# Third Trimester foetal complications in pregnancy with diabetes

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## Abstract

Diabetes in pregnancy starts affecting the foetus even in the pre-conception period. The complications encountered in third trimester are foetal macrosomia and intrauterine foetal demise; birth of a macrosomic baby further leads to shoulder dystocia, birth trauma, brachial plexus injury. Additionally, pregnancies with overt/pre-gestational diabetes may be complicated with foetal growth restriction, congenital abnormalities diagnosed in third trimester and foetal hypertrophic obstructive cardiomyopathy. Even minor degrees of hyperglycaemia is associated with adverse pregnancy outcome. Optimizing maternal glycaemic control and foetal surveillance is crucial for optimizing the perinatal outcome and minimizing aforesaid complications. The management of macrosomia is controversial regarding timing and mode of delivery, but most authorities agree for primary caesarean if estimated foetal weight at the end of pregnancy is 4500 gram or more.

**Keywords:** Diabetes in pregnancy, Foetal complications, Macrosomia, Shoulder dystocia, Stillbirth, Foetal cardiomyopathy.

## Introduction

Diabetes in pregnancy can be pre-gestational, i.e. already a known case of type I or II diabetes; or it is first recognized in pregnancy, which traditionally was considered as 'gestational diabetes mellitus'. But according to the new International Association of Diabetes in Pregnancy Study Groups (IADPSG) terminology, glucose intolerance first recognized in pregnancy can be classified as either overt diabetes mellitus (ODM) or gestational diabetes mellitus (GDM).[1] The incidence of gestational diabetes has increased in recent years due to the obesity epidemic and will increase further with the new diagnostic criteria by IADPSG, and adopted by the American Diabetes Association.[2]

Diabetes in pregnancy is a high-risk condition for both mother and baby. The relevance of even minor degrees of hyperglycaemia to adverse pregnancy outcome was clearly demonstrated by the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study[3] which confirmed that the risk of adverse pregnancy outcomes increases with increasing maternal glucose in a continuous association, even below the traditional cut-offs for gestational diabetes. More importantly, there was no demonstrable threshold effect for any of these increased risks.[3]

Foetal complications of diabetes in pregnancy (both gestational/overt and pre-gestational) in the third trimester macrosomia with its consequences and unexplained foetal demise or stillbirths. Additionally, pregnancies with overt/pre-gestational diabetes may be complicated with foetal growth restriction, congenital abnormalities diagnosed in third trimester and foetal hypertrophic obstructive cardiomyopathy. The outcomes of women with type 1 and type 2 diabetes are equally poor.

## Macrosomia and its consequences

Macrosomia is defined as a birth weight of more than 4000 grams. Both gestational and pre-gestational diabetes mellitus are independent risk factors for macrosomia, which complicates 34% of gestational diabetes, 40% of pre-gestational type 1 and 2 diabetes compared to 9% in women with optimum glycaemic control (i.e. <110mg/dL mean capillary glucose levels).[4,5] Macrosomic infants of diabetic mothers are anthropometrically different from other large-for-gestational age infants[6] with excessive fat deposition on shoulders and trunk (larger chest-to-head ratio and shoulder-to-head ratio) predisposing to shoulder dystocia. Such babies are also defined as large-for-gestational age (LGA) infants in which birth weight is greater than 90th percentile for that population. According to Boulet et al,[7] macrosomic newborn infants can be categorized into 3 groups:

**Grade 1 macrosomia:** Newborn infants who weigh 4000 to 4500 g: Delivery of macrosomic foetus is associated with prolonged labour, an increased likelihood of operative delivery, shoulder dystocia, clavicular fractures, and brachial plexus injury that may be permanent leading to litigations.

**Grade 2 macrosomia:** Newborns with weights between 4500 and 4999 g: In addition to the above complications, these are further at significant risk for neonatal morbidity including perinatal asphyxia, 5-minute Apgar score of <3, assisted ventilation, meconium aspiration, and hyaline

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membrane disease.

**Grade 3 macrosomia:** defined as a birth weight of > 5000 grams: These have increased infant mortality rates compared to grade 1 and 2 macrosomia.

Delivery of macrosomic baby increases the maternal risk of postpartum haemorrhage, perineal tears, laceration of anal sphincter and postpartum infection. Labour complications, birth injuries, and newborn morbidity rise with each grade. Hence, although a definition of macrosomia as >4000 gram (grade 1) may be useful for the identification of increased risks of labour and newborn complications, >4500 g (grade 2) may be more predictive of neonatal morbidity caused by birth trauma, and >5000 g (grade 3) may be a better indicator of infant mortality risk.[7]

Third trimester 1 hour post-prandial glucose measurements has been reported as the strongest predictor for macrosomia.[8] In HAPO cohort, the risk of macrosomic infant was double compared with euglycaemic women.[1]

Estimated foetal weight (EFW) by ultrasound remains the key for obstetric management in pregnancies complicated by diabetes with sensitivity of 68% and specificity of 96% to detect macrosomia.[9] The positive predictive value for detection of macrosomia exceeds 90% when the abdominal circumference or estimated foetal weight is above the 95th percentile. However, they may be error of up to 25% in estimating true birthweight.[10]

The management of macrosomia is controversial regarding timing and mode of delivery. Induction at 38 weeks in diabetics may reduce the risk of macrosomia (RR 0.56, 95%CI 0.32-0.98), while not increasing caesarean rates (RR 0.81, 95%CI0.52-1.26) as found in a randomized trial,[11] included in a Cochrane review,[12] but no conclusive recommendation was made. In fact, elective induction in suspected macrosomic pregnancies does not decrease the risk of caesarean, instrumental delivery and perinatal mortality,[13] rather it may increase the risk of foetal lungs immaturity and poor bishop, thus increasing caesarean rates. In fact, if cervix is unfavourable, it is better to wait for spontaneous labour.[14]

Most authorities agree for primary caesarean if EFW at the end of pregnancy is 4500 gram or more. The controversy arises when EFW is between 4000 and 4500 gram. Some favour caesarean as shoulder dystocia is common in diabetic macrosomia and others believe that the margin of error of sonographic EFW and relatively small number of foetal injuries (1 in 500 deliveries), in such weight do not justify caesarean. According to a simplified treatment algorithm proposed by Chauhan et al[1,5] elective caesarean is indicated for estimated foetal weight >4500 gram in diabetics, >4000 gram with prior history of shoulder dystocia or caesarean delivery and >5000 gram in uncomplicated pregnancies. Some investigators have used the threshold of 4000 gram16 or 4250 gram[17] to offer elective caesarean delivery. Elective caesarean may also be offered to cases with history of neonatal brachial plexus injury in previous macrosomic foetus due to high risk of recurrence during subsequent vaginal delivery.

If the patient with suspected grade 1 macrosomia is allowed a trial of labour, caesarean should be performed if there is protracted labour, failure to descend or secondary arrest of cervical dilation. Vacuum or forceps should not be used in such patients. Persistent occipito-posterior position that do not rotate spontaneously should also be delivered by caesarean. Finally, the obstetrician should be prepared for possibility of shoulder dystocia and should be versed with the maneuvres.[17]

Following are the risks associated with delivery of a macrosomic baby:

**Shoulder dystocia:** Shoulder dystocia is a complication of vaginal delivery. Clinically it is recognized, either by a turtle sign (retraction of foetal head tightly against maternal perineum, after it has delivered) or the lack of delivery of anterior shoulder after typical gentle downward traction on the foetal head. Shoulder dystocia is 5 times as frequent in diabetic pregnancy and the probability is 2.2% in <4000 gram, 13.9% in 4000 - 4499 gram and 52.5 in ≥4500 gram birth weight compared to 0.7%, 6.7% and 14.5% in non-diabetic pregnancy.[18] In fact, the level of foetal truncal asymmetry (abdominal circumference minus biparietal diameter) measured sonographically correlates with the incidence and severity of shoulder dystocia in patients with diabetes.[19] Shoulder dystocia is an obstetric emergency and should be immediately managed with maneuvers including combination of McRoberts maneuver, suprapubic pressure, foetal rotation, or delivery of the foetal posterior arm.

Shoulder dystocia can lead to foetal brachial plexus injury in 4-40%, fractures of foetal humerus and clavicle in 10%, hypoxic ischaemic brain injury in 0.5-23% and foetal death in 0.4% cases.[20] The risk correlates with the duration of head-to-body delivery and is especially increased when the duration is 45 minutes.[20] Maternal complications of shoulder dystocia include post-partum haemorrhage, vaginal lacerations, anal tears, and uterine rupture.

**Brachial plexus injury:** Reported rate of brachial plexus injury in infants with 5000 gram birth weight is as high as

20%. It is estimated that to prevent one case of brachial plexus injury, 443 women with 4.5 kg EFW need to have elective caesarean, thus elective caesarean has no significant effect on reducing incidence of brachial plexus injury.[15]

**Birth trauma:** Both gestational and pre-gestational diabetes mellitus are independent risk factors for birth trauma, humerus and clavicular fracture, as well as intrapartum asphyxia.

## Unexplained foetal demise/Stillbirths

Foetal demise in absence of obvious factors such as placental insufficiency, abruption, foetal growth restriction or oligohydramios is declared 'unexplained'. Reported incidence is 1% in pre-gestational diabetes and 0.54%, 0.36% and 0.18% in untreated and treated gestational diabetes and nondiabetic mothers, respectively.[21] In a large retrospective study published in 2015, relative risk RR of stillbirth was 2.5 in type 2 and 1.4 in type 1 diabetes compared to non-diabetes.[22]

These are typically macrosomic babies with foetal hyperinsulinaemia as the possible cause of death. Foetal hyperinsulinaemia increases foetal metabolic rate and oxygen demand in foetus leading to chronic hypoxaemia and lactic acadaemia. Other risk factors include poor glycaemic control which leads to villous oedema and placental dysfunction, hence foetal hypoxia and acidosis. Extramedullary haematopoiesis as evidenced by relative foetal erythraemia in cord blood supports chronic hypoxia as the cause of foetal death. Foetal hypertrophic cardiomyopathy, maternal diabetic vasculopathy, preeclampsia and ketoacidosis further contribute by reducing placental blood flow and foetal oxygenation are other contributing factors. Foetal demise occurs most often after 36 weeks of pregnancy, but can be seen as early as second trimester in women with vascular complications. Still births within 72 hours of seemingly normal foetal heart tracings have been reported. Hence foetal surveillance starting form 28 weeks is important in managing pregnancies with diabetes for early detection and management of foetus at risk. In every antenatal visit, importance of daily foetal movement count should be re-emphasized to the pregnant women.

## Congenital malformations detected in third trimester

In a non-compliant women with pre-gestational diabetes taking irregular antenatal care visits, congenital malformations may be detected in third trimester. There is 2-6 folds increase in major malformations in infants of type 1 and 2 diabetic mothers with incidence ranging from 5-10%. These occur primarily due to maternal hyperglycaemia and associated derangements in maternal metabolism during period of embryogenesis. But hyperketonaemia, somatomedin inhibition and excess free oxygen radicals are other contributory factors.

**Intra-uterine growth restriction (IUGR):** Women with unexplained foetal growth restriction have greater maternal insulin sensitivity resulting in decreased nutrients available for placental transport to the foetus.[5] In contrast, in women with vascular disease, IUGR is associated with preeclampsia. This reinforces the need for frequent foetal surveillance.

## Foetal hypertrophic cardiomyopathy

Diabetes affects foetal heart both during early and late gestation. Uncontrolled glycaemic status during first trimester affects embryogenesis by inhibiting gene expression needed for foetal heart development. In late pregnancy, foetal hyperinsulinaemia causes myocardial hyperplasia and hypertrophy, leading to hypertrophic obstructive cardiomyopathy which mainly involves interventricular septum and right, left posterior ventricular walls due to abundant insulin receptors in these areas.[23] Such foetuses when born develop congestive heart failure due to left ventricular outflow obstruction. This cardiac hypertrophy is usually transient and resolves after birth, requiring no therapy. A prenatal interventricular septal thickness of 4.5 mm on ultrasound is found to be a predictor of hypertrophic cardiomyopathy and is associated with twofold higher risk of intrauterine foetal death and threefold higher risk of perinatal mortality.[23]

To summarize, pregnancy with diabetes is associated with foetal complications that can be minimized by good glycaemic control and foetal surveillance during pregnancy. Serial ultrasound estimation of foetal weight, growth parameters and amniotic fluid, starting at 28 weeks is mandatory while managing these women, to

**Summary of third trimester fetal complications in pregnancy with diabetes.**

- Macrosomia.
- Consequences of Macrosomia: Shoulder Dystocia.
  Brachial Plexus Injury.
  Birth Trauma: Humerus, Clavicle fracture.
  Intrapartum asphyxia.
  Maternal risks: Prolonged or obstructed labour, increased caesarean, PPH, vaginal lacerations, perineal tears, uterine rupture.
- Unexplained Foetal Demise/Stillbirth.
- Congenital abnormalities diagnosed in third trimester.
- Intrauterine Growth Restriction.
- Fetal hypertrophic obstructive cardiomyopathy.

timely detect macrosomia, polyhydramnios, or IUGR in cases with pre-existing diabetic vasculopathy.

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