. Knöfler M, Mösl B, Bauer S, Griesinger G, Husslein P. TNF-alpha/TNFR1 in primary and immortalized first trimester cytotrophoblasts. *Placenta*. 2000; 21 (5–6): 525–35.
53. Siwetz M, Blaschitz A, El-Heliebi A, Hiden U, Desoye G, Huppertz B, Gauster M. TNF- α alters the inflammatory secretion profile of human first trimester placenta. *Lab Invest*. 2016; 96 (4): 428–38. DOI: 10.1038
54. Christian LM, Porter K. Longitudinal changes in serum proinflammatory markers across pregnancy and postpartum: effects of maternal body mass index. *Cytokine*. 2014; 70 (2): 134–40. DOI: 10.1016
55. Crocker IP, Cooper S, Ong SC, Baker PN. Differences in apoptotic susceptibility of cytotrophoblasts and syncytiotrophoblasts in normal pregnancy to those complicated with preeclampsia and intrauterine growth restriction. *Am J Pathol*. 2003; 162(2):637–43.
56. Sadowsky DW, Adams KM, Gravett MG, Witkin SS, Novy MJ. Preterm labor is induced by intraamniotic infusions of interleukin-1beta and tumor necrosis factor-alpha but not by interleukin-6 or interleukin-8 in a nonhuman primate model. *Am J Obstet Gynecol*. 2006; 195(6):1578–89.
57. Stewart FM, Freeman DJ, Ramsay JE, Greer IA, Caslake M, Ferrell WR. Longitudinal assessment of maternal endothelial function and markers of inflammation and placental function throughout pregnancy in lean and obese mothers. *J Clin Endocrinol Metab*. 2007; 92 (3): 969–75.
58. Stone RA, Silvis A, Jude D, Chaffin D. Increasing body mass index exacerbates inflammation in obese gravidas. *Obstet Gynecol*. 2014; 123(Suppl 1):81S.
59. Aye IL, Lager S, Ramirez VI, Gaccioli F, Dudley DJ, Jansson T, Powell TL. Increasing maternal body mass index is associated with systemic inflammation in the mother and the activation of distinct placental inflammatory pathways. *Biol Reprod*. 2014b; 90(6):129. DOI: 10.1095
60. Friis CM, Paasche Roland MC, Godang K, Ueland T, Tanbo T, Bollerslev J, Henriksen T. Adiposity-Related Inflammation: Effects of Pregnancy. *Obesity*. 2013; 21: E124–E130. DOI: 10.1002

61. Aye IL, Jansson T, Powell TL. TNF- α stimulates System A amino acid transport in primary human trophoblast cells mediated by 38 MAPK signaling. *Physiol Rep*. 2015; 3 (10): pii-e12594. DOI: 10.14814
62. Jones HN, Jansson T, Powell TL. IL-6 stimulates system A amino acid transporter activity in trophoblast cells through STAT3 and increased expression of SNAT2. *Am J Physiol Cell Physiol*. 2009a; 297: C1228–C1235. DOI: 10.1152
63. Lager S, Jansson N, Olsson AL, Wennergren M, Jansson T, Powell TL. Effect of IL-6 and TNF- α on fatty acid uptake in cultured human primary trophoblast cells. *Placenta*. 2011; 32 (2): 121–7. DOI: 10.1016
64. Ruan H, Dong LQ. Adiponectin signaling and function in insulin target tissues. *J Mol Cell Biol*. 2016; 8 (2): 101–9. DOI: 10.1093
65. Jansson N, Nilselfelt A, Gellerstedt M, Wennergren M, Rossander-Hulthé L, Powell TL, Jansson T. Maternal hormones linking maternal body mass index and dietary intake to birth weight. *Am J Clin Nutr*. 2008; 87 (6): 1743–9.
66. Duval F, Santos ED, Poidatz D, Sérazin V, Gronier H, Vialard F, Dieudonné MN. Adiponectin Inhibits Nutrient Transporters and Promotes Apoptosis in Human Villous Cytotrophoblasts: Involvement in the Control of Fetal Growth. *Biol Reprod*. 2016; 94(5):111. DOI: 10.1095
67. Aye IL, Jansson T, Powell TL. Interleukin-1 β inhibits insulin signaling and prevents insulin-stimulated system A amino acid transport in primary human trophoblasts. *Mol Cell Endocrinol*. 2013; 381(1–2):46–55. DOI: 10.1016
68. Triantafyllou GA, Paschou SA, Mantzoros CS. Leptin and Hormones: Energy Homeostasis. *Endocrinol Metab Clin North Am*. 2016; 45(3):633–45. DOI: 10.1016
69. Dos Santos E, Duval F, Vialard F, Dieudonné MN. The roles of leptin and adiponectin at the fetal-maternal interface in humans. *Horm Mol Biol Clin Investig*. 2015; 24(1):47–63. DOI: 10.1515
70. Tessier DR, Ferraro ZM, Gruslin A. Role of leptin in pregnancy: consequences of maternal obesity. *Placenta*. 2013; 34(3):205–11. DOI: 10.1016
71. Bouret SG. Nutritional programming of hypothalamic development: critical periods and windows of opportunity. *Int J Obes Suppl*. 2012; (Suppl 2):2. S19–24. DOI: 10.1038
72. Knight M, Kurinczuk JJ, Spark P, Brocklehurst P; UK Obstetric Surveillance System. Extreme obesity in pregnancy in the United Kingdom. *Obstet Gynecol* 2010;115(5):989–997.
73. Weiss JL, Malone FD, Emig D, et al; FASTER Research Consortium. Obesity, obstetric complications and cesarean delivery rate—a population-based screening study. *Am J Obstet Gynecol* 2004; 190(4):1091–1097.
74. Ovesen P, Rasmussen S, Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. *Obstet Gynecol* 2011;118(2 Pt 1):305–312
75. Kayem G, Kurinczuk J, Lewis G, Golightly S, Brocklehurst P, Knight M. Risk factors for progression from severe maternal morbidity to death: a national cohort study. *PLoS ONE* 2011;6(12): e29077.
76. Reddy UM, Branum AM, Klebanoff MA. Relationship of maternal body mass index and height to twinning. *Obstet Gynecol* 2005; 105(3):593–597.
77. Hoekstra C, Willemsen G, van Beijsterveldt CE, Lambalk CB, Montgomery GW, Boomsma DI. Body composition, smoking, and spontaneous dizygotic twinning. *Fertil Steril* 2010;93(3): 885–893.
78. Kim SS, Zhu Y, Grantz KL, et al. Obstetric and neonatal risks among obese women without chronic disease. *Obstet Gynecol* 2016; 128: 104–12.
79. Huda SS, Forrest R, Paterson N, Jordan F, Sattar N, Freeman DJ. In preeclampsia, maternal third trimester subcutaneous adipocyte lipolysis is more resistant to suppression by insulin than in healthy pregnancy. *Hypertension* 2014; 63: 1094–101.
80. Wang Z, Wang P, Liu H, et al. Maternal adiposity as an independent risk factor for pre-eclam-

- psia: a meta-analysis of prospective cohort studies. *Obes Rev* 2013; 14: 508–21.
81. Salihi HM, De La Cruz C, Rahman S, August EM. Does maternal obesity cause preeclampsia? A systematic review of the evidence. *Minerva Ginecol* 2012; 64: 259–80.
 82. Yariv Yogev, Patrick M. Catalano, Pregnancy and Obesity, *Obstet Gynecol Clin N Am* 36 (2009) 285–300.
 83. Kalter H. Five-decade international trends in the relation of perinatal mortality and congenital malformations: stillbirth and neonatal death compared. *Int J Epidemiol* 1991; 20: 173–9.
 84. Odland V, Haglund B, Pakkanen M, et al. Deliveries, mothers and newborn infants in Sweden, 1973–2000. Trends in obstetrics as reported to the Swedish Medical Birth Register. *Acta Obstet Gynecol Scand* 2003; 82: 516–28.
 85. Nohr EA, Bech BH, Davies MJ, et al. Prepregnancy obesity and fetal death. *Obstet Gynecol* 2005; 106: 250–9.
 86. Riley L, Wertz M, McDowell I, Obesity in Pregnancy: Risks and Management, *American Family Physician*, 2018, Volume 97, Number 9.
 87. ACOG. ACOG practice bulletin # 105: bariatric surgery and pregnancy. *Obstet Gynecol* 2009; 113(6): 1405–1413.
 88. Kominiarek MA. Preparing for and managing a pregnancy after bariatric surgery. *Semin Perinatol* 2011; 35(6): 356–361.
 89. Norgaard LN, Gjerris ACR, Kirkegaard I, et al. Fetal growth in pregnancies conceived after gastric bypass surgery in relation to surgery-to-conception interval: a Danish National cohort study. *PLoS ONE* 2014; 9(3): e90317.
 90. Santoro N, Lasley B, McConnell D, et al. Body size and ethnicity are associated with menstrual cycle alterations in women in the early menopausal transition: The Study of Women's Health across the Nation (SWAN) daily hormone study. *J Clin Endocrinol Metab* 2004; 89: 2622–31. DOI:10.1210
 91. Luke B, Brown MB, Stern JE, Missmer SA, Fujimoto VY, Leach R. SART Writing Group. Female obesity adversely affects assisted reproductive technology (ART) pregnancy and live birth rates. *Hum Reprod* 2011; 26: 245–52. DOI:10.1093
 92. Bausenwein J, Serke H, Eberle K, et al. Elevated levels of oxidized low-density lipoprotein and of catalase activity in follicular fluid of obese women. *Mol Hum Reprod* 2010; 16: 117–24. DOI:10.1093
 93. Valckx SD, Arias-Alvarez M, De Pauw I, et al. Fatty acid composition of the follicular fluid of normal weight, overweight and obese women undergoing assisted reproductive treatment: a descriptive cross-sectional study. *Reprod Biol Endocrinol* 2014; 12: 13. DOI:10.1186
 94. La Vignera S, Condorelli R, Bellanca S, et al. Obesity is associated with a higher level of pro-inflammatory cytokines in follicular fluid of women undergoing medically assisted procreation (PMA) programs. *Eur Rev Med Pharmacol Sci* 2011; 15: 267–73.
 95. Patrick M Catalano, Kartik Shankar, Obesity and pregnancy: mechanisms of short term and long term adverse consequences for mother and child, *BMJ* 2017; 360: j1.
 96. Committee on Nutritional Status During Pregnancy and Lactation. *Nutrition During Pregnancy*. Washington, DC: National Academy Press; 1990: parts I and II.
 97. Weight Gain During Pregnancy: Reexamining the guidelines. IOM Brief Report, May, 2009. Available at: <http://www.iom.edu>. Accessed September 2009.
 98. ACOG Committee Opinion Number 315, September 2005. Available at: <http://www.acog.org>. Accessed September 2009.
 99. Taraneh Shirazian, MD, and Sreekala Raghavan, BS, Obesity and Pregnancy: Implications and Management Strategies for Providers, *MOUNT SINAI JOURNAL OF MEDICINE*, 2009, 76:539–545.
 100. Poston L et al. Effect of a behavioural intervention in obese pregnant women (the UPBEAT study): a multicentre, randomised controlled trial. *Lancet Diabetes Endocrinol.*, 2015; 3(10):

767-77.

101. Dodd, JM et al. Antenatal lifestyle advice for women who are overweight or obese: the LIMIT randomised trial. *BMJ*, 2014; 348, g1285.
102. Dodd, JM et al. Effects of antenatal lifestyle advice for women who are overweight or obese on maternal diet and physical activity: the LIMIT randomised trial. *BMC Med*, 2014; 12, 161.
103. Thangaratinam, S. et al. Effects of interventions in pregnancy on maternal weight and obstetric outcomes: meta-analysis of randomised evidence. *BMJ*, 2012; 344, e2088.
104. Dodd JM, Managing obesity during pregnancy—what are the options? *Nat Rev Endocrinol* 2015 Dec;11(12):691-2.