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Clinical Guidelines for Management of Diabetes in Pregnancy



Federation of Obstetric & Gynaecological Societies of India

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CHAPTER 2

Metabolic Alterations in Diabetic Pregnancy

Siddharth N Shah, Nihar Mehta, Tanvi Tuteja

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INTRODUCTION

Gestational diabetes is diabetes first detected in pregnancy. Although type 1 diabetes is more likely to develop in pregnancy, the great majority of women have pretype 2 diabetes, and many will go on to develop diabetes later in life. If type 1 diabetes is suspected during pregnancy or after delivery, autoimmunity should be confirmed by measurement of antibodies against islet cell antigens [antibodies directed against glutamic acid decarboxylase (GADA), islet antigen-2 antibody (IA-2A)]. Maturity onset diabetes of the young (MODY) may also present in pregnancy, and genetic testing is recommended when family history suggests that this phenotype may be present. However, in general gestational diabetes mellitus (GDM) can be regarded as pretype 2 diabetes.[1]

Gestational diabetes mellitus is a disease of the mother that associates with altered feto-placental vascular function. It describes a heterogeneous group of hyperglycemic metabolic disorders detected in pregnancy. It is characterized by inadequate beta cell secretion for the level of insulin resistance present whether the insulin response is normal or elevated.[2]

In normal pregnancy, insulin resistance emerges in the second trimester and progresses over the late third trimester, thereby increasing maternal glucose, free fatty acids (FFA), and amino acids in order to provide adequate energy to the fetus. In normal pregnancy, insulin resistance leads to an appropriate increase of insulin secretion, and blood glucose levels remain in the normal range. Due to the increasing demand of the developing fetus and increased transplacental nutrition transfer, maternal glucose levels are even lower than in healthy nonpregnant women.[1,3]

INSULIN RESISTANCE

The metabolic/endocrine changes accompanying the second half of gestation and inducing physiological pregnancy-related insulin resistance unmask and worsen the underlying pre-existing metabolic disturbances (pregestational insulin resistance and relative insulin secretion defect), leading to the full clinical picture of GDM.[4,5]

Impaired first phase insulin secretion, prolonged and increased second phase insulin release, reduced insulinogenic indices, increased hepatic glucose output (relative to prevailing hyperinsulinemia), changes in insulin kinetics, reduced glucose absorption from the gut, and varying degrees of insulin resistance have been described. These abnormalities have been described in women with GDM, as compared to pregnant women with normal glucose tolerance, based upon fasting or dynamic tests (oral and intravenous glucose tolerance tests).[1]

OTHER METABOLIC DISTURBANCES

Gestational diabetes mellitus associates with metabolic disturbances[1] such as abnormal handling of the locally released vasodilator adenosine, and biosynthesis and metabolism of cholesterol lipoproteins, or metabolic diseases resulting in endoplasmic reticulum stress and altered angiogenesis.

1. Increased fractional release of amylin and proinsulin relative to insulin secretion may be a cause or consequence of dysfunctional insulin secretion and action.[6] In addition, increased ectopic fat mass (intramyocellular and intrahepatic fat) and a slightly impaired flux through myocellular ATP synthase (fATP), the final step of mitochondrial oxidative phosphorylation, has also been found in women with GDM.[7]
2. Impaired lipid metabolism with increased FFA concentrations (insulin resistance of the adipose tissue with increased lipolysis) is also characteristic of the condition.
3. At present, changes of adiponectin and leptin appear to be the most important disturbances, although an increase of tumor necrosis factor-alpha (TNF-α) and plasma cortisol levels also parallel the increase of insulin resistance during pregnancy.[8]
4. TNF-α may impair the postreceptor insulin signaling cascade in skeletal muscle by activating pathways that increase sphingomyelinases and ceramides.
5. A decrease of adiponectin and increase of leptin has consistently been described, with changes in resistin, visfatin, chemerin, vaspin, fetuin-A, and many other proteins released from adipose tissue, the liver or the gastrointestinal tract have also been described, but with inconsistent results.[9]
6. Inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and soluble adhesion molecules [endothelial cell adhesion molecule (ECAM), vascular cell adhesion molecule (VCAM), and intercellular adhesion molecule (ICAM)] and vascular markers [e.g. asymmetric dimethylarginine (ADMA)] were found to be increased in some studies. In women with GDM or in those with a history of GDM, early endothelial dysfunction associates with the development of glucose dysregulation and other risk factors for atherosclerosis.

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7. Another interesting association can be seen between bone markers and insulin secretion and sensitivity in GDM. Increased osteocalcin and C-telopeptide (CTX) levels in GDM could be regarded as compensatory mechanisms which try to cope with increased demand on insulin secretion, while decreased osteopontin levels may relate to insulin resistance in GDM.[10]

CONCLUSION

To conclude insulin is a key factor playing a modulatory role in GDM-associated altered angiogenesis, and metabolism of lipids in human fetoplacental vascular bed. Clinical management of insulin sensitivity is considered a therapeutic target in treatment of mothers with GDM and this could result in reversal of insulin resistance along with GDM-associated alterations in angiogenesis and lipid metabolism. Thus, a better understanding of the mechanisms behind the alterations along with treatment of these women with diet/exercise and insulin help in preventing adverse fetal outcomes from this disease.

REFERENCES

1. Pathogenesis of GDM. In: The Living Textbook of Diabetes. Available online at https://www.diapedia.org/41040851394/rev/19 Accessed on January 6, 2018.
2. Salzer L, Tenenbaum-Gavish K, Hod M. Best Pract Res Clin Obstet Gynaecol. 2015;29(3):328-38.
3. Kautzky-Willer A. Endocrine changes in diabetic pregnancy. In: Djelmis J, Desoye G, Ivanisevic M (Eds). Diabetology of pregnancy. Basel, New York: Karger; 2005. pp 18-33.
4. Xiang AH, Peters RK, Trigo E, et al. Multiple metabolic defects during late pregnancy in women at high risk for type 2 diabetes. Diabetes. 1999;48(4):848-85.
5. Catalano PM. Obesity, insulin resistance, and pregnancy outcome. Reproduction. 2010;140(3):365-71.
6. Kautzky-Willer A, Thomaseth K, Ludvik B, et al. Elevated islet amyloid pancreatic polypeptide and proinsulin in lean gestational diabetes. Diabetes. 1997;46(4):607-14.
7. Prikoszovich T, Winzer C, Schmid AI, et al. Body and liver fat mass rather than muscle mitochondrial function determine glucose metabolism in women with a history of gestational diabetes mellitus. Diabetes Care. 2011;34(2):430-6.
8. Buckley BS, Harreiter J, Damm P, et al. Gestational diabetes mellitus in Europe: prevalence, current screening practice and barriers to screening. A review. Diabet Med. 2012;29(7):844-54.
9. Worda C, Leipold H, Gruber C, et al. Decreased plasma adiponectin concentrations in women with gestational diabetes mellitus. Am J Obstet Gynecol. 2004;191(6): 2120-4.
10. Winhofer Y, Kiefer FW, Handisurya A, et al. CTX (crosslaps) rather than osteopontin is associated with disturbed glucose metabolism in gestational diabetes. PLoS One. 2012;7(7):e40947.

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Clinical Guidelines for Management of Diabetes in Pregnancy

With increase in the prevalence of Diabetes in pregnancy (including both gestational diabetes and pre-gestational/overt diabetes), several challenges are being faced in the management of this important medical disorder. This book on *Clinical Guidelines for Management of Diabetes in Pregnancy* is an endeavour to meet the needs of the Obstetricians, Physicians and Endocrinologists who are jointly involved in the management of this important medical disorder. The book is aimed to provide a comprehensive approach to diabetes in pregnancy yet is easy to understand and comprehend. The "Practical Obstetrics Committee of FOGSI" has collaborated with leading clinicians in the field to bring out this book.

This book includes latest guidelines and management protocols, tables, flowcharts and key points for the benefit of the practicing clinicians and postgraduate students. The unique point about this book is that the authors of the chapters are all experts in their respective fields of Obstetrics, Medicine, Endocrinology, Neonatology and Ophthalmology who have added their knowledge and expertise of several years to enrich the contents of the book so that the reader will get a holistic view of dealing with day-to-day common problems and clinical management of pregnant women with diabetes.



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ISBN 978-93-5270-395-1