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RESEARCH ARTICLE

MANAGEMENT OF DIABETES AND PREGNANCY: A CATCH 22 SITUATION?

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ABSTRACT

Now a days prevalence of diabetes in increasing due to earlier onset of diabetes and the better treatment opportunities. Early onset Diabetes in young females is commonly associated with pregnancy. Diabetes in pregnancy can lead to adverse effects both on the mother and the baby due to hyperglycemia. In addition, pregnancy itself can also cause altered blood glucose levels due to hormonal changes and leads to deleterious effects on the complications of diabetes. So management of diabetes requires multidisciplinary approach.

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INTRODUCTION

Now as younger people are developing diabetes, there are more chances that diabetic women may become pregnant. And pregnancy is associated with hormonal changes that can alter the blood glucose control. Placenta also secretes some hormones that effect glucose control. Normally, blood glucose is primarily controlled by two hormones secreted from the endocrine portion of pancreas. Glucagon secreted from the alpha cells of islet of Langherns increase the blood glucose and the Insulin secreted from the beta cells decrease the blood glucose. Insulin secretion is stimulated by the interaction of nutrients, hormones, and the autonomic nervous system. There is continuous slow release of insulin with increase in secretion at the time of meals. The release of glucagon is stimulated by low blood glucose, protein-rich meals and adrenaline.There are some other hormones like cortisol and Growth Hormone that also raises blood glucose. Pregnancy is associated with markedalteration in blood glucose levels in diabetics. During initial 16-20 weeks there is slight decrease in blood glucose levels leading to increased risk of hypoglycemia if prepregnancy drugs are continued in the same dose. Later on as pregnancy progresses there is hyperglycemia requiring high doses of insulin and other hypoglycemic drugs.

After delivery there is rapid decrease in requirement of hypoglycemic drugs. In first 16-20 weeks there is both increase in the insulin secretion and insulin sensitivity (2). The exact mechanism for increase in insulin secretion and sensitivity is not known. Leptin, secreted by placenta is found to increase the secretion of insulin from the beta cells (3). Findings of some studies that show an increase in C Peptide levels during initial stages of pregnancy favours this.(4) There is also role of TNF alpha in increasing insulin sensitivity (5). As insulin is an anabolic hormone so it helps in the excess utilization of glucose during the first trimester so that nutrients are available later on when the metabolic demands of growing foetus increases. During pregnancy placenta acts as an endocrine organ and secretes hormones. The two major hormones secreted by placenta are Human Chorionic Gonadotropin (hcg) and Human Chorionic somatomammotropin (Hcs). Hcs a protein hormone secreted by syncytiotrophoblast of placenta. The chemical structure of this hormone is very similar to the human growth hormone and prolactin. It helps in the development of breast and also acts as maternal growth hormone leading to decreased glucose utilization so that it is available for the developing foetus.The amount of hCS secreted is proportional to the size of the placenta.

As the size of placenta is greatest at term , so the levels of hcs also peaks at term. These hormonal changes in pregnancy help in the growth of foetus, growth of maternal breast, enlargement of uterus to accommodate the growing baby. In normal pregnancy, pancreatic insulin secretion increases to compensate for peripheral insulin resistance, caused by placental hormones. Hcsinduce peripheral insulin resistance and thereby reduce maternal glucose utilization, while concomitantly increasing maternal lipolysis. The net result is an increased maternal reliance on fatty acids and ketones, leaving an abundant supply of glucose for the foetus. Increased fatty acids and ketones in the maternal circulation also serve as substrates for steroid hormone production by the placenta. Some later studies show a significant role of TNF alpha in changing insulin sensitivity (6). TNF alpha is secreted from placenta. TNF-alpha inhibits insulin signalling and insulin mediated glucose uptake (7). Rapid decrease in insulin resistance with the delivery of the baby signifies the role of placental hormones in metabolism of glucose.

Effects of Diabetes on pregnancy: If a pregnant lady is diabetic then the pregnancy is considered as a high risk pregnancy. As diabetes increases the risk of poor fetal outcome and congenital malformations and also predisposes the mother for eclampsia and preeclampsia. Maternal diabetes mellitus has long been associated with congenital malformations and peripartum complications in the mother. But the exact mechanism for the same is not known even till now. As offsprings with diabetic fathers do not have an increased risk of congenital malformations so it almost rules out the possibility of underlying genetic factors. Maternal Hyperglycemia is the main factor responsible for teratogenicity. Many studies show that there is no increased risk of congenital malformations in infants with prediabetic mothers or those with well controlled type 2 diabetes mellitus (8). In diabetics there is not only hyperglycemia but other metabolic abnormalities also like glycosylation of proteins and ketosis. The latest study known as HAPO (Hyperglycemia and Adverse Pregnancy Outcome) study was basically done to investigate the effects of hyperglycemia on the pregnancy outcome (9). Maternal blood glucose levels were assessed with the help of glucose tolerance test and HBA1c.Significant associations were found between higher HbA1c levels and Poor pregnancy outcome.

Effect of diabetes on diabetic retinopathy: Pregnancy is a state that is associated with major changes in haemodynamics. There is an increase in total blood volume leading to increase in cardiac output and also vasodilatation leading to decrease in peripheral vascular resistance during pregnancy. In a normal pregnancy there are some autoregulatory mechanisms which prevent changes in retinal blood flow. But if the person is diabetic then there is impaired autoregulation of retinal blood flow leading to aggravation of diabetic retinopathy changes (10).

Maternal Risks

- Miscarriages
- Polyhydroamnios
- Preterm labour
- Preeclampsia
- Intra Uterine FetalDeath
- Higher incidence of infections like vaginal candidiasis, UTI, endometrial infections or wound infections
- Acute complications like DKA
- Worsening of preexisting microvascular complications like retinopathyor nephropathty
- Hypoglycemia
- Assissted labour or caesarean section
- Risk of Type 2 diabetes mellitus

Fetal Risks (11)

- Higher incidence of still births
- Shoulder dystocia, prolonged labour, birth trauma and Erbs palsy
- Macrosomia
- Neonatal Hyperbilirubinemia
- Neonatal asphyxia
- Neonatal hypoglycemia
- Low for gestational age
- Congenital malformations-
- Congenital heart disease (Atrial Septal Defect, Ventricular Septal Defect, Coarctation of Aorta, Transposition of Great Arteries)

Nervous System and Skeletal System Involvement in the form of neural tube defects, anencephaly, microcephaly, holoprosencephaly, caudal regression, sacral agenesis Gastrointestinal system involvement in the form of duodenal atresia, anorectal atresia, and small left colon syndrome Renal system involvement in the from of renal agenesis, hydronephrosis, and ureteric abnormalities

Diabetes and Obesity later in life

Clinical Implications: Asalready discussed earlierDiabetes significantly affect the outcome of pregnancy and pregnancy significantly alters the blood glucose control in a prediabetic and a diabetic. Good blood glucose control is very important to achieve the best possible outcome of a pregnancy associated with diabetes.

Diagnosis of Diabetes in pregnancy: For the diagnosis of diabetes in first trimester the diagnostic crtiteria is same for as that for non pregnant state. There is a need to check for blood glucose during initial pregnancy. If it is suggestive of normal glucose tolerance then patient has to go for repeat blood glucose testing at around 24-28 weeks of gestation. But only those with risk factors for gestational diabetes requires repeat testing. There are different diagnostic criteria for diagnosis of diabetes in non pregnantstate and gestational diabetes as there are changes in insulin sensitivity during pregnancy.

Table 1. Blood glucose values for Diagnosis of Gestational Diabetes

S.No	Time	Non Pregnant State	One Step Strategy For GDM	Two Step Strategy For GDM
1.	Fasting	126	92	95
2.	I hour		180	180
3.	2 hours	200	153	155
	3 hours			140

One-step strategy (12): Perform a 75-g OGTT, with plasma glucose measurement when patient is fasting and at 1 and 2 h, at 24–28 weeks of gestation in women not previously diagnosed with diabetes. The OGTT should be performed in the morning after an overnight fast of at least 8 h.

Two-step strategy (13)

Step 1: Perform a 50-g GLT (nonfasting), with plasma glucose measurement at 1 h, at 24– 28 weeks of gestation in women not previously diagnosed with diabetes. If the plasma glucose level measured 1 h after the load is 130 - 140 mg/dL, proceed to a 100-g OGTT.

Step 2: The 100-g OGTT should be performed when the patient is fasting. The diagnosis of GDM is made when at least twoof the four plasma glucose levels (measured fasting and at 1, 2, and 3 h during OGTT) are met or exceeded (Carpenter-Coustan criteria)

Management

Preconceptional Counselling in Diabetics who are planning pregnancy is also very important as there is a need for disciplined approach towards management of diabetes during pregnancy (14). As pregnancy alters the blood glucose levels, so there may be a need of frequent self monitoring of blood glucose and also frequent visits to the Endocrinologist. They also need to be screened for complications of pregnancy specifically diabetic retinopathy as there is risk of progression of retinopathy by an ophthalmologist. Blood glucose targets for women with type 1 or type 2diabetes are as follows:(15) Fasting glucose <95 mg/dL and either One-hour postprandial glucose<140mg/dL or Two-hour postprandial glucose <120mg/dL

There are some differences in the management of Type 1, Type 2 diabetes mellitus and gestational diabetes.Blood glucose levels can be assessed by HbA1c and capillary blood glucose. For gestational diabetes, advise on lifestyle modification is the first and foremost. As the patient has no previous experience of managing diabetes, she has to be advised about medical nutrition therapy by a nutritionist and the need to continue physical activity. Metformin is the drug of choice if blood glucose is not much raised. Otherwise insulin is the drug of choice. In Type 2 diabetes mellitus, again along with lifestyle modification metformin is the first choice. If not controlled then insulin is added. Sulphonylurea like glyburide can be given safely with few complications. (16).

In Type 1 diabetes mellitus Insulin is the only treatment. Both Human insulin and Insulin Analogues are used.Insulin can be given both as MDI (Multiple Daily Injections) or CSII (Continous Subcutaneous Insulin Injections). There is no superiority of one method over the other. (17) As diabetes increases the risk for congenital malformations in the offspring there need to be a proper follow up with the obstetrician. With the birth of the baby there is sudden drop in insulin resistance as placenta is the source of hormones causing hyperglycemia (18). So postpartum insulin dose needs to be reduced to avoid hypoglycemia. In gestational diabetes blood glucose values return to normal but follow up is needed to look for development of type 2 diabetes mellitus later in life. First screening is recommended at 4–12 weeks postpartum with a75-g OGTT using nonpregnancy criteria.Life Long screening has to be done as there is 30-50% chances of development of Type 2 diabetes (19). During lactation also there needs to be proper monitoring of blood glucose in diabetics because of erratic life style but breast feeding is to be continued as it confers metabolic benefits to the mother (20).

CONCLUSION

With the increasing prevalence of diabetes in young there are more cases of diabetes complicating pregnancies. Both these conditions affect each other creating a type of vicious cycle. Diabetes increases the risk of congenital malformations in the baby and also complicates the pregnancy like increased risk of pre eclampsia and others. In addition to that, pregnancy alters the insulin resistance throughout the whole gestation period. This requires multidimensional approach in the management of both pregnancy and diabetes.

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