Chettinad Health City Medical Journal
Volume 11, Issue 2 - 2022, Pg. No. 69-74
Peer Reviewed & Open Access Journal

Review Article

Role of Insulin Resistance in Gestational Diabetes Mellitus: A Literature Review

Irfat Ara[1], Mudasir Maqbool[2], Imran Gani[2]

[1]Research Officer, Regional Research Institute of Unani Medicine, Srinagar, Jammu and Kashmir, India.
[2]Research Scholar, Department of Pharmaceutical Sciences, University of Kashmir, Srinagar, Jammu and Kashmir, India.
DOI: https://doi.org/10.24321/2278.2044.202218

I N F O

Corresponding Author:
Mudasir Maqbool, Department of Pharmaceutical Sciences, University of Kashmir, Srinagar, Jammu and Kashmir, India.
E-mail Id:
bhatmudasir.scholar@kashmiruniversity.net
Orcid Id:
https://orcid.org/0000-0002-9036-008X
How to cite this article:
Ara I, Maqbool M, Gani I. Role of Insulin Resistance in Gestational Diabetes Mellitus: A Literature Review. Chettinad Health City Med J. 2022;11(2):69-74.

Date of Submission: 2022-06-06
Date of Acceptance: 2022-06-22

A B S T R A C T

Several physiologic, hormonal, and molecular processes contribute to the emergence of hyperglycaemia during pregnancy. Increased insulin resistance is seen during the course of a healthy pregnancy. During the early stages of normal pregnancies, the pancreatic β-cells secrete more insulin, which slows the rise in plasma glucose levels. This regulation explains the abnormally modest increases in plasma glucose levels brought on by elevated insulin resistance. The aim of this review was to evaluate the role of insulin resistance in gestational diabetes mellitus (GDM). The authors extensively searched various electronic databases like PubMed, Scopus, and Google Scholar for the collection of material regarding the role of insulin resistance in GDM. It was seen that hyperglycaemia results from the combination of the pregnancy's increased insulin tolerance and pancreatic beta-cell insufficiency. Scientific studies have revealed that individuals who present with GDM are more likely to acquire chronic insulin resistance because of the superimposition of lower insulin production by the cells in that condition (GDM). Due to their significance in the development of postpartum diabetes mellitus, inflammation markers in GDM have been widely researched. Inflammation during GDM induces adaptive reactions in the placenta, which can have a substantial effect on the programming of foetal development.

Keywords: Pregnancy, Insulin, β-cells, Pathophysiology, Gestational Diabetes Mellitus

Introduction

Gestational diabetes mellitus (GDM) is one of the most common maternal complications, and its frequency has increased globally alongside the rise of type 2 diabetes. The term gestational diabetes mellitus refers to any dysglycaemia that develops or is identified for the first time during pregnancy. It has become a global public health problem and one of the world's leading public health concerns for both mothers and children. It causes various pregnancy problems and has been linked to adverse maternal and foetal outcomes, including a higher risk of pre-eclampsia, caesarean sections, increased foetal weight with accompanying issues, and hypoglycaemia.[1] Maintaining glycaemic control during pregnancy greatly reduces the frequency of adverse outcomes, according to studies.[2] According to the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, obesity and GDM are separate and combined risk factors for adverse pregnancy outcomes.[3,4]

Pregnancy is characterised by elevated insulin resistance.[5] As pregnancy continues, increased insulin resistance is observed during the second and third trimesters.[6] This increase in insulin resistance is believed to promote foetal growth by ensuring higher glucose levels in the mother.[7] It also leads to the increased utilisation of lipolysis pathways as energy sources in the mother, resulting in an increase in free fatty acids (FFA). GDM is characterised by an increased supply of nutrients to the foetus, resulting in excessive growth. Due to the release of adipocytokines and the diabetogenic action of placental hormones, there is an increase in insulin resistance throughout pregnancy.[8-10] The increased resistance is mostly the result of the diabetogenic effects of pregnancy hormones including cortisol, oestrogen, progesterone, human placental lactogen (hPL), and placental growth hormone (hPGH).[11,12] Increased adiposity during pregnancy is another factor linked to the development of insulin resistance. This is attributed to the influence of adipocytokines, which are hormones generated from adipocytes. It was hypothesised that insulin resistance is caused by post-receptor alterations that influenced insulin receptor-mediated processes. The steroid hormones cortisol, progesterone, and oestrogen have well-documented hyperglycaemic effects. As pregnancy continues, progesterone output rises, and this hormone is linked to insulin resistance in multiple ways.[13,14] HPL and hPGH are placental hormones that have extensive metabolic interactions and are principally responsible for ensuring that the foetus receives an adequate amount of carbohydrates. It has been demonstrated that hPL levels increase significantly during pregnancy and that hPL leads to peripheral insulin resistance.[15,16] A recent study has shown that adipose tissue and its accompanying cytokines, known as adipokines, play a significant role in the development of insulin resistance. Previously, placental hormones were thought to be predominantly responsible for the development of insulin resistance. Adiponectin, tumour necrosis factor-alpha (TNF-α), leptin, retinol binding protein-4 (RBP-4), interleukin-6 (IL-6), visfatin, and resistin have been evaluated as insulin resistance mediators. Adipocytes secrete adiponectin, and adiponectin levels are seen to decline as pregnancy develops. It has been demonstrated that GDM is associated with lower plasma adiponectin concentrations. In laboratory investigations, the effect of TNF-α on raising insulin resistance has been demonstrated.[17-19] Multiple studies have demonstrated a correlation between TNF levels and insulin resistance. It has also been reported that TNF-α reduces insulin secretion in GDM pregnancies. A study revealed that GDM is associated with elevated levels of TNF-α and decreased levels of adiponectin. According to reports, adipose tissue is connected with the release of adipokines that mediate insulin resistance. These adipokines influence glucose metabolism and insulin resistance via their effects on skeletal muscle, liver, and pancreatic β-cells, as well as molecular pathways that influence glucose transport.[19-23]

Role of Hormones in Gestational Diabetes Mellitus

The placenta influences various hormonal axes throughout pregnancy. Pregnancy hormones are secreted into maternal blood by the placenta. In some cases, the placenta secretes hormones that either bypass or completely replace normal hormonal regulation. There are certain similarities between the hormones of non-pregnant women and placental hormones, because of which, placental hormones may also regulate hormone release. Human placental growth hormone (hPGH), human placental lactogen (hPL), and human chorionic gonadotropin (hCG) are examples of pregnancy hormones. Throughout pregnancy, hormones such as prolactin, oestrogen, and cortisol are present in enhancing levels. The growth hormone axis is an example of maternal metabolism takeover. The pituitary growth hormone (GH) is nearly fully replaced by hPGH in the maternal blood at around 20 weeks of gestation and is secreted tonically.[24,25] Also, the level of hPGH in the blood is similar to that of acromegaly, which is more than tenfold as compared to GH in the non-pregnant state. In comparison with GH, hPGH exhibits a somatogenic effect.[26] The hPGH may cause raised insulin levels and may lower insulin-dependent uptake of glucose and glycogenesis. It may also cause a decrease in insulin's ability to hinder hepatic glucogenesis. Its effects on pregnancy in humans are still not clear. It looks like in pregnancy, hPGH is what controls the levels of insulin-like growth factors (IGFs). This shows that hPGH, IGFs, GH, and insulin-like growth factor binding proteins (IGF-BPs) all work together. During pregnancy, this could be the pathway that links the growth hormone axis with insulin resistance.[27-31] Intriguingly, during pregnancy, the growth hormone axis is also linked with the pregnancy-associated plasma protein A (PAPP-A) because of its association with IGF-BPs. This confirms the importance of the growth hormone axis during gestation. Progesterone, estradiol, cortisol, prolactin, hPGH, and hPL have been characterised as mediators of the shift in insulin sensitivity during pregnancy. In contrast, Kirwan JP et al. analysed the association between the variations in the levels of plasma of leptin, cortisol, progesterone, hCG, hPL, and oestrogen throughout pregnancy and those in insulin sensitivity. Only a substantial association between cortisol levels and insulin sensitivity was discovered by the scientists.[19,32,33] Instead, McIntyre HD et al. discovered that triglycerides, IGFBP1, and leptin were substantially linked with maternal insulin sensitivity estimates. Thus, insulin resistance has not been explained by any single hormone. In the maternal blood, various placental hormones have relatively short half-lives,

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202218

the impact of which is gone within 24 to 48 hours following birth, leading to the restoration of non-pregnant physiology in many ways.[28,34,35] This means that within one or two days after giving birth, mothers with type 1 diabetes have insulin needs that are the same as or even lower than they were before they got pregnant.[36,37]

Pancreatic β-cell Function

In normal pregnancies, β-cells undergo hyperplasia, hypertrophy, and increased secretory activity to counteract increased insulin resistance. It has been argued that one facet of the continuum of insulin resistance leads to GDM. Insulin sensitivity is known to have been reduced in females with poor glucose tolerance during pregnancy.[38,39] This compromises pancreatic beta cells and renders them incapable of compensating for increasing insulin resistance during pregnancy. This leads to GDM hyperglycaemia. Pancreatic-cell dysfunction is the inability of cells to recognise and respond effectively to circulating glucose levels.[38,40] Changes in placental hormones and cytokines have been linked to pancreatic β-cell dysfunction, lipotoxicity, glucotoxicity, and elevated indicators of inflammatory and oxidative stress in GDM.[41]

Discussion

There are a variety of potential causes for GDM. Some of them are elevated BMI, obesity, weight gain during pregnancy, dietary habits, family history, and past medical history. These factors work in an additive fashion to exacerbate insulin resistance and β-cell dysfunction. GDM was distinguished from normal pregnancies by abnormal glucose and lipid metabolism.[41,42] Hyperinsulinemia, hyperglycaemia, and hyperlipidaemia are metabolic abnormalities associated with it. These changed metabolic consequences have been demonstrated to modify gene expression, raise oxidative stress markers, increase lipid peroxidation levels, increase inflammatory markers, and alter the production and secretion of vasoactive molecules. Genes with altered expression have been discovered in GDM mothers. Several genes are expressed differently in the placenta of GDM patients.[43-46] The degree of total antioxidant potential was shown to be lower in the serum of GDM mothers as compared to controls during pregnancy. In GDM pregnancies, the blood concentrations of oxidative stress markers appeared to be greater than in control pregnancies. Indicators of oxidative stress in placental tissues of GDM-affected babies have improved, according to studies. In the maternal blood and placenta of GDM pregnancies, there was an increase in oxidative damage and a decrease in antioxidant defence systems, according to a prospective study. In women with GDM, an increase in malonyldialdehyde (MDA) levels, which serve as a template for lipid peroxidation, has been found.[47-49] It was also claimed that no substantial change in lipid peroxidation was seen in GDM pregnancies. Inflammatory markers in GDM have been extensively researched due to their role in the development of postpartum diabetes mellitus. The involvement of inflammation in the placenta during gestational diabetes may have a significant role in foetal growth.[50,51] As a result of these biochemical changes in GDM, there was an improvement in the release of vasoactive molecules. In gestational diabetes, alterations in the normal levels of endothelial dysfunction markers such as soluble vascular cell adhesion molecule-1 (sVCAM-1) and endothelial nitric oxide synthase (eNOS) have been identified in both maternal and cord blood. Therefore, it has been established that these metabolic alterations lead to placental endothelial dysfunction. Hypoxia affects the placenta in gestational diabetes. In an experimental study on the placenta of mice, there was an increase in both hypoxia and inflammatory responses. These enhancements have been described as modifications to the microvascular and microscopic structures of the placenta.[52] As evidenced by placental structural changes, the placenta has the ability to adapt to its hormonal and metabolic environment. According to the Pederson Hypothesis, the increased glucose availability to the foetus also causes excessive foetal growth. The extended theory further adds that high glucose causes the foetal pancreas to release considerable quantities of insulin. It may lead to foetal hyperinsulinemia, which can influence the oxygen demand that causes hypoxia,[53] as a result of which, placental alterations like hypercapillarisation and developmental programming were triggered. The reciprocal impacts of the maternal, foetal, and placental metabolic environment depended on the form and function of the placenta.[46] As a result, these factors influence pregnancy outcomes.

Conclusion

Gestational diabetes mellitus (GDM) is a serious pregnancy complication in which people without previously diagnosed diabetes have chronic hyperglycaemia after delivery. In certain instances, pancreatic-cell dysfunction leads to poor glycaemic regulation on the basis of chronic insulin resistance, resulting in hyperglycaemia. Elevated insulin resistance is a characteristic of pregnancy. Around the second or third trimester, rising insulin resistance is observed. This increase in insulin resistance is believed to ensure that higher glucose levels in the mother support foetal growth. It also increases the utilisation of the mother's lipolysis pathways as energy sources, leading to an increase in free fatty acids. Inflammatory markers in GDM have been examined primarily due to their significance in the development of postpartum diabetes mellitus. Inflammation triggers adaptive responses in the placenta during gestational diabetes, which may play a significant role in foetal developmental programming. The ability to tailor the best possible treatment for pregnant women

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202218

with diabetes, beneficial for the mother and the next generation, depends on having a thorough understanding of the mechanisms underlying the development of insulin resistance during pregnancy and its impact on the offspring. This requires knowledge of the causes and effects of insulin resistance in pregnancy.

Acknowledgement

The authors would like to acknowledge all the authors whose work has been reviewed in the preparation of the manuscript.

Conflict of Interest: None

References

1. HAPO Study Cooperative Research Group. The hyperglycemia and adverse pregnancy outcome (HAPO) study. Int J Gynecol Obstet. 2002;78:69-77. [Google Scholar]
2. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med. 2005;352:2477-86. [PubMed] [Google Scholar]
3. Biswas T, Uddin MJ, Mamun AA, Pervin S, Garnett SP. Increasing prevalence of overweight and obesity in Bangladeshi women of reproductive age: findings from 2004 to 2014. PloS One. 2017;12:e0181080. [PubMed] [Google Scholar]
4. Balarajan Y, Villamor E. Nationally representative surveys show recent increases in the prevalence of overweight and obesity among women of reproductive age in Bangladesh, Nepal, and India. J Nutr. 2009;139:2139-44. [PubMed] [Google Scholar]
5. Kühl C. Insulin secretion and insulin resistance in pregnancy and GDM: implications for diagnosis and management. Diabetes. 1991;40:18-24. [PubMed] [Google Scholar]
6. 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;165:1667-72. [PubMed] [Google Scholar]
7. Moyce BL, Dolinsky VW. Maternal β-cell adaptations in pregnancy and placental signalling: implications for gestational diabetes. Int J Mol Sci. 2018;19:3467. [PubMed] [Google Scholar]
8. Phelps RL, Metzger BE, Freinkel N. Carbohydrate metabolism in pregnancy: XVII. Diurnal profiles of plasma glucose, insulin, free fatty acids, triglycerides, cholesterol, and individual amino acids in late normal pregnancy. Am J Obstet Gynecol. 1981;140:730-6. [PubMed] [Google Scholar]
9. Catalano PM, Kirwan JP, Haugel-de Mouzon S, King J. Gestational diabetes and insulin resistance: role in short- and long-term implications for mother and fetus. J Nutr. 2003;133:1674S-83S. [PubMed] [Google Scholar]
10. Dirar AM, Doupis J. Gestational diabetes from A to Z. World J Diabetes. 2017;8:489. [PubMed] [Google Scholar]
11. Ryan EA, Enns L. Role of gestational hormones in the induction of insulin resistance. J Clin Endocrinol Metab. 1988;67:341-7. [PubMed] [Google Scholar]
12. Sonagra AD, Biradar SM, Dattatreya K, Murthy JD. Normal pregnancy-a state of insulin resistance. J Clin Diagn Res. 2014;8:CC01. [PubMed] [Google Scholar]
13. Briana DD, Malamitsi-Puchner A. Reviews: adipocytokines in normal and complicated pregnancies. Reprod Sci. 2009;16:921-37. [PubMed] [Google Scholar]
14. Wada T, Hori S, Sugiyama M, Fujisawa E, Nakano T, Tsuneki H, Nagira K, Saito S, Sasaoka T. Progesterone inhibits glucose uptake by affecting diverse steps of insulin signaling in 3T3-L1 adipocytes. Am J Physiol Endocrinol Metab. 2010;298:E881-8. [PubMed] [Google Scholar]
15. Handwerger S, Freemark M. The roles of placental growth hormone and placental lactogen in the regulation of human fetal growth and development. J Pediatr Endocrinol Metab. 2000;13:343-56. [PubMed] [Google Scholar]
16. Beck P, Daughaday WH. Human placental lactogen: studies of its acute metabolic effects and disposition in normal man. J Clin Invest. 1967;46:103-10. [PubMed] [Google Scholar]
17. Worda C, Leipold H, Gruber C, Kautzky-Willer A, Knöfler M, Bancher-Todesca D. Decreased plasma adiponectin concentrations in women with gestational diabetes mellitus. Am J Obstet Gynecol. 2004;191:2120-4. [PubMed] [Google Scholar]
18. Frost RA, Lang CH. Skeletal muscle cytokines: regulation by pathogen-associated molecules and catabolic hormones. Curr Opin Clin Nutr Metab Care. 2005;8:255-63. [PubMed] [Google Scholar]
19. Kirwan JP, Mouzon SH, Lepercq J, Challier JC, Huston-Presley L, Friedman JE, Kalhan SC, Catalano PM. TNF-α is a predictor of insulin resistance in human pregnancy. Diabetes. 2002;51:2207-13. [PubMed] [Google Scholar]
20. McLachlan KA, O'Neal D, Jenkins A, Alford FP. Do adiponectin, TNFα, leptin and CRP relate to insulin resistance in pregnancy? Studies in women with and without gestational diabetes, during and after pregnancy. Diabetes Metab Res Rev. 2006;22:131-8. [PubMed] [Google Scholar]
21. Altinova AE, Toruner F, Bozkurt N, Bukan N, Karakoc A, Yetkin I, Ayvaz G, Cakir N, Arslan M. Circulating concentrations of adiponectin and tumor necrosis

factor-α in gestational diabetes mellitus. Gynecol Endocrinol. 2007;23:161-5. [PubMed] [Google Scholar]
22. Xu J, Zhao YH, Chen YP, Yuan XL, Wang J, Zhu H, Lu CM. Maternal circulating concentrations of tumor necrosis factor-alpha, leptin, and adiponectin in gestational diabetes mellitus: a systematic review and meta-analysis. ScientificWorldJournal. 2014;2014:926932. [PubMed] [Google Scholar]
23. Rabe K, Lehrke M, Parhofer KG, Broedl UC. Adipokines and insulin resistance. Mol Med. 2008;14:741-51. [PubMed] [Google Scholar]
24. Fuglsang J, Lauszus F, Flyvbjerg A, Ovesen P. Human placental growth hormone, insulin-like growth factor I and-II, and insulin requirements during pregnancy in type 1 diabetes. J Clin Endocrinol Metab. 2003;88:5042. [PubMed] [Google Scholar]
25. Zehravi M, Maqbool M, Ara I. Polycystic ovary syndrome and infertility: an update. Int J Adolesc Med Health. 2022;34:1-9. [PubMed] [Google Scholar]
26. MacLeod JN, Worsley I, Ray J, Friesen HG, Liebhaber SA, Cooke NE. Human growth hormone-variant is a biologically active somatogen and lactogen. Endocrinology. 1991;128:1298-302. [PubMed] [Google Scholar]
27. Barbour LA. Metabolic culprits in obese pregnancies and gestational diabetes mellitus: big babies, big twists, big picture: The 2018 Norbert Freinkel Award Lecture. Diabetes Care. 2019;42:718-26. [PubMed] [Google Scholar]
28. McIntyre HD, Chang AM, Callaway LK, Cowley DM, Dyer AR, Radaelli T, Farrell KA, Huston-Presley L, Amini SB, Kirwan JP, Catalano PM; Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Cooperative Research Group. Hormonal and metabolic factors associated with variations in insulin sensitivity in human pregnancy. Diabetes Care. 2010;33:356-60. [PubMed] [Google Scholar]
29. McIntyre HD, Serek R, Crane DI, Veveris-Lowe T, Parry A, Johnson S, Leung KC, Ho KK, Bougoussa M, Hennen G, Igout A, Chan FY, Cowley D, Cotterill A, Barnard R. Placental growth hormone (GH), GH-binding protein, and insulin-like growth factor axis in normal, growth-retarded, and diabetic pregnancies: correlations with fetal growth. J Clin Endocrinol Metab. 2000;85:1143-50. [PubMed] [Google Scholar]
30. Fuglsang J, Ovesen P. Aspects of placental growth hormone physiology. Growth Horm IGF Res. 2006;16:67-85. [PubMed] [Google Scholar]
31. Zehravi M, Maqbool M, Ara I. Correlation between obesity, gestational diabetes mellitus, and pregnancy outcomes: an overview. Int J Adolesc Med Health. 2021;33(6):339-45. [PubMed] [Google Scholar]
32. Monget P, Oxvig C. PAPP-A and the IGF system. Ann Endocrinol. 2016;77(2):90-6. [PubMed] [Google Scholar]
33. Zehravi M, Maqbool M, Ara I. Polycystic ovary syndrome and reproductive health of women: a curious association. Int J Adolesc Med Health. 2021;33(6):333-7. [PubMed] [Google Scholar]
34. Fuglsang J, Sandager P, Møller N, Fisker S, Orskov H, Ovesen P. Kinetics and secretion of placental growth hormone around parturition. Eur J Endocrinol. 2006;154(3):449-57. [PubMed] [Google Scholar]
35. Lønberg U, Damm P, Andersson AM, Main KM, Chellakooty M, Lauenborg J, Skakkebaek NE, Juul A. Increase in maternal placental growth hormone during pregnancy and disappearance during parturition in normal and growth hormone-deficient pregnancies. Am J Obstet Gynecol. 2003;188:247-51. [PubMed] [Google Scholar]
36. Roeder HA, Moore TR, Ramos GA. Changes in postpartum insulin requirements for patients with well-controlled type 1 diabetes. Am J Perinatol. 2016;33(7):683-7. [PubMed] [Google Scholar]
37. Zehravi M, Maqbool M, Ara I. Healthy lifestyle and dietary approaches to treating polycystic ovary syndrome: a review. Open Health. 2022;3:60-5. [Google Scholar]
38. Clark CM, Qiu C, Amerman B, Porter B, Fineberg N, Aldasouqi S, Golichowski A. Gestational diabetes: should it be added to the syndrome of insulin resistance? Diabetes Care. 1997;20:867-71. [PubMed] [Google Scholar]
39. Catalano PM. Carbohydrate metabolism and gestational diabetes. Clin Obstet Gynecol. 1994;37:25-38. [PubMed] [Google Scholar]
40. Buchanan TA, Xiang AH. Gestational diabetes mellitus. J Clin Invest. 2005;115:485-91. [PubMed] [Google Scholar]
41. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. Int J Mol Sci. 2018;19:3342. [PubMed] [Google Scholar]
42. Solomon CG, Willett WC, Carey VJ, Rich-Edwards J, Hunter DJ, Colditz GA, Stampfer MJ, Speizer FE, Spiegelman D, Manson JE. A prospective study of pregravid determinants of gestational diabetes mellitus. JAMA. 1997;278:1078-83. [PubMed] [Google Scholar]
43. Biri A, Onan A, Devrim E, Babacan F, Kavutcu M, Durak I. Oxidant status in maternal and cord plasma and placental tissue in gestational diabetes. Placenta. 2006;27:327-32. [PubMed] [Google Scholar]
44. Coughlan MT, Vervaart PP, Permezel M, Georgiou HM, Rice GE. Altered placental oxidative stress status in gestational diabetes mellitus. Placenta. 2004;25:78-84. [PubMed] [Google Scholar]
45. Madazlı R, Tuten A, Calay Z, Uzn H, Uludag S, Ocak V.

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202218

The incidence of placental abnormalities, maternal and cord plasma malondialdehyde and vascular endothelial growth factor levels in women with gestational diabetes mellitus and nondiabetic controls. Gynecol Obstet Invest. 2008;65:227-32. [PubMed] [Google Scholar]
46. Radaelli T, Varastehpour A, Catalano P, Mouzon SH. Gestational diabetes induces placental genes for chronic stress and inflammatory pathways. Diabetes. 2003;52:2951-8. [PubMed] [Google Scholar]
47. Enquobahrie DA, Williams MA, Qiu C, Meller M, Sorenson TK. Global placental gene expression in gestational diabetes mellitus. Am J Obstet Gynecol. 2009;200:206. [PubMed] [Google Scholar]
48. Toescu V, Nuttall SL, Martin U, Nightingale P, Kendall MJ, Brydon P, Dunne F. Changes in plasma lipids and markers of oxidative stress in normal pregnancy and pregnancies complicated by diabetes. Clin Sci. 2004;106:93-8. [PubMed] [Google Scholar]
49. Lappas M, Mittion A, Permezel M. In response to oxidative stress, the expression of inflammatory cytokines and antioxidant enzymes are impaired in placenta, but not adipose tissue, of women with gestational diabetes. J Endocrinol. 2010;204:75. [PubMed] [Google Scholar]
50. Wolf M, Sauk J, Shah A, Smirnakis KV, Jimenez-Kimble R, Ecker JL, Thadhani R. Inflammation and glucose intolerance: a prospective study of gestational diabetes mellitus. Diabetes Care. 2004;27:21-7. [PubMed] [Google Scholar]
51. Heitritter SM, Solomon CG, Mitchell GF, Skali-Ounis N, Seely EW. Subclinical inflammation and vascular dysfunction in women with previous gestational diabetes mellitus. J Clin Endocrinol Metab. 2005;90:3983-8. [PubMed] [Google Scholar]
52. Myatt L, Kossenjans W, Sahay R, Eis A, Brockman D. Oxidative stress causes vascular dysfunction in the placenta. J Matern Fetal Med. 2000;9:79-82. [PubMed] [Google Scholar]
53. Redinger RN. The pathophysiology of obesity and its clinical manifestations. Gastroenterol Hepatol. 2007;3:856. [PubMed] [Google Scholar]

ISSN: 2278-2044
DOI: https://doi.org/10.24321/2278.2044.202218