Maternal complications in pregnancy with diabetes

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Abstract

Maternal complications of diabetes in pregnancy include obstetric complications such as pre-eclampsia, preterm labour, polyhydramnios, increased operative delivery and increased infective morbidity. These can be minimized with optimal glycaemic control. Additionally, pregnancies with overt/pregestational diabetes may have diabetes related complications such as hypoglycaemia, worsening of retinopathy, nephropathy and diabetic ketoacidosis. Women with pre-existing diabetic vasculopathy should be managed with multi-disciplinary approach with maternal and foetal surveillance to detect any deterioration. Such patients have a poor pregnancy outcome. Gastropathy and coronary artery disease in diabetics is a contraindication to pregnancy.

Keywords: Diabetes in pregnancy, Complications, Maternal, Nephropathy, Retinopathy.

Introduction

Diabetes in pregnancy can be pre-gestational or first recognized during pregnancy which can be further categorized into overt or gestational according to IADPSG.[1] It is a high-risk condition for both mother and baby. Obstetric complications of diabetes in pregnancy include pre-eclampsia, preterm labour, polyhydramnios, protracted labour, increased operative delivery and increased infective morbidity. Additionally, complications of overt/pre-gestational diabetes that can affect pregnancy may be categorized as those related to glycaemic control such as hypoglycaemia and diabetic ketoacidosis (DKA); those related to microvascular complications like retinopathy, nephropathy and gastropathy; and those related to macrovascular complications of which the most relevant is coronary heart disease. The outcomes with both type 1 and 2 diabetes are equally poor. Presence of retinopathy or nephropathy, representing vascular compromise, is a risk factor for foetal growth restriction and has a poor pregnancy outcome (odds ratio 2.6).[2]

Pregnancy itself has a negative effect on diabetes. Blood glucose control becomes significantly more difficult when insulin resistance of pregnancy is added to the insulin deficiency of diabetes. Pregnancy also predisposes to starvation ketosis and diabetic ketoacidosis due to enhanced lipolytic activity. Besides pregnancy aggravates the microvascular complications.

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Obstetric Complications

Pre-eclampsia: Women with poorly controlled diabetes, both gestational and overt, are at two times higher risk of developing gestational hypertension and pre-eclampsia.[1] Impaired vascular reactivity in pregnant women with type-1 diabetes makes them more susceptible to develop preeclampsia. Incidence varies from 11-22% reaching upto 36% in patients with vasculopathy. Higher maternal BMI is also associated with greater risk, with the odds of preeclampsia increasing approximately 8 fold from the lowest to highest category of BMI. Also frequency of preeclampsia rises with increasing OGTT plasma glucose (fasting, 1-hr and 2-hr).[3]

Preterm delivery: Spontaneous preterm delivery is seen in approximately 20% among diabetic women.[1] Women with type-1 diabetes have highest risk for preterm delivery.[4] Likely causes are polyhydramnios, infection and iatrogenic as in patients with vasculopathies and pre-eclampsia. If preterm labour occurs, antenatal steroids may be given as for non-diabetic patient, but it leads to marked deterioration in control requiring appropriate increase in insulin doses.

Polyhydramnios: Women with both pregestational and gestational diabetes are at increased risk of developing polyhydramnios. Rather, if polyhydramnios develops in third trimester, patient's glycaemic state should be re-checked. Various causes have been implicated for its occurrence in diabetes including high osmotic pressure of amniotic fluid, associated congenital anomalies, foetal hyperglycaemia and foetal polyuria.[5]

Labour Dystocia and Traumatic Vaginal Delivery: Vaginal delivery of macroscopic baby may lead to prolonged labour, vaginal lacerations, perineal tears and obstructed labour with uterine rupture in extreme cases.

Caesarean Delivery: The risk of caesarean delivery is significantly greater with diabetes of any type. Reported rates are 52% in type 1, 48% in type 2 and 37% in gestational diabetes.[4] Likely causes include macrosomia, prolonged labour, preeclampsia and induction of labour in women on insulin.

Postpartum Haemorrhage: Risk of post-partum haemorrhage increases due to polyhydramnios, prolonged labour and delivery of macrosomic baby.

Infective Morbidity: Women with diabetes are more prone to develop urinary tract infection and vaginal moniliasis, hence, should be subjected to per-speculum examination, urine microscopic and culture especially when blood glucose is not controlled. There is also the risk of post-caeserean wound infection.

Diabetic Retinopathy

Pregnancy is an independent risk factor for worsening of diabetic retinopathy, defined as deterioration of at least one stage.[6] Stages of diabetic retinopathy include background, non-proliferative and proliferative disease. Proliferative retinopathy, designated as Class R of Modified White Classification; is characterized by neovascularization of retinal capillaries. These fragile vessels may cause vitreous haemorrhage, scarring and retinal detachment. Raised intra-ocular pressure in labour also causes bleeding leading to sudden vision loss.

Prevalence of diabetic retinopathy during pregnancy is 5-27% in type I diabetes, with vision-threatening progression occurring in 2-5%.[7] Prevalence in type 2 diabetes is lower, 2.9-14% in early pregnancy, with a low risk of progression unless blood glucose and hypertension is poorly controlled.[6] The adverse effect of pregnancy on the retinal microvasculature is relatively transient, with risk of progression decreasing after delivery by first year postpartum.

The risk factors for progression include poor glycaemic control, preexisting retinopathy, diabetes of longer duration, pregnancy (odds ratio 2.3, due to circulating IGF-I)[8,9] and associated chronic hypertension/pre-eclampsia.

Maternal complications of diabetes in pregnancy.

◆ Obstetric complications (both in gestational and pre-gestational diabetes):
- Pre-eclampsia
- Preterm labour- both spontaneous and iatrogenic
- Polyhydramnios
- Protracted labour, obstructed labour leading to uterine rupture
- Traumatic vaginal delivery: vaginal lacerations, perineal tears
- Increased caesarean delivery
- Postpartum haemorrhage
- Increased infective morbidity- urinary tract infections, moniliasis, wound infections

◆ Diabetes related complications (in overt and pre-gestational diabetes):
- Related to glycaemic control- hypoglycaemic episodes, diabetic ketoacidosis
- Related to microvascular complications: retinopathy, nephropathy, gastropathy*
- Related to macrovascular complications: Coronary artery disease*

*Pregnancy is contraindicated.

Pre-existing status wise progression is seen in 10%, 21%, 18% and 54% of patients with no retinopathy, micro-aneurysms only, mild non-proliferative and moderate to severe proliferative retinopathy at baseline, respectively.[10] Progression to proliferative retinopathy occurs in 40% after 15 years compared to only 18% in <15 years duration of diabetes.[10] Hence, known diabetics should plan pregnancy at a young age. Interestingly, rapid glycaemic control also worsens retinopathy. Previously treated retinopathy do not worsen in pregnancy.

Ideally, retinal assessment should be done pre-conceptionally. During pregnancy, retinal assessment is recommended in first antenatal visit, which if normal should be repeated at 28 weeks and additionally at 16-20 weeks if retinopathy is found.[11] Proliferative retinopathy is an emergency which is treated with laser panretinal photocoagulation.[6] ADA also recommends to control blood pressure to <130/80 to reduce risk of progression. Infrequently, women with florid disc neovascularization unresponsive to laser, may be offered termination of pregnancy due to risk of vision loss.[12] Increased ophthalmologic surveillance should be continued for at least one year postpartum. Besides, women with worsening of retinopathy during pregnancy are counseled not to have another pregnancy.

Macular oedema is another ophthalmologic complication that develops in 10% women with poorly controlled type 2 diabetes; risk further increases if preeclampsia co-exists.[6] It may cause irreversible loss of central vision and is treated with laser.

Diabetic retinopathy per se is not a contraindication to vaginal birth. However, epidural anaesthesia with assisted second stage or caesarean birth, is recommended in untreated proliferative disease, due to potential risk of valsalva induced retinal haemorrhage during labour.

Diabetic Nephropathy

Renal disease representing Class F of Modified White classification, develops in 25-30% of type-1 and upto 20% in type-2 diabetes, with a peak incidence after 16 years of onset of diabetes.[13] Diabetic nephropathy is a progressive disease categorized as: microalbuminuria (albuminuria 30-300 mg/24 hours with normal glomerular filtration rate); macroalbuminuria (albuminuria > 300 mg/24 hours with progressive decline in GFR); and end-stage renal disease (declining creatinine clearance, increasing serum creatinine and urea) requiring dialysis or transplantation. In women with overt nephropathy, end-stage disease occurs in 50% in 10 years and in 75% by 20 years.

Nephropathy in pregnancy is associated with increased

risk of hypertension, preeclampsia (32-65%), nephrotic syndrome, preterm delivery (57-91%), anaemia (42%), foetal growth restriction (12-45%) and perinatal mortality.[14]

Patients should be screened for microalbuminuria at booking and should be referred to a nephrologist if serum creatinine is >1.5 mg/dL or protein excretion is >2 g/day.[9] Tight blood glucose and blood pressure control, close foetal surveillance and timely delivery are needed to optimize pregnancy outcome. Reno-protective agents such as angiotensin converting enzyme inhibitors or Angiotensin II receptor blockers are contraindicated in pregnancy as they are teratogenic and may cause foetal proximal tubal dysgenesis and oligohydramnios. These should be discontinued before pregnancy. Alternatives are methyldopa, labetolol and reno-protective calcium channel blockers. Control of hypertension in pregnant women with diabetic nephropathy is crucial to prevent further deterioration of renal function.[12] Best predictors of perinatal outcome are proteinuria and creatinine clearance.

Diabetic Gastropathy

Gastroparesis i.e. delayed gastric emptying in absence of mechanical obstruction occurs in long-standing diabetes. Patients present with continuous vomiting leading to starvation ketosis. Treatment involves prokinetics, and antiemetics. Hospitalization for correction of electrolyte disturbances, intermittent gastric intubation and enteral feeds may be required.

Gastroparesis is one of the few diabetic complications in which pregnancy is contraindicated, as there is significant risk of morbidity, worsening of disease and poor perinatal outcome. Gastropathy unrecognized before pregnancy may be confused with hyperemesis gravidarum.

Coronary Artery Disease

Coronary artery disease (CAD) is a macrovascular complication which is unusual in younger type 1 diabetics but women with type 2 diabetes are older, obese which increases their risk of developing CAD. Such patients should be counseled against pregnancy as it is associated with maternal and foetal mortality and intensive care at a tertiary centre is required to optimize the outcome.

In pregnancy, myocardial infarction and acute coronary syndrome may present with atypical features such as abdominal or epigastric pain and vomiting. It may be difficult to distinguish these symptoms from pregnancy-related symptoms. Therefore, there should be a low threshold for cardiology consultation. Troponin I is the marker of choice for diagnosis, as levels are not altered by pregnancy. The shorter the interval between myocardial infarction and delivery, the worse the outcome. Mode of delivery is decided as per obstetrical indications, as caesarean does not protect women from immediate post-partum changes in stroke volume and cardiac output. Myocardial infarction is not an indication for immediate delivery, as maternal mortality is increased in women delivered within 2 weeks of myocardial infarction.

Hypoglycaemic Episodes

Hypoglycaemia is the most common adverse event during pregnancy in type 1 diabetes, Recurrent episodes are reported in upto 61% women of whom 25% have severe hypoglycaemia.[2] Asymptomatic nocturnal hypoglycaemia is also common in pregnancy. Risk of hypoglycaemia increases due to diminished compensatory response of counter-regulatory epinephrine, cortisol and glucagon, to hypoglycaemia. Reassuringly, there is no association of poor pregnancy outcome with recurrent hypoglycaemia (OR 1.1, 95% CI 0.7-1.7) or severe hypoglycaemia (OR 1.3, 95% CI 0.7-2.3).[2] Risk of hypoglycaemia is less with type 2 diabetes seen in 21% women.

These episodes are more frequent in first trimester but can also occur in the third trimester and occur if physical activity changes or meals are omitted. Patients can present with anxiety, nausea, palpitations, tremor, sweating and dizziness and these symptoms can be misinterpreted as being due to pregnancy itself and therefore overlooked.

Hypoglycaemic episodes have high mortality for both mother and foetus. These episodes are managed by giving a glass of glucose water or orange juice or 15 gram glucose. Intravenous glucose (20 mL of 50% solution) or glucagon injection (1mg intramuscular or subcutaneous) may be required if the patient is unconscious. To prevent recurrent hypoglycaemia, a snack should be eaten after the initial treatment.

Diabetic Ketoacidosis (DKA)

This is a serious metabolic complication and a medical emergency in diabetic pregnancy, the prevalence being 1-2%. It most commonly occurs in second or third trimester and in new-onset type 1 diabetes, although it may affect type 2 diabetes or, more rarely, gestational diabetes. Predisposing factors include infection, hyperemesis gravidarum, missed insulin dose, newly diagnosed diabetes, gastroparesis and use of steroids and beta agonists as needed for managing preterm labour.

During pregnancy DKA may develop even at glucose levels reaching 200 mg/dL; and is characterized by

osmotic diuresis, depleted intravascular volume, high anion gap and metabolic acidosis. If uncorrected, DKA may lead to maternal mortality and foetal death in 10-35% cases.[13]

Symptoms include polydipsia, polyuria, nausea, vomiting, malaise, headache with severe dehydration. Hyperventilation and altered mental status occur as a result of ketoacidosis, with characteristic smell of ketones. A diabetic pregnant woman presenting with persistent vomiting should be evaluated for DKA. Undiagnosed diabetics receiving beta-agonists may also present with DKA. Hyperglycaemia (which may be minimal in pregnancy), low plasma bicarbonate < 15 mEq/L (anion gap acidosis), pH < 7.3 and ketonaemia/ ketonuria makes the diagnosis of DKA. It is a medical emergency requiring fluid resuscitation, insulin infusion, correction of serum electrolytes and electronic foetal monitoring for > 24 weeks gestation. Recurrent late deceleration are likely during acute episode which usually resolves as maternal condition improves, hence immediate delivery is rarely indicated because of foetal indication. Mother's condition must be stable before induction or emergency caesarean. Early diagnosis, aggressive treatment and management of precipitating factor such as infection can minimize morbidity.

To summarize, pregnancy with diabetes is associated with obstetric complications that can be minimized by good glycaemic control and maternal surveillance during pregnancy. Women with pre-existing diabetic vasculopathy should be managed with a multi-disciplinary approach with maternal and foetal surveillance to detect any deterioration and timely management.

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