Diabetes in Pregnancy – Dr. Hana

Introduction

- Diabetes occurs in 2–5% of all UK pregnancies and its prevalence is rising.
- Forty years ago the majority of women with diabetes attending an antenatal clinic had type 1 diabetes and were young, non-obese and of low parity.
- Today the majority of women have type 2 diabetes, or gestational diabetes (GDM), and are older, more obese and of higher parity.

The types of diabetes encountered in obstetric practice

- **Type 1 diabetes**: Absolute insulin deficiency due to an autoimmune destruction of the pancreatic β-cell. Presents typically under the age of 20 years old.
- **Type 2 diabetes**: Relative insulin deficiency due to increased insulin resistance. Presents typically over age of 20.
- **Gestational diabetes**
- **Monogenetic diabetes MODY (Maturity Onset of Diabetes of the Young)**: Results from a single gene mutation causing defects in pancreatic β-cell insulin secretion. Present from birth & typically diagnosed under age of 20.
- **Mitochondrial diabetes**: Arises from a mutation in mitochondrial DNA leading to a defect in insulin secretion. Associated with a number of other medical problems including neural sensory deafness, a tendency for stroke and lactic acidosis.
- **Secondary diabetes**: Diabetes due to other medical conditions, i.e. pancreatitis, cystic fibrosis, glucocorticoids and other drugs.

Gestational diabetes:

- Glucose intolerance of variable severity with onset or 1st recognition during pregnancy.
- The incidence of gestational diabetes is reported as 2-3%.
- Normal pregnancy is characterized by:
  - Mild fasting hypoglycemia
  - Postprandial hyperglycemia
  - Hyperinsulinemia
- Due to peripheral insulin resistance which ensures an adequate supply of glucose for the baby. Insulin resistance
  1. Production of placental somatomammotropin
  2. Increased production of cortisol, estriol, & progesterone
  3. Increased insulin destruction by kidney & placenta

Risk factors

- Diabetes mellitus (DM) type II in a first-degree relative (Family history of diabetes)
- Body mass index >30 kg/m2
- Gestational diabetes in a previous pregnancy
- Age: >35 years old
- Ethnicity – belonging to a non-white ethnic group
- Poor obstetric history
  - Previous polyhydramnios
  - Previous congenital malformation
  - Previous unexplained fetal death
  - Previous large neonate (>4000-4500)gm
  - Prior neonatal hypoglycemia
Screening for diabetes in pregnancy

- All antenatal women are screened for DM at 26-28 weeks gestation with 1 hour random oral glucose challenge test (50 gm glucose) the threshold for a positive test is ≥ or more than 140mg/dl.
- For patients at risk or have glycosuria, a random oral glucose challenge test (50 gm glucose) is performed at booking. If negative, the test is repeated again at 26-28 weeks gestation.
- No single screening test has been shown to be perfect in terms of high sensitivity and specificity for GD. Urinary glucose is unreliable, different criteria exist across Europe and the USA for its diagnosis, there has been a general trend to move towards the World Health Organization (WHO) criteria based on a 75-g oral glucose tolerance test (OGTT).

(OGTT) World Health Organization (WHO) criteria for glucose tolerance based on a 75g oral glucose tolerance test 24-32 w

<table>
<thead>
<tr>
<th>Fasting plasma glucose</th>
<th>1 hour PM (Post Meal)</th>
<th>2 h glucose PM</th>
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<td>&gt; 5.1 mmol/l</td>
<td>10 mmol/l</td>
<td>8.5 mmol/l</td>
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Pre-pregnancy counselling

Aim

1. Achieve the best possible glycemic control before pregnancy
2. Educate diabetic women about the implications of pregnancy
3. Information about risks of uncontrolled diabetes with pregnancy and the effect of pregnancy on progression of diabetes
4. Advise to take high dose (5mg) folic acid pre-conception and for 1st 12 weeks.
5. Hyperglycemia exerts its teratogenic effects during the period of organogenesis-1st 42 days of pregnancy.
6. The level of HbA1c in early pregnancy correlates well with the risk of early fetal loss and congenital abnormality
   a. HbA1c > 10% the risk of fetal loss during pregnancy is around 30%, the risk of congenital abnormalities is the same. Therefore diabetes therapy should be intensified and adequate contraception used until glucose control is good
   b. Targets for therapy pre-pregnancy should be to maintain
      i. HbA1c at 6.1%
      ii. FBS glucose level < 5.5 mmol/L,
      iii. 2H post-meal glucose < 7.8 mmol/L.
7. Preconception clinic provide an opportunity to screen for diabetic microvascular disease retinopathy, nephropathy and neuropathy. In addition women at risk of maternal macrovascular disease can be identified.
8. Information given on when to stop potentially harmful drugs, such as Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers.
9. General healthy lifestyle advice on healthy weight management, diet, exercise, alcohol & cigarette smoking
10. Women who have significant diabetic nephropathy (proteinuria > 2g /24 hs) should be informed of their high risk of pre-eclampsia & preterm birth.
11. For women with type 2 diabetes previously on oral hypoglycemic agents switching to insulin remains standard practice; however, certain oral hypoglycemic agents are now being prescribed to women with gestational diabetic pregnancies.
1st trimester

- REFERRAL TO A COMBINED MULTIDISCIPLINARY DIABETIC OBSTETRIC ANTENATAL CLINIC
- This team should comprise of an obstetrician, diabetologist, specialized midwife, diabetic nurse and dietician who are jointly involved with the care of all pregnant diabetic women attending the hospital.

1-DATING ULTRASOUND SCAN

- Ideally a dating scan should be performed within the first 10 weeks following conception as this allows both the viability of the pregnancy to be confirmed and an accurate gestational age obtained.

2-SCREENING FOR DIABETIC COMPLICATIONS

- Diabetic women with type 2 diabetes are more prone to diabetic maculopathy. A dilated retinal examination each trimester should be performed with referral to an ophthalmologist if retinopathy is present.
- Screening for diabetic nephropathy comprises measurement of albumin/creatinine ratio & creatinine level if is elevated; meticulous attention should be paid to blood pressure control for women with significant proteinuria or serum creatinine above 120 µmol/L, aspirin or heparin should be considered.
- Women with diabetic autonomic neuropathy are at increased risk of gastroparesis that can increase in early pregnancy, causing nausea and vomiting, poor glycemic control and an increased risk of hypoglycaemia. Dietary advice and non-pharmacological treatment should be given prior to treatment with antiemetics such as antihistamines.
- Older women with type 2 diabetes are at increased risk of CAD. A previous history of CAD or its diagnosis in pregnancy is associated with significant maternal morbidity.

3-SCREENING FOR NON-DIABETIC CO-MORBIDITIES

- Women with type 1 diabetes are more susceptible to other autoimmune diseases. The prevalence of autoimmune thyroid disease is sufficiently high to warrant all type 1 women, to be screened for it early in pregnancy.
- Women with type 2 diabetes are likely to have the other components of the metabolic syndrome including obesity, hypertension, dyslipidaemia and insulin resistance.
- Obesity, independently of diabetes, is a risk factor for late stillbirth, birth trauma and maternal complications postpartum.

4-SCREENING FOR CHROMOSOMAL ANOMALIES

- Screening for Down’s syndrome at 13 weeks +6 days by combined test (nuchal translucency, β human chorionic gonadotrophin and pregnancy associated plasma protein).

5-ASSESSMENT AND OPTIMIZATION OF GLYCEMIA

- The first HbA1c measurement taken in pregnancy provides a crude assessment of the risk of major congenital malformations, which is between 2 and 3 times that of non-diabetic pregnancies. With the risk increasing with increasing HbA1c values.
- Keeping fasting glucose levels during the critical period of organogenesis below 6 mmol/l and 1 hour postprandial glucose levels below 7.8 mmol/l has been shown to decrease the fetal malformations rate.
- This tight degree of glycaemic control usually by giving multiple injections of short- and long-insulin injections throughout the day or an insulin pump. The newer quicker analogue insulins are well suited for targeting postprandial glycaemia. And NovoRapid is licensed for use in pregnancy.
- Blood sugar profile
  - The adjustment of the insulin dose is based on frequent daily blood glucose monitoring that should include a fasting value, a 1-h postmeal value and a bedtime reading.
- Diabetic ketoacidosis associated with a high fetal loss.
  - Advice needs to be given on how to manage and monitor low levels of ketonemia (<1.5 mmol/l) and when to seek hospital advice urgently if unwell or if blood ketones are higher than 1.5 mmol/l.
Dietary recommendations in diabetic patient

- Total caloric intake should be 30 calories/kg for normal weight, 24 cal/kg for obese patients
  - 50-55% CHO
  - 25% protein
  - 20% fat
- Divide meals into six portions daily, three meals & three snacks between meals. The most important snack is the bedtime snack.
- Most women with impaired glucose & GDM are initially managed with dietary advice.
- Insulin should be added to patients who have fasting hyperglycemia despite their dietary regimen.
- Patients require insulin injection at least twice daily.
- A mixture of short acting and medium acting insulin is given 20-30 minutes before breakfast and dinner. The dose is determined based on body weight, TM of pregnancy & sugar level.
- The initial dose is
  - 1st TM 0.6 units/kg
  - Second TM 0.7 u/kg
  - 3rd TM 0.8 u/kg
- Obese patients usually require 0.1 u above the recommended dose in each TM.
- Total daily dose is calculated & 2/3 of the dose is given in the morning (7am) & the remaining 1/3 is given in the evening (5pm).
- The morning dose is divided as 2/3 NPH & 1/3 regular insulin, while the evening dose is divided as ½ regular & 1/2 NPH.
- Insulin is given by SC route with an insulin syringe in the thigh, upper arm, buttocks or abdominal wall.

ADVICE ON HYPOGLYCEMIA PREVENTION

- All women must be aware of the risk of hypoglycemia as they intensify their insulin management.
- Individual advice on the timing of meals and snacks to minimize hypoglycemia needs to be given.
- Family members should be instructed on how and when to administer glucagon.
- Women should carry identification cards specifying that they are taking insulin.
- Warning signs of hypoglycemia vary from person to person include feeling shaky, sweating, tingling in the lips, going pale, heart pounding, confusion & irritability.

Management of hypoglycemia

- Ensure that those close to the patients have been instructed in the 1st recognition & 1st aid management of hypoglycemia.
- 1st aid management consists of administration of a sugary fluid followed by a starchy snack.
- If left untreated & the patient becomes unconscious, administration of IV glucose 10-25% in a central vein is indicated. Glucagon injections are preferable if available.
2nd trimester

1-OPTIMIZATION OF GLYCAEMIC CONTROL

- By the middle of the second trimester maternal insulin resistance starts to increase due to high concentrations of circulating maternal fatty acids and placental hormones.
- By term, in non-diabetic women, insulin secretion has to increase 2–3 fold to control blood glucose levels postprandially.

2-SCREENING FOR CONGENITAL ABNORMALITIES

- A detailed anomaly ultrasound scan should be offered to all diabetic women between 18 and 20 weeks’ gestation to look for major congenital abnormalities. Structure most commonly affected in diabetic pregnancies are the spine, skull, kidneys and heart. Fetal echocardiography between 20 and 24 weeks’ gestation should be offered to view the four chambers of the heart together with the ventricular outflow tracts.

3-SURVEILLANCE FOR MEDICAL OBSTETRIC COMPLICATIONS

- Women with diabetes have an increased risk of hypertension in pregnancy, including pre-eclampsia. In addition to serial clinic blood pressure measurements and urine analysis for protein, uterine artery Doppler wave-form analysis at 24 weeks may be helpful in identifying those women most at risk.
- Women should be screened for retinopathy using digital photographs at 26 w if there was any evidence of retinopathy in the 1st trimester, referral to ophthalmologist is required if the retinopathy has progressed.

4-ASSESSMENT OF FETAL GROWTH

- Ultrasound scans for assessment for fetal growth usually starts at the end of the second trimester and is repeated thereafter every 4 weeks, or more frequently if needed.
- Baseline measurement of fetal abdominal circumference at 26 weeks expressed as a percentile can be compared with later scans to provide evidence for growth acceleration or restriction.
- Measurement of liquor volume should also be serially recorded, as polyhydramnios is more common in diabetic pregnancies.

3rd trimester

1-OPTIMIZATION OF GLYCAEMIC CONTROL

- Achieving good glycemic control tends to become easier as the insulin resistance protects women from severe hypoglycemia.
- When glucocorticoid steroids are required for lung maturation insulin requirements over the next 72 h may need to double.

2-ASSESSMENT OF FETAL GROWTH

- Evidence on serial ultrasounds of a rising abdominal circumference percentile in relation to the head circumference or bi-parietal diameter is indicative of accelerated fetal growth.

3-TIMING AND MODE OF DELIVERY

- The risk of late unexpected stillbirth among women with diabetes is approximately fourfold higher than for the nondiabetic population and it is for this reason that most authorities advocate delivery between 38 and 39 weeks.
- The risk of birth trauma increases with increasing birthweight.
- C.S may be indicated if when complications dictate urgent delivery & when malpresentation is present.
- C.S is not indicated on account of diabetes alone.
PROTOCOLS FOR INSULIN DURING LABOUR AND DELIVERY

- Women being admitted for a planned induction should be encouraged to take their normal insulin doses the night before. Once admitted they should continue with their short-acting bolus insulin to cover meals only switching to an intravenous insulin sliding scale once in labor or a decision has been taken to perform a Caesarean section.
- Ideally elective Caesarean sections should be planned for early morning, with the women instructed to take their normal bolus insulin with their evening meal and two thirds of their usual basal insulin the night before admission. Once on the ward an intravenous insulin sliding scale can be started, with the dose adjusted downwards straight after delivery.

Post-partum

- Insulin requirements drop to prepregnancy values immediately.
- Following delivery of the placenta. For women with type 1 diabetes they can recommence their prepregnancy insulin regime as soon as they are eating and drinking normally. This dose of insulin should be clearly written in the notes as part of the delivery plan.
- For women who have type 2 diabetes previously on oral agents, these too can be restated immediately following pregnancy. Insulin is not excreted into breast milk and is considered completely safe for use during breastfeeding. Insulin requirement often fall in mothers with type 1 diabetes who breastfeed due to the small increase in metabolic rate that occurs with lactation. The use of Metformin by breastfeeding mothers is also considered safe, as very little of the drug is excreted in breast milk.

Complication of diabetes in pregnancy

### Maternal complications
- Preterm labor
- Incidence of PIH may be increase
- PPH
- Infection: High incidence of chorioamnionitis, postpartum endometritis, UTI, candidiasis of vulva & vagina

### Neonatal complications
- Respiratory distress syndrome
- Neonatal hypoglycemia
- Polycythemia & jaundice
- Hypocalcaemia & hypomagnesaemia
- Hypertrophic cardiomyopathy in infants of type I diabetes mothers

### Fetal complications
- Approximate threefold increase in fetal malformation
- Increased rate of spontaneous miscarriage in poorly controlled diabetes with pregnancy
- Unexplained IUFD
- IUGR
- Fetal thrombosis

Effects of pregnancy on diabetes

1. More insulin is necessary to achieve metabolic control
2. Progression of diabetic retinopathy
3. Worsening of diabetic nephropathy
4. Increased risk of death for patient with diabetic cardiomyopathy
5. Ketosis

Indications of hospitalization

- On initial calculation of insulin dose, especially in unreliable patients
- Patient with PIH
- Sever vascular diabetic disease
- At any time if there are concerns about glycemic control, especially if hyperemesis gravidarum develops
- In cases of diabetic complications, e.g. diabetic ketoacidosis