Obstetric management of pregnancy complicated by Diabetes Mellitus

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“Diabetes may develop during pregnancy and cease with termination of pregnancy, recurring some times after that, Hydramnios is common that pregnancy is very liable to be interrupted by the death of the fetus and the dead child is often enormous”

Duncan (1882)
• GDM, Pre-GDM, and even simple maternal glycaemia of pregnancy and impaired glucose tolerance have wide ranging impact on pregnancy outcomes from beginning to end.

From conception to delivery and even beyond for both mother and offspring.
Causes of Concern:

Gestational and pre-gestational diabetes are common complications of pregnancy that can be associated with severe maternal and fetal morbidity which are due to:

- Increase congenital malformation
- Still birth
- Macrosomia
- Pre-term labour
- Increased pregnancy complications (Hydramnios and PIH)
- Progression of diabetic complications secondary to pregnancy

Aim in obstetric management is to prevent these factors and improve the perinatal and maternal outcome
CONGENITAL ANOMALIES

- Congenital anomalies accounts for 50% of perinatal mortality
- Major congenital malformation - Diabetic embryopathy are 3 to 5 fold increased. It is due to multifactorial etiology. It can affect any system.
- Diabetic specific malformations - sacral dysgenesis, femoral hypoplasia - unusual facies phenotype.

Periconceptional care for diabetic woman is the most important and effective intervention to reduce the incidence of congenital anomaly in the offspring.
CAUSES FOR MAJOR CONGENITAL MALFORMATION

- Hyperglycemia has been shown to be teratogenic for the developing embryo.

Other factors

- Myoinositol, arachidonic acid deficiency, hyperketonemia and excess of free oxygen radicals.

Recent evidence is hyperglycemic altered gene expression leading to aberrant cell signaling and resultant embryopathy.
TO REDUCE CONGENITAL MALFORMATION

Intensified glycemic control during periconception and first trimester of pregnancy is important in reducing the incidence of CA.

Various studies have shown that periconceptional care and strict glycemic control (CBG 60 to 130 mg and low HbA1c in first trimester), lowers the CA to 1.4% vs. 10.5% in the control.

Achieving normoglycemia before and after conception reduces the rate of anomalies.
PRECONCEPTIONAL COUNCELLING

1. Folic acid administration
2. Adequate blood sugar control to reduce the major congenital malformation
3. HbA1c monitoring monthly until stable at a level less than 1% above the upper limit of normal.

use contraception throughout this period to avoid inadvertent pregnancy
4. Evaluation with history, physical examination and lab investigations for diabetic complications.

a. Diabetic nephropathy
   - 24 hours urine volume
   - 24 hr urine protein
   - creatinine clearance
   - serum creatinine
   - urine culture

b. Diabetic retinopathy
   - retinal examination after dilation by ophthalmologist.
   - If retinopathy detected – background or proliferative & treat
c. Cardiovascular system
  • Determination of BP is of utmost importance.
  • Chronic hypertension-review of anti hypertension medicine.
    (ACE inhibitors – should be replaced by less embryotoxic drug)
  • ECG-Any suspicion of CAD should be further evaluated with the exercise stress test.

d. Evidence of autonomic dysfunction
  • Lack of awareness of hypoglycaemia (autonomic neuropathy)
  • Orthostatic hypotension (autonomic neuropathy)
  • Excessive nausea vomiting sensation (Gastroparesis diabeticorum)

e. Endocrine
  • Thyroid dysfunction is frequently associated with type 1 diabetes.
  • Thyroid function should be routinely evaluated in the pre conception period

Unplanned pregnancy is common among diabetic woman, they should be counseled early for the importance of preconception care in the progression of this disease

Pre conception care can significantly reduce pregnancy complication with a dramatic impact on the diabetic mother and her infant
Ladder of preconception care in diabetic women

- **Established Disease**
  - Highlight the importance of preconception care
  - Contraception

- **Preconception**
  - Education
  - Planned metabolic control
    - Folic acid
    - Complication; Nephropathy, hyper tension, Retinopathy, CV disease, Neuropathy, hypothyroidism

- **Early pregnancy**
  - Metabolic control
    - Folic acid
    - Treat complications

- **Council**
  - Impact on pregnancy
  - Impact on diabetes
  - Treat complication
  - Concerns Severe gastroparesis, CAD
Still Birth

Type 1 & Type 2 DM are associated with 3 to 5 times increased risk for still birth

75% of unexplained still birth are associated with hyperglycaemia and elevated HbA1C

Incidence of fetal death is greater in Type2 than type1 (obesity, HT, maternal age)

In GDM (Langer 5.4 vs. 1.8/1000) risk is smaller than Type1.

The increased risk is noted in all types of diabetes, despite an intense fetal surveillance programme and aggressive obst. management
Causes of still birth

Causes are multiple and varied

- Hyperglycaemia is one of the cause
- In 90% the cause can be ascertained
- Causes can be pathologic, obstetric & vascular (Maternal or Fetal)
- Fetal malformations, fetal aneuploidy, placental malformations, placental insufficiency, infections and so on
PATHOPHYSIOLOGY OF SB

In human studies the cause is not clear, may be undetected hyperglycaemia and ketoacidosis & unnoticed hypoglycemia. Bradley and colleagues noted deviations in fetal blood pH and plasma lactate with significant acidosis in the III trimester.

In animal studies hyperglycaemia and hypoxia, greater oxidative stress. Increased supply of nutrients to the uterus resulted in poor implantation and increased malformation rates.
Prevention of still birth in diabetic pregnancy

Key to prevention is the comprehensive multidisciplinary care, with aggressive blood sugar control.
Reducing extremes in BS may be an important tool to reduce the risk of stillbirth.
Achieve and maintain euglycaemia by aggressive management and monitoring of blood sugar (seven times a day)
Increased monitoring of blood sugar and fetal surveillance results in fewer still birth, less risk of macrosomia & less injury for neonate.
To prevent still birth

I. Antepartum fetal surveillance

1. Kick count: Simple, inexpensive, non invasive and improved maternal bonding

2. NST with Amniotic fluid volume and biophysical profile
   Weekly or twice weekly to monitor fetal wellbeing in all forms of DM.

3. Doppler velocimetry: of maternal and fetal vessels.
   Gradations of abnormal foetal blood velocity are associated with an increase in foetal acidaemia.
   Reversed end diastolic flow is a strong predictor of subsequent foetal death.

Raised S/D of foetal umbilical artery seen in maternal vasculopathy associated with HT, renal insufficiency, IUGR, and neonatal metabolic complications, **but not associated with hyperglycaemia**

Doppler studies is better than NST or BPP in identifying adverse outcome. (Bracero- colleagues)
Pregnant diabetics appear to have improved outcome with some form of antepartum surveillance

• The best method, the best timing interval for testing, the optimal gestational age to begin testing and more accurate interpretation of testing are still in evolution

• The lesson is that antepartum fetal testing no matter the form seems to improve perinatal outcome to a modest to significant degree
To Prevent Still Birth……..

Timing of delivery:
Important key for improved outcome. The goal is to deliver a live baby with an acceptable risk of caesarean in optimum time.

Indications for delivery:
1. Apparent inability to adhere the treatment regimens.
2. Hyperglycemia despite intensive efforts to gain control.
3. Abnormal fetal testing (NST, BPP, Doppler velocimetry)
4. Fetal growth restriction and fetal macrosomia

Once decided for delivery (induction), close intrapartum monitoring to ensure the lowest risk of cerebral palsy. Scrupulous control of maternal blood sugar during course of labour will decrease the risk of intrapartum still birth.

An organised multi disciplinary approach for the management of diabetic pregnancy is essential for the success of pregnancy.
MACROSOMIA

DETECTION AND PREVENTION

Excessive fetal growth – usually 4000 to 4500g, our standard > 3500g.

The adverse outcome of macrosomic baby:

The challenges in the diagnosis of excessive fetal growth:
1. When to detect the excessive fetal growth.
   - Near term for management decision
   - Earlier gestation to impact the abnormal growth rate.
   Can the growth rate be corrected through changes in diabetic management.

2. Is there an optimum method for estimating fetal weight (ultrasound, clinical maneuver, maternal perception - how reliable??)

3. Is the birth weight is really the whole story or the fetal fatness - large proportion of birth trauma and shoulder dystocia still occur with birth wt below 4000g.
Macrosomia: Early detection and implications for treatment and prevention:

1. At what point in gestation should we attempt to detect overgrowth.
2. When does it start?
3. Does that correlate to when it can be detected.
4. What are the limitations of our ability to detect it.
5. Can it be altered once detected or is it biologically / physiologically programmed in the course of diabetes in pregnancy.
The predictors of fetal overgrowth

1. Abdominal circumference > 75th percentile – single ultrasound examination at 28 to 32 weeks. (sensitivity 89%, specificity 76%)
2. Increased Hb A1c before 18 weeks.
Detection-Altered fetal growth and new Ultrasound –”Horizon”

“MACROSOMIA” produced by maternal glucose intolerance is different from that associated with other predisposing factors. Diabetic macrosomia is characterised by truncal and upper extremity adiposity. so the new horizons are to evaluate the fetal fat distribution.

1. Humeral soft tissue thickness (Landon and colleagues) - sensitivity 88%, specificity 75%
2. Cheek to cheek diameter (CCD) - increases the accuracy when incorporated into the weight calculating formula.
3. Assessment of enlargement of the cardiac interventricular septum
4. Volumetric technique using 3D USG. It helps in the measurement of the adiposity of the fetus.
Summarize

Early detection and tight control of blood sugar can control macrosomia and LGA.

However, strictest diabetic control (mean blood glucose <86mg%) can result in SGA.

Langer had suggested glucose control is continuum, with the targets flexible i.e. in first trimester one set of norms are target to prevent early outcomes (spontaneous abortion or congenital malformations).

For macrosomia the optimal glycemic threshold has to be identified. As our understanding of the pathophysiology of diabetes in pregnancy grows we can fine tune our therapy and surveillance to meet the needs of an individual diabetic woman and her fetus.
PRE-NATAL MANAGEMENT IN DIABETIC PREGNANCY

Goals:-

- Detection of diabetic embryopathy
- Strict control of blood sugar levels
- Detection of macrosomia
- Detection of fetal distress and prevention of antepartum death
- Timing of delivery and improve maternal and fetal outcome
- Choose between caesarean section or vaginal delivery for improved outcome
- Adequate intrapartum and postpartum management
• Detection of diabetic embryopathy
  • Efforts to detect embryopathy should start soon after conception
  • A. HbA1C performed 4 to 6 wks after conception, will reflect level of blood sugar in periconceptional period.
  • HbA1C > 8.5 - Anamolies 20 to 25%
  • when HbA1C is normal, the probability of major malformation < 2%
  • B. USG by vaginal probe from 10 to 14 wks. will detect defects like anencephaly, prosencephaly
  • I trimester screening for aneuploidy - NT
  • NT is increased in chromosomally abnormal fetus with congenital heart disease
  • In addition serum Beta HCG & PAPPA will help for aneuploidy
  • A negative I trimester screening does not end the search for diabetic embryopathy
Continue……

II Trimester Screening

- Serum alpha fetoprotein at 16wks
- It is one of the analyte in triple and quadruple tests.
- Normally MSAFP is lower in diabetic women— if abnormal, needs comprehensive USG examination for fetal spine.
- Genetic amniocentesis
- Detailed anatomic survey at 18 to 20 wks
- Fetal echo at 22 to 24 wks.
Assessment of fetal well being:

- Indication for surveillance depends on severity and stability of DM
- Pts on insulin require fetal surveillance during last 10 wks.
- Wkly or biweekly NST and biophysical profile
- Brittle or diabetic requiring >100 units of insulin or with growth restricted fetus, start surveillance at 28 wks.
- Stable DM without complications start surveillance as late as 34 wks GA
LABOUR AND DELIVERY

• Preterm labour – tocolysis with beta adrenergic drug – increases glycogenolysis and lipolysis and tendency towards metabolic acidosis and hence pt should receive continuous insulin infusion to antagonise the effect of, labour inhibiting medication.

• The drug of choice is nifedipine - if not able to tolerate, terbutaline 2.5 mg every 4hrs may be used.

30% of preterm labour is due to infection so use appropriate antibiotic
STEROIDS:

For accelerating lung maturity, steroid is to be used in all situations in diabetic pregnancy for delivery before 38wks.

Pre-term PROM:

Whenever PPROM is there - there is a strong possibility of infection which will be very severe in diabetics than non-diabetics, hence the expectant line of management of diabetics with PPROM should be an exception rather than a rule.
TIME OF DELIVERY

• Stable well controlled diabetics - no need to interrupt before term.
• Avoid prolongation of pregnancy to prevent the super adding of the complications of prolonged pregnancy to the fetal complications of DM.
• Unstable DM: As soon as fetal lung maturity is attained.

Fetal and maternal complications in unstable pts are numerous, so no advantage of prolongation of pregnancy once lungs are mature.
MODE OF DELIVERY

• Diabetes is not a PRIORI indication for C-section
• However multiple indications for C-Section are present in these pts
• More than 50% of pts can be safely delivered vaginally
INTRAPARTUM MANAGEMENT

- No contraindication for induction of labour
- Caesarean—done as first thing in the morning when pt is in euglycaemic state
- Vaginal delivery:
  - Labour progress is monitored by partogram
  - No contraindication for labour acceleration and for painless labour, anticipate shoulder dystocia
  - Multidisciplinary team should be available
  - Strict control of blood sugar is required even during labour
  - III stage should be actively managed
  - Prophylactic antibiotic should be given
Postpartum management

- After delivery of placenta the insulin resistance is lost and hence dose of insulin has to be adjusted.
- They are prone for infection and sub involution so use prophylactic antibiotic.
- Encourage breast feeding.
- Early postpartum follow-up 1 to 2 wks after delivery is helpful in assessing changing glycaemic control in Type1 & 2 DM and medical therapy may be instituted if needed.
- Early visit also allow the physician to identify problems with breastfeeding and encourage the following of dietary and exercise guidelines.
Breastfeeding

• Breast feeding should be encouraged.
• Offspring of diabetic mothers are at increased risk for childhood obesity and for Type 2 diabetes later in life.
• Breastfed infants are at a lower risk of later development of obesity or diabetes.
• A longer duration of exclusive breastfeeding and later introduction of formula may also be protective of developing beta cell autoimmunity and later risk for type 1 diabetes.
GLYCAEMIC FOLLOW-UP

• Maternal education to prevent childhood obesity, a forerunner of type 2 diabetes in young adults
• Diabetic mothers should be stressed on ABCs of diabetes (A1c, Blood pressure & Cholesterol)
• Strict glycaemic control in type 1 & type 2 DM, significantly cut in half the risk for microvascular complications
• Glycaemic goals for both types of diabetes are similar (FBS 80-120mg and before bed levels 100-140mg, Hba1C <7%)
• Glycaemic management in type 2 should be monitored every 3 months with HbA1c levels
• Normalizing serum lipid levels prevents macrovascular disease—fasting lipid profiles delayed 3 to 6 mths to allow the reversion of physiological change.
• Women with GDM have 50 to 60% lifetime risk for developing DM.
• If FBS>121mg 21 fold risk of postpartum DM.
• Post-partum glycaemic status should be established 6 wks post-partum using WHO GTT, repeated in 1yr and then at minimum every 3yrs.thereafter.
• Women with GDM and postpartum IGT has 16% annual incidence rate of developing diabetes.
Contraception

BREAST FEEDING:

• LAM: exclusive breastfeeding is used as a birth control method.

• Women should begin breastfeeding immediately after delivery and avoid supplementation and they need to breastfeed frequently—every 4hrs during daytime 6hrly during night time.

• LAM + Condom - effective method and encourage exclusive breastfeeding.
• HORMONAL CONTRACEPTION:
  • Women who desire HC can be reassured that the level of hormone transferred to breast milk is less than 1% of maternal dose – comparable to hormone level observed during ovulatory cycles.
  • No effect on infant growth and wt with either progestin only or COC use.
  • Progestin only pill can be started on D21 but COC should not be started before 6wks.postpartum.
  • Emergency contraception given within 72hrs of unprotected coitus is not indicated before 21 days postpartum.
HORMONAL CONTRACEPTION AND DIABETES:

• Type 1 DM-COC or POP on short term use minimal metabolic effect, on long term use no increased risk of or progression of retinopathy, renal disease or HT

• Long term use does not increase the risk of developing diabetes

• Use of progestin only pill during lactation increased the diabetic risk almost three fold and this risk is increased with longer duration of uninterrupted dose. Thus progesterone only method should not be prescribed to women with prior GDM while they are breast feeding (Xiang, Kjos et al)

• Alternative methods: 1. LAM plus condom

2. non hormonal method or starting low dose

COC 6 to 8 wks post partum.
INTRAUTERINE DEVICE:

• Provides excellent long-acting pregnancy protection in diabetic women.
• Medicated copper IUD is not associated with increased risk of PID in type 1 and type 2 diabetes.
• Progestin medicated IUD – data not available.
• Copper medicated device can be inserted within 48 hrs of delivery otherwise should be delayed up to 6 weeks postpartum.
• Selection of candidates and monitoring of IUD similar to general population.
• No need for general antibiotic prophylaxis with insertion or removal of IUD.
Indian scenario

- Incidence 9.84%. High in women with spontaneous abortion.
- Incidence of GDM varies widely.
- Excessive weight gain seen in GDM is 32% (control - 1.7%).
- Fetal macrosomia 32% (control - 6.8%).
- PIH 48% (control - 18.8%).
- Hydramnios 28% (control - 4.3%).
- Vulvovaginitis 4% (control - 1.3%).
- IUD 12% (control - 1.7%).
- Fetal malpresentation 16% (control - 6%).
- C. section 44% (control - 13.3%).
- Postpartum complications increased.
- MMR is 10 times higher.
- Perinatal morbidity increased.
- Strict glycemic control improves obstetric outcome. It should precede the onset of pregnancy.
The I.O.G. Experience

- No. of cases in 3 months – 34 (GDM – 20, Pre GDM – 14)
- Perinatal morbidity – 58.82%
- Perinatal mortality – 17.64%
- Maternal morbidity (PIH) – 29.54%
- Other maternal morbidities – fibroid, bronchial asthma, hypothyroid.
- Age group – 58.8% (25 to 30 yrs)
- Gestational age at delivery - < 34 – 6 (17.6%)
  34 to 37 – 3 (8.8%)
  >37 – 24 (70.5%)
- Mode of delivery – labour naturale – 8 (32%)
  assisted breech – 3
  LSCS – 23 (67.6%)
- Birth weight < 3.5 kg – 29 (85%)
  > 3.5 kg – 5 (14.7%)
To conclude

- DM is one of the challenging medical complication during pregnancy
- 90% of diabetes cases encountered during pregnancy are gestational onset
- Rapidly increasing incidence of type2 pre gestational DM is caused in part by an increased prevalence of obesity
- Overt diabetes has a more significant impact on pregnancy outcome
- The embryo as well as the fetus and mother can experience serious complications directly from diabetes
- The success of pregnancy outcome related to the degree of control but more importantly to the intensity of any maternal cardiovascular or renal disease
- Management of diabetic problems involve:
  1. New treatment and monitoring modalities
  2. Efficacy and safety of insulin analogues and oral hypoglycemic agents
  3. Preventing or detecting excess fetal growth.
  4. Reducing adverse events of delivery with team approach.
The maternal health and fetal outcome depends upon the care by the committed team of diabetologists, obstetricians and neonatologists.