ejpmr, 2018,5(1), 373-374

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

DIABETES IN PREGNANCY: *LONG TERM EFFECTS ON OFFSPRING BEGINS IN UTERO*

Mishra Archana*[1], Arya Priyanka[2] and Saxena Pikee[3]

[1]Associate Professor, Department of Obstetrics and Gynaecology, VMMC and SJH, New Delhi, India.
[2]Senior Resident, Department of Obstetrics and Gynaecology, VMMC and SJH, New Delhi, India.
[3]Professor, Department of Obstetrics and Gynaecology, LHMC and SSKH, New Delhi, India.

***Corresponding Author: Dr. Mishra Archana**

Associate Professor, Department of Obstetrics and Gynaecology, VMMC and SJH, New Delhi, India.

Article Received on 20/11/2017 **Article Revised on 10/12/2017** **Article Accepted on 30/12/2017**

Exposure to an adverse fetal and/or early postnatal environment may lead to a number of chronic diseases in the future life of offspring. One such condition is diabetes in pregnancy- both preexisting DM and gestational diabetes mellitus.

Diabetes in pregnancy can be 1 of 3 types: pre-existing type 1 diabetes, pre-existing type 2 diabetes and gestational diabetes (diabetes with onset or first diagnosis in pregnancy). Drastic increase in prevalence of all 3 types of pregnancy diabetes have been noted in recent years[1] and hence a matter of concern. The prevalence of GDM in India varies from 3.8 to 21% in different parts of the country, depending on the geographical locations and diagnostic methods used[2] and nearly 125 million people in India are expected to develop Type2 DM by 2040.

Diabetes in pregnancy is associated with both short term and long term consequences in offspring and mother. While GDM is associated with an increase in adverse fetal and neonatal outcomes such as fetal macrosomia, birth injury, neonatal hyperbilirubinemia, hypoglycemia, hypocalcemia, polycythemia, idiopathic respiratory distress syndrome, perinatal mortality; pregestational diabetes is associated with an increase risk of congenital malformations in fetus and both macrosomia and fetal growth retardation. These are the short term effects of diabetes in pregnancy, but of major concern are the long term impacts of diabetes in pregnancy on the health of offspring.

At critical and delicate period of fetal development, the process by which a stimulus induces long-term impacts on fetus is termed as metabolic memory.[3] This phenomenon is thought to reflect permanent effects of unbalanced fetal nutrition on structural as well as physiological systems (programming) on fetus.

According to Pederson hyperglycemia–hyperinsulinism hypothesis - maternal hyperglycemia results in fetal hyperglycemia due to trans-placental transmission of glucose and hence hypertrophy of fetal islet tissue and insulin hypersecretion.[4] Freinkel modification of Pederson's hypothesis suggested that in diabetic pregnancies, maternal fuels such as lipids and amino acids in addition to elevated glucose concentrations reach the fetus and stimulate the fetal pancreas and liver to secrete more insulin and insulin-like growth factors.[5] As a result, fetal fuels are consumed at an increased rate leading to greater tissue anabolism and macrosomia. Freinkel postulated that this will have long-lasting effects on the structure and metabolic functions of the fetus, and may cause obesity associated with metabolic syndrome, hypertension, insulin resistance and type 2diabetes in later life[6], this is known as 'fuel-mediated teratogenesis'. Maternal hypercholesterolemia during pregnancy is associated with greatly increased fatty streak formation in human fetal arteries and accelerated progression of atherosclerosis during childhood and high chances of coronary artery disease.[7]

Studies have shown that increased fetal insulin and IGF levels in macrosomic babies have mitogenic effects on the fetal breast tissue. This theory explains the increased incidence of breast carcinoma in women who where macrosomic at the time of birth.

Maternal diabetes has also been implicated in adverse psychological outcomes in the offspring, including lower psychomotor development and cognitive function.[8] Some researchers have also suggested a link between exposure to maternal diabetes and the development of schizophrenia.[9]

Studies on Pima Indians have shown that besides a genetic transmission of diabetes, the diabetic intra-uterine milieu can also lead to development of diabetes in the offspring. Impaired glucose tolerance is more frequent in children of mothers who had diabetes during pregnancy than in children of mothers who developed diabetes after pregnancy.[10] Studies have shown that

35% of patients with gestational diabetes were offspring of diabetic mothers compared with only 5% of normoglycemic mothers. Studies have shown that oxidative stress due to free radical damage and lipid peroxidation affects fetal 'programming' and the transmission of a diabetogenic tendency to the next generation through permanent alteration of DNA and tissue damage in the developing fetus.

Diabetes is a major public health problem, especially in emerging countries such as India. There is now strong evidence indicating that maternal hyperglycemia creates a hostile intrauterine environment and programmes the growing fetus for the risk of non communicable diseases in later life. A meticulous glycemic control has been shown to reduce the immediate effects of GDM on the fetus however its role in preventing the long-term NCD outcomes in the offspring is not known. This warrants further studies in this field. Early detection of diabetes in pregnancy, optimal diabetic control, good antenatal and perinatal care for all women and adequate lactation and nutrition after birth are priorities.

REFERENCES

1. Bell R, Bailey K, Cresswell T, Hawthorne G, Critchley J, et al. Trends in prevalence and outcomes of pregnancy in women with pre-existing type I and type II diabetes. BJOG. 2008; 115: 445–52.
2. Gestational Diabetes Mellitus. Current guidelines for diagnosis and management. Medicine update, 2010; 20.
3. C. N. Hales and D. J. P. Barker, "The thrifty phenotype hypothesis," British Medical Bulletin, 2001; 60: 5–20.
4. Pedersen, J., Weight and length at birth of infants of diabetic mothers. Acta Endocrinol (Copenhagen), 1954; 16: 330–342.
5. Freinkel N. Banting Lecture. Of pregnancy and progeny. Diabetes, 1980; 29: 1023–1035.
6. Krishnaveni, G. V. et al., Exposure to maternal gestational diabetes is associated with higher cardiovascular responses to stress in adolescent Indians. J. Clin. Endocrinol. Metab., 2015; 100: 986–993.
7. W. Palinski and C. Napoli, "The fetal origins of atherosclerosis: maternal hypercholesterolemia, and cholesterol-lowering or antioxidant treatment during pregnancy influence in utero programming and postnatal susceptibility to atherogenesis," The Journal of Federation of American Societies for Experimental Biology, 2002; 16(11): 1348–1360.
8. Camprubi Robles, M., Campoy, C., Garcia Fernandez, L., Lopez Pedrosa, J. M., Rueda, R. and Martin, M. J., Maternal diabetes and cognitive performance in the offspring: a systematic review and meta-analysis. PLOS ONE, 2015, 10, doi:10.1371/journal.pone. 0142583.
9. Van Lieshout, R. J. and Voruganti, L. P., Diabetes mellitus during pregnancy and increased risk of schizophrenia in offspring: a review of the evidence and putative mechanisms. J. Psychiatry Neurosci., 2008; 33: 395–404.
10. Pettitt DJ, Aleck KA, Baird HR, Carraher MJ, Bennett PH, Knowler WC. Congenital susceptibility to NIDDM. Role of intra-uterine environment. *Diabetes*, 1988; 37: 622.