i. History of recurrent hypoglycaemia
ii. Hypoglycaemia unawareness
iii. Poor diabetes control
iv. Brittle diabetes
v. Non-compliance with medical treatment
vi. Patients who are 'unwilling 'or 'unable' to monitor and manage their blood glucose levels

b) Self-Monitoring of Blood Glucose (SMBG): Misconception that pricking blood invalidates their fast needs to be allayed. Patients with T1DM should monitor their blood glucose:

i. Multiple times a day to understand the trend of the excursions and keep a Ramadan logbook of these records
ii. Post-*iftar* to detect hyperglycemia after heavy meal
iii. Whenever they experience symptoms of hypoglycaemia

c) Dietary advice: This needs to be individualised and includes having a well-balanced meal with 40-50% carbohydrates with low glycemic index, 20- 30% protein and <35% of fat, with daily calories divided equally between *iftar and suhoor* with 1-2 snacks in between, while including plenty of fruits and vegetables and avoiding caffeinated, sweetened drinks and deserts. These can be represented by the 'Ramadan Plate Method" for visualisation to patient. To aid with this, a mobile and web-based application known as Ramadan Nutrition Plan (RNP) has been designed to help physicians design individualised medical nutrition therapy (MNT) for patients with diabetes during Ramadan fasting. In order to ensure adequate spacing between the meals, the dinner should be taken as soon as possible at *iftar* and *suhoor* should be delayed as much as possible. The practice of staying up late at night to consume *suhoor* before eventually going to sleep should be discouraged.

d) Underscore the importance of breaking the fast immediately if any of these situations arises:

i. Blood Glucose < 70mg/dL
ii. Blood Glucose > 300mg/dL
iii. Symptoms of hypoglycaemia, hyperglycaemia, dehydration or acute illness occur

2. Pharmacological Management

a. Patients on Basal-Bolus Regimen have to make the following adjustments:

i. Long/intermediate-acting insulin

1. If taking once a day, then reduce it by 15-40% and take at *iftar*
2. if taking twice a day, then take the usual morning dose at *iftar*, and reduce the evening dose by 50% and take it at *suhoor*]

ii. Premeal insulin

1. Normal *iftar* dose,
2. Reduce *suhoor* dose by 25-50%

b. Patients on insulin pump

i. Basal rate is to be kept same as before, but reduce it by 20-40% in the last 3-4 hours of fasting and increase dose by 0-30% in the first 2 hours after *iftar*

ii. Bolus rate is to be decided by normal carbohydrate counting and insulin sensitivity principles

Target pre-iftar/pre-suhoor and post-iftar/post-suhoor BG is 90-130 mg/dl, and insulin is to be self-titrated in increments of 2 units till target BG is reached. Patients should be advised to follow up after the festivities are over to discuss the challenges they faced, and readjustment of medications.

Smoking, Alcohol and other substance abuse in T1DM

Adolescents tend to indulge in experimental behavior in a bid to develop an individual identity. The stress associated with a chronic illness like T1DM may further provoke indulgence in high-risk behavior in these individuals.

Smoking

Harmful effects of cigarette smoking are established across all age groups. However, adolescents with T1DM are predisposed to a larger magnitude of deleterious effect, be it impact on metabolic control or on micro- and macro- vascular complications. Smoking is associated with worse glycemic control in T1DM along with a tendency to have higher diastolic blood pressure and atherogenic lipid profile, leading to an increase in cardiovascular risk. Smoking also causes vascular damage, endothelial dysfunction and activation of coagulation pathway which in the background of vascular stiffness and poor cardiovascular profile, leads to an increased risk of cardiovascular events. Microvascular complications are also seen with increased frequency and an increased progression to micro albuminuria and nephropathy, worsening of retinopathy, and deterioration of neuropathy has been reported in smokers with T1DM. On account of these factors, the mortality has been reported to be higher in smokers in several T1DM cohorts.

There is good evidence to suggest that the deleterious effects induced by smoking are reversible upon its cessation. This makes for a compelling argument for the need of active intervention to curb smoking in patients with T1DM. As cigarette smoking in children with T1DM increases with age, it becomes essential to actively counsel children against the initiating of smoking from younger age, which puts physicians taking care of these patients at the forefront of combating smoking. ADA recommends smoking cessation counselling as a routine component of diabetes care. Multiple strategies, including the 5 A's plan of Ask, Advise, Assess, Assist, and Arrange have been proposed as an effective method to address smoking among adolescents with T1DM. Psychotherapy, nicotine patch and other nicotine cessation modalities may be tried in motivated patients. ADA recommends against the use of e-cigarettes.

Alcohol

Even though alcohol consumption is reported to be lower in individuals with T1DM compared to their peers, they are still at a higher risk of experiencing severe harm from it, as alcohol consumption is associated with worse glycemic control as well as higher rates of DKA and hypoglycemia. The metabolism of alcohol reverses the NADH/NAD-ratio (redox-shift) which inhibits gluconeogenesis. Besides, alcohol is also known

to inhibit glycogenolysis and enhance lactate and beta-hydroxybutyrate production. Lower release of glucose from the liver leads to hypoglycaemia and accumulation of beta-hydroxybutyrate causes ketosis. Further, the risk of hypoglycemia is compounded by reduced recognition of physiological warning signs (hypoglycemia unawareness) by patient along with mistaken identification of these signs by third party as those of intoxication. Chronic alcohol consumers also have reduced diabetes self-care behaviors, poor compliance with medications, and worse glycemic control and HbA1c levels.

Thus, patients with T1DM need to be adequately questioned and counselled regarding harms of both binge drinking as well as chronic consumption of alcohol. They should be educated regarding 'responsible drinking', which includes avoiding binge drinking, consuming carbohydrates while drinking alcohol, watching out for delayed hypoglycemia and preventing it by frequent monitoring or consumption of extra carbohydrate or decreasing the dose of insulin. Patients should never drink alone, and their peers should be informed about the diagnosis of diabetes and risk of hypoglycemia and DKA, and necessary steps that may be required if situation arises.

Other illicit drugs

Self-reported usage of street drugs is common in T1DM, with results varying from 10-77% depending upon survey method and countries involved. Risk of hypoglycemia and DKA remains high due to impaired self-care associated with intoxication, as well as having overall a poor glycemic control and HbA1c levels. Studies have indicated that past and current drug abuse is significantly associated with acute events leading to mortality in T1DM. Most of the individuals were unaware of the negative health consequences of these drugs on their disease or how to manage the complications. Thus, it becomes imperative for physicians taking care of these individuals to frequently ask them about usage of these drugs tacitly, and to counsel them for cessation and psychotherapy referral as required, for an overall positive health.

Summary

The diagnosis of T1DM means the start of a long and close relationship of the patient, family, and others, with the diabetes care team. The aim of a physically and emotionally healthy person and family can only be achieved by effective education, taking all aspects into consideration, at a pace which is appropriate for the age, socio-economic-cultural background, motivation, availability of technology and medical status of the child and caregivers. Outcomes can be very rewarding, as well managed children grow up to become confident, self- reliant "heroes".

Checklist of related topics

1. Diagnosis, symptoms, need for lifelong self-care with insulin
2. Pathophysiology, "cause" – no one's fault, not communicable, difference from T2D, other forms of diabetes, honeymoon phase (not cured)
3. Blood glucose (and ketone) testing, recording, discerning patters
4. Handling insulin: types, action profiles, transport, storing, devices, injecting, adjusting, sites
5. Hypoglycemia, I-cards, glucagon, Sick days, any illness/ surgery
6. Diet changes, carbohydrate counting, exercise, sports

7. Psychological responses, family dynamics, cognitive behavior therapy, coping mechanisms, avoiding burnout
8. Diabetes technology
9. Peer support, self-help groups
10. Special occasions: festivals, travel, diabetes camp, school camp/excursion
11. Detection and management of co-morbidities, complications
12. Careers, marriage, contraception, planning conception, driving,
13. Smoking, alcohol, drugs, other additions and risk taking behaviors
14. Financial issues
15. Transition to adult services

Suggested Reading

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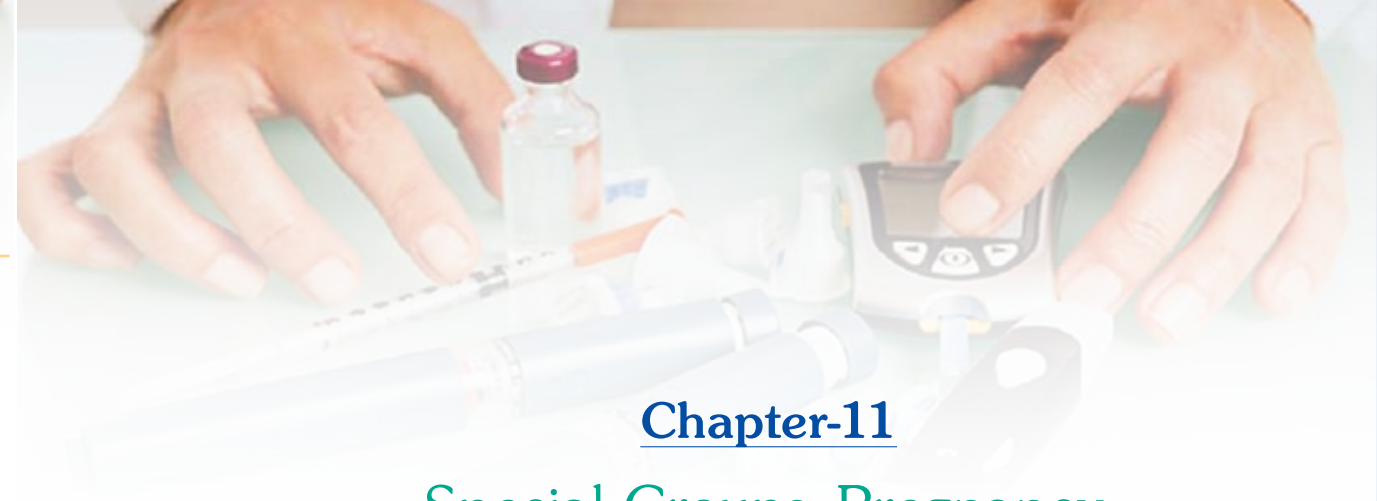

Chapter-11

Special Groups: Pregnancy, Travel and Surgery

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Section A-Pregnancy

Introduction

Type 1 diabetes mellitus (T1DM) affects approximately 0.1-0.2% of all pregnancies and has a higher association with poor outcomes for both mother and her off spring[1]. The risk of perinatal death and stillbirth has been reported to be 4 to 6-fold higher in T1DM as compared to the general population[2]. Data (1996-2008) from England revealed a four and two times higher prevalence for fetal and infant death respectively, without any significant difference among women with pre- existing T1DM (n=1206) or type 2 diabetes mellitus (T2DM) (n=342). The study found that this adverse effect was largely moderated by glycemic control[3].The risk of congenital malformations (like neural tube defects, caudal regression, microcephaly or anencephaly, congenital heart disease) can be as high as 15% in offsprings of T1DM women with HbA1c above 14%[2,4-6]. The risk is also higher for miscarriage, intrauterine death, preterm birth, macrosomia and associated complications in women with poor periconceptional glycemic control.

In view of the strong link between poor glycemic control and adverse pregnancy outcomes, achieving euglycemia during preconception and pregnancy is important for improving pregnancy outcomes. The early recognition and care of associated complications like nephropathy, retinopathy, and comorbidities like hypertension is also essential for improving pregnancy outcomes.

Women in the reproductive age group should be aware of the importance of planned pregnancy, and education regarding it should begin during adolescence as part of routine diabetes care[5]. A woman who plans pregnancy would need about 6 months to achieve and maintain optimal glycemic control. The components of care from preconception (Table I) to postpartum phase are discussed below. This chapter aims to provide a description of components that can help in improving outcomes of pregnant women with T1DM.

Glycemic targets

Preconception

Near normoglycemia is the target when planning pregnancy. According to guidelines the goal of pre-pregnancy HbA1c should be < 7%[6-9]. Lower HbA1c (of < 6.5%) can be targeted if it can be achieved safely (especially avoiding the risk of severe or frequent hypoglycemic episodes)[6-9]. On the contrary, a woman with HbA1c > 10% should be strongly discouraged from getting pregnant till she achieves better control because of the high risk of adverse

Table I: Preconception care of women with diabetes

A.	Preconception counselling: Aim to inform woman to have optimal glycemic control before pregnancy.
B.	Optimization of insulin therapy preferably with multiple daily dose insulin or continuous subcutaneous insulin.
C.	HbA1c levels should be as close to normal as possible without undue hypoglycemia.
D.	Medications should be reviewed. Comorbidities and complications should be assessed and taken care of.
E.	Folic acid (5 mg) daily should be prescribed daily before conception to reduce the risk of neural tube defects.
F.	Measurement of serum TSH and thyroid peroxidase is recommended before conception.
G.	Discussion on contraception and providing the most appropriate method.

Abbreviations: TSH-Thyroid stimulating hormone, HbA1c-Glycated hemoglobin

pregnancy outcomes beyond this level[6]. A monthly measurement of HbA1c is suggested by UK NICE (National institute for Clinical excellence) guidelines in the pre-conception period[6]. Clear guidance on self-monitored capillary glucose targets is still required. Some suggest glycemic targets of 80-110 mg/dl for fasting and pre-meals and 100-155 mg/dl for 1-hr post-meals[10]. As per the UK NICE guidelines,the recommended target includes:

- A fasting plasma glucose (FPG) of 90–126 mg /dl on waking
- Plasma glucose of 72–126 mg /dl before meals at other times of the day.
- After meal plasma glucose level of 90–162 mg/dl.

Women may require monitoring of blood glucose around 6-8 times in a day to achieve these targets without hypoglycemia. To increase compliance on decided strategy the monitoring frequency needs to be individualized. This is based on shared decisions,and striking a balance between the need for achieving glycemic targets and available resources.

Insulin storage/technique, self-adjustment of insulin doses required at certain times, sick day rules, ketone testing and hypoglycemia care are important components of education for safety achieving glycemic targets. The woman herself or any family member should have necessary skills for the same.

The woman should undergo a review for drugs with potential teratogenic effect (like ACE inhibitors or angiotensin receptor blockers, statins) and evaluation for glycemic and blood pressure control, diabetes related complications and thyroid status (Table I). This is in addition to other investigations done as routine for all women in preconception period or special investigations required an individual basis.

During Pregnancy

The American Diabetes Association (ADA) has recommended targets for women with T1DM, similar to women with GDM, which are as follows[7]:

- FPG ≤ 95 mg/dl and
- Either one-hour postprandial ≤ 140 mg/dl or
- Two-hour postprandial ≤ 120 mg/dl.

The UK NICE recommends almost similar target levels for pregnant women except a slightly lower target (of < 115 mg/dl) for two hour postprandial glucose, if these can be achieved without causing problematic hypoglycemia.

Less stringent and individualized targets can be set in case efforts to achieve recommended targets result in significant hypoglycemia[7]. The HbA1c is used as an additional measure of glycemic control (a monthly measurement is suggested) and should not be a replacement of self-monitoring of blood glucose, due to physiological changes in pregnancy affecting its accuracy. The data suggest that HbA1c of < 6-6.5% is associated with lower rates of adverse fetal outcomes[7].

Fetal Growth monitoring

It is important to have an objective assessment of fetal growth in addition to close clinical monitoring of the pregnancy, since poor glycemic control is associated with accelerated fetal growth. Ideally a scan is done at 28 weeks and then 4 weekly to monitor growth. If this is not feasible in resource limited settings, at least one at 28 and another at 36 weeks is advisable. The presence of polyhydramnios and accelerated growth may be due to less than optimal glycemic control and needs to be factored in along with the blood glucose values.

Growth restriction can happen in women who have long standing type 1 diabetes and vasculopathy. Similarly, the tailing off of growth can also be a warning for impending preeclampsia. The risk of preeclampsia is higher in women with T1DM, and poor glycemic control increases it further.

In women with T1DM, there is higher risk of stillbirth. This is due to fetal hyperglycemia and hyperinsulinemia which induce fetal hypoxemia and maternal vasculopathy, causing poor utero placental circulation. This therefore, unlike pure placental dysfunction in IUGR or preeclampsia, does not lend itself to surveillance by fetal doppler examination. Indeed there are no good studies based on which one could make recommendations on the frequency or the best method of fetal surveillance. As of now, combination of a Non Stress test and amniotic fluid volume is monitored depending on local institutional protocols.

The NICE 2015 guidelines have elaborated in detail the antenatal management of women with diabetes during pregnancy and the same have been adapted here and presented in Table II. This table refers to physical activity and not antenatal management.

Insulin therapy

Multiple subcutaneous insulin injections (MSII) are standard of care to achieve glycemic control given higher efficacy and better safety than premix or split mix regimens[11]. According to NICE 2015 guidelines, insulin pump can be offered to women during pregnancy if glycemic control is difficult to achieve with MSII due to significant hypoglycemia. In view of increased potential of hypoglycemia in pregnancy, rapid acting analogs like aspart or lispro and long acting analogs like detemir are preferred over conventional insulins[11].

Insulin requirements may vary throughout pregnancy. It may increase in the first 9 weeks, thendecrease from 9-16 weeks, before further increasing until the 37th week[12]. With progression in pregnancy, the insulin requirements may increase by two to three times with a shift towards more prandial insulin requirement. The insulin requirements can be 40-50% higher for up to 1 week after the initiation of glucocorticoid treatment for premature fetal lung maturation.

Medical nutrition therapy

An individualized nutrition plan which is culturally sensitive and socio- economically viable and which provides adequate calories for fetal and maternal health, achieves glycemic goals without hypoglycemia, and helps in appropriate gestational weight gain should be made with the help of an expert dietician. The Dietary Reference Intakes (DRI) recommends a minimum of 175 g of carbohydrate, a minimum of 71 g of protein, and 28 g of fiber[7]. A less carbohydrate-restricted approach may improve maternal adherence when combined with higher quality carbohydrates, lower fat, appropriate caloric intake, and ethnically acceptable foods[13]. Three major meals and three to four adequately spaced snacks help in avoiding hypoglycemia while preventing glycemic fluctuations, provided women also pay attention to timings, content and quality of meals/snacks.

Exercise

Exercise facilitates the glucose uptake, improves glucose clearance and sustains insulin sensitivity. Furthermore, exercise also regulates counter-regulatory hormones and decreases hepatic glucose output as evident in fasting blood glucose levels. Women without medical and obstetric contra indications (Table III) should be encouraged to doat least 30 min/day of physical activity[14]. Carbohydrates consumed (20 g of glucose) before, during, and after physical activity will help avoid hypoglycemia, especially if glucose is < 90 mg/dl[15].If starting glycemia is 90–124 mg/dl, one should ingest 10 g of glucose before starting aerobic exercise. If starting glycemia is 126–180 mg/dl aerobic exercise can be started without glucose ingestion[15].

During Labor

Women with T1DM should be managed with insulin infusion and intravenous dextrose (5%) running separately. Monitor glucose hourly and the level should be maintained intervals between 72 and 126 mg/dl[6]. During cesarean section blood glucose monitoring should be reduced to 30 minutes which should continue till the baby is born and mother is conscious. An anesthetic assessment should be done in third trimester for women with diabetes and comorbidities such as obesity or autonomic neuropathy[6].

Hypoglycemia

The aim to achieve near normoglycemia also increases risk of hypoglycemia. Severe hypoglycemia (hypoglycemia requiring help from another person to restore the blood glucose level) is 3 to 5 times more frequent in first half of pregnancy than before conception. It is mainly because of increased nausea and vomiting in the first trimester, thereafter the incidence is lower. Up to 45% of women with T1DM experience severe hypoglycemia during pregnancy. However, 60% of the severe hypoglycemic episodes are accounted for by only 10% of pregnant women with T1DM[16,17]. A history of severe hypoglycemia in the year preceding pregnancy and self-estimated impaired hypoglycemia awareness are significant risk factors for severe hypoglycemia. A simple question “Do you recognize symptoms when you have hypoglycemia?” can identify subjects with impaired awareness. The woman with impaired awareness has threefold increased risk of severe hypoglycemia compared to woman who has normal awareness[18]. A longer duration of diabetes, intensive insulin treatment resulting in lower HbA1c in early pregnancy, and fluctuating plasma glucose values (< 70 to > 180 mg/dl) contribute to a higher risk of severe hypoglycemia during pregnancy[16,17].

Limited evidence in humans suggests that hypoglycemia has no short or long- term adverse effect on the fetus[16]. However, consequences of severe hypoglycemia like convulsions, road traffic accidents, maternal death in extreme cases, are rare but dangerous complications of

Table II: Timetable of antenatal appointments – adapted and modified from UK NICE guidelines

Booking appointment Ideally by 10 weeks	• Review medicines for diabetes and its complications. • Patient should get blood pressure measurement, per speculum examination, hemogram, kidney function tests, liver function test, TSH, urine routine microscopy and culture. • Measure HbA1c levels in every trimester. • Confirm viability of pregnancy and gestational age at 7–9 weeks. Early viability scan is recommended since women with diabetes are at a higher risk of miscarriage. Dating is important to plan delivery and avoid prematurity. • Offer retinal assessment for women with pre-existing diabetes unless the woman has been assessed in the last 3 months. • Offer renal assessment for women with pre-existing diabetes if this has not been performed in the last 3 months. • Arrange contact with the joint diabetes and antenatal clinic every 1–2 weeks throughout pregnancy for all women with diabetes.
11-14 weeks	• Neural tube/nasal bone (NT/NB) scan with dual screen test for chromosomal anomalies.
18-20 weeks	• A detailed ultrasound needs to be performed between 18-20 weeks along with a fetal echocardiogram to rule out neural tube defects, cardiac and other structural abnormalities that are associated with diabetes. • Retinal assessment if diabetic retinopathy was present at their first antenatal clinic visit.
28-32 weeks 36 weeks	• Offer ultrasound monitoring of fetal growth and amniotic fluid volume • Need for antenatal steroids (ANS) to be evaluated • Women with uncontrolled sugars or high insulin requirement should be reconsidered for referral to higher centre with NICU facility • Daily fetal movement count should be explained • Retinal assessment of all women • Offer ultrasound monitoring of fetal growth and amniotic fluid volume.
	Provide information and advice about: • Timing, mode and management of birth • Analgesia and anesthesia • Changes to blood glucose-lowering therapy during and after birth • Care of the baby after birth • Initiation of breastfeeding and the effect of breastfeeding on blood • Contraception and follow-up.
37^{+0}-38^{+6} weeks	• Offer induction of labor, or caesarean section if indicated, otherwise await spontaneous labor. • Timing of delivery should be individualized Neonatal care: Neonate should be monitored for hypoglycemia, respiratory distress, hyperbilirubinimia.

Abbreviations: UK NICE guidelines: United Kingdom The National Institute for Health and Care Excellence guidelines, TSH: thyroid stimulating hormone, HbA1c: Glycated hemoglobin, NT/NB: Neural tube/nasal bone, NICU: Neonatal Intensive Care Unit, ANS: antenatal steroids

Table III Contraindications to physical activity during pregnancy

Contrain-dications	Medical	Obstetric
Absolute	• Hemodynamically significant heart disease • Restrictive lung disease	• Incompetent cervix • Multiple gestation at risk for premature labour • Persistent second or third trimester bleeding • Placenta previa after 26 weeks gestation • Premature labour during the current pregnancy • Ruptured membranes • Pre-ec lampsia , pregnancy induced hypertension
Relative	• Severe anemia • Unevaluated maternal cardiac arrhythmias • Chronic bronchitis • Uncontrolled diabetes • Extreme morbid obesity • Extreme underweight (BMI <12 kg/m^2) • History of extremely sedentary lifestyle • Poorly controlled hypertension • Poorly controlled hyperthyroidism • Poorly controlled seizures • Orthopaedic limitations • Heavy smoker	• Intrauterine growth restriction in the current pregnancy

Abbreviation: BMI-Body mass index

severe hypoglycemia. Certain preventive measures as listed in Table IV can help in reducing the risk of hypoglycemia during pregnancy[16].

Table IV: Hypoglycemia prevention in T1DM during pregnancy

- Early identification of high-risk patients, particularly women with self-estimated impaired hypoglycemia awareness and / or history of severe hypoglycemia the year preceding pregnancy
- Reduction of insulin dose by approximately 10% at 8-16 weeks
- Cautious use of supplementary insulin in early pregnancy
- Use of rapid- and long-acting insulin analogues
- Avoid pre-bedtime plasma glucose values below 108mg/dl
- Perform frequent blood glucose monitoring including between 02:00 and 04:00 am
- Prescription of glucagon for administration at home by partner
- Use of continuous subcutaneous insulin infusion (insulin pump) therapy combined with real-time continuous glucose monitoring

Abbreviations: T1DM-Type 1 diabetes mellitus

CGMS and Insulin pump

Continuous glucose monitoring system (CGMS) provides detailed information regarding

glucose patterns that can be used for optimizing diet, lifestyle and insulin doses. It also can alert users to impending hypoglycemia or hyperglycemia allowing them to take earlier corrective action and therefore minimize out of rangeexcursions[19]. CONCEPTT was a multicenter, open-label trial where women with T1DM < 14-week gestation were randomized to capillary glucose monitoring with and without real-time CGM (used continuously from randomization until delivery). The study found that the numbers needed to treat with CGM to prevent one complication were six for both neonatal intensive care admission and large for gestational age, and eight for neonatal hypoglycemia. Sensor-integrated insulin delivery improves time in range compared to stand-alone pump therapy[21]. The first trial of sensor-integrated insulin delivery in pregnancy, which included 16 women with T1DM found that it improves time in target by 15% without increasing hypoglycemia as compared to sensor-augmented insulin delivery system[22].

Insulin pump therapy is an attractive option, given many unique challenges in pregnancy of T1DM women. Women with recurrent troublesome hypoglycemic episodes and those with hypoglycemia awareness can be good candidates for insulin therapy, preferably starting preconception. Good evidence is lacking in context for the use of currently available insulin pumps in T1DM during pregnancy[19].

Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) must be excluded in all pregnant women with T1DM who become unwell, even if blood glucose values are not too high as seen in DKA (< 200 mg/dl) (euglycemic DKA can occur in pregnancy). The risk for DKA is enhanced in pregnancy due to increase in insulin resistance and enhanced lipolysis/ketosis associated with pregnancy. It is rarely life threatening for mother if it is recognized and treated promptly (Table V). However, fetal loss rates remain in the order of 10–25% for a single episode of DKA[23,24].

Other general measures to be taken care

Preconception evaluation and optimization of thyroid status

All pregnant women should be screened for thyroid disorders in preconception period using TSH, T4 and TPO, and should be managed and monitored as delineated in guidelines[11].

Folic acid supplementation

Folic acid supplementation with a daily dose of 5 mg should be started 3 months before planned conception, to reduce the risk of neural tube defects[11].

Cessation of smoking, alcohol and illicit drugs

Smoking, alcohol and illicit use of drugs is associated with adverse pregnancy outcomes. Women should be advised to stop their use in preconception period and thereafter. Referral to de-addiction clinic/expert may be done if required.

Associated metabolic diseases

Hypertension

There is two to four fold higher risk of hypertension in women with diabetes. Hypertension may be present in women with T1DM. Blood pressure (BP) <130/80 mm Hg) should be achieved before conception. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers should be discontinued prior to conception[11]. Women

Table V: Diabetic ketoacidosis (DKA) in Pregnancy - When to suspect DKA?

A high index of suspicion for DKA in diabetic pregnant women with nausea, vomiting, abdominal pain, fever, hyperventilation, hypotension, and change in mental status, in addition to symptoms related to hyperglycemia

Predisposing factors include

- Infection
- Omission of insulin doses
- Obstetrical use of β-sympathomimetic drugs and glucocorticoids.
- Protracted vomiting, starvation and dehydration
- Undiagnosed diabetes
- Insulin pump failure
- Poor glycemic control

Risks to mother

- Acute renal failure
- Adult respiratory distress syndrome
- Myocardial infarction
- Cerebral edema
- Death

Risks to fetus

- Preterm delivery
- Acidosis and hypoxia could result in fetal demise
- Adverse neurobehavioural outcomes and lower IQ

Educate

- All women with pre-existing diabetes who are planning pregnancy or already pregnant should be educated about DKA; prevention with self-monitoring of blood glucose (SMBG), medical nutrition therapy, and appropriate insulin therapy; and sick day management.
- The patient should be taught to perform urine ketone measurements at times of illness or when persistent glucose levels exceed 200 mg/dl and to promptly report positive values.

The management of DKA during pregnancy include

Multidisciplinary approach

- Intravenous fluid therapy
- Intravenous insulin therapy
- Electrolyte correction
- Evaluation of the need for bicarbonate administration
- Identification and treatment of any precipitating factors
- Monitoring of maternal and fetal responses

Fetal monitoring

- Continuous fetal heart rate monitoring and biophysical tests are used to assess fetal wellbeing in cases occurring after 24 weeks' gestation.
- Immediate delivery may not be necessary for ominous patterns, since correction of DKA often reverts the patterns to normal (usually after 4-8 hours).
- If fetal status does not improve or if the maternal condition continues to deteriorate despite aggressive therapy, delivery is warranted.

Abbreviations: DKA-Diabetic ketoacidosis, IQ-Intelligence quotient, SMBG- self monitoring of blood glucose

should be switched to safer alternatives like methyldopa, labetalol, or calcium channel blockers (nifedipine slow release).

In pregnancy, as per UK NICE guidelines (not specific to diabetes), treatment should be initiated if blood pressure is >150/100mm Hg for uncomplicated chronic hypertension/ gestational hypertension/preeclampsia and at >140/90 mm Hg for target-organ damage secondary to chronic hypertension. Treatment goal is <160/110 mm Hg (but systolic ≥ 120 mmHg and diastolic ≥ 80 mm Hg, as uteroplacental and blood flow may get compromised below these levels) for chronic hypertension,<160/110 mm Hg for gestational hypertension and preeclampsia[25,26].

Dyslipidemia

In the case of women taking a statin, it has to stop if they are attempting to conceive. Use of fibrates and/or niacin is also not advisable. Bile acid-binding resins are safe alternatives in case hypercholesterolemia requires treatment[11].

Overweight/obesity

Pre-pregnancy overweight/obesity is an additional adverse factor, which adds to the insult for both the mother and her offspring. Therefore, optimization of weight before pregnancy is also desirable. Women having excess weight should preferably lose weight before pregnancy and those with BMI above 27 kg/m^2 should be strongly advised and encouraged to lose weight before conceiving[6].

Complications associated with Type 1 diabetes

The presence of active (requiring treatment for regression/stabilization) proliferative retinopathy, severe diabetic nephropathy with glomerular filtration rate reduced to < 30ml/min/1.73 m^2, severe autonomic neuropathy or severe coronary heart disease could pose serious increased risks during pregnancy and these complications should be evaluated in detail and necessary action taken[2].

Diabetic Retinopathy

Pregnancy increases the short-term risk of progression of diabetic retinopathy. In data compiled from 11 studies (till 2015) including 1026 T1DM pregnant women, the chances of progression to proliferative diabetic retinopathy (PDR) during pregnancy were only 0.5% if there was no diabetic retinopathy at baseline. However, the incidence was 10% if some degree of non- proliferative diabetic retinopathy (NPDR) was present at baseline[27]. Therefore, the presence of retinopathy especially moderate to severe NPDR is a risk factor for PDR in pregnancy. Longer duration of diabetes, poor blood glucose control, hypertension, and pre-eclampsia are other factors, which increase the risk of progression of retinopathy in pregnancy. In the DCCT trial, pregnancy was associated with 1.63- and 2.48-fold increased risk of developing short-term retinopathy in the intensive and conventional group, respectively[28]. The risk persisted for 1 year after delivery. It is recommended that all women with diabetes who are planning a pregnancy have a detailed ocular assessment (if it has not been done in the last 6 months). If retinopathy is documented, the patient should be apprised of the specific risks of worsening of diabetic retinopathy during pregnancy[11]. A baseline detailed eye examination should be done during the first (if not performed in the last 3 months) and in the third trimester for all. Patients with mild retinopathy should

be evaluated every trimester, and those with severe lesions should be evaluated monthly. Finally, strict follow-up should continue for 1 year after delivery[6-8,11,27].

If the degree of retinopathy warrants therapy, conception should be deferred until the retinopathy has been treated and found to have stabilized[11]. Laser photocoagulation for severe non-proliferative or proliferative retinopathy (PDR) prior to pregnancy reduces the risk of visual impairment in pregnancy. If not performed prior to pregnancy, it is still considered safe to receive during pregnancy. Data are lacking to guide treatment recommendations for diabetic macular edema (DME) during pregnancy[8]. It may often regress after pregnancy without specific therapy. However, an expert retina specialist should be involved for taking individualized decisions.

There is also insufficient evidence regarding safety of intravitreal anti-vascular endothelial growth factor injections (anti-VEGF) for DME or PDR during pregnancy. In case these are required, a negative pregnancy test should be ensured, contraception should be provided and conception should be delayed for 3 months after the last intravitreal injection. It should be avoided especially during first trimester due to potential risk of defective embryogenesis, and should be used cautiously if absolutely necessary in second and third trimester after discussion of the potential risks and benefits with the patient.

Diabetic Nephropathy

The risks of adverse pregnancy outcomes are higher for women with chronic kidney disease (CKD), and women should be screened for it prior to conception. In a recent systematic review and meta-analysis, pregnancy with CKD had nine fold greater odds of preeclampsia, four fold greater odds of premature delivery, eight fold greater odds for small for gestational age/low birth weight, two fold greater odds for cesarean section and failure of pregnancy[29]. Urine albumin to creatinine ratio, serum creatinine, and estimated GFR) should be measured prior to conception to assess the renal function[11].In the preconception period, estrogen-containing preparations usually are contraindicated in women with diabetic nephropathy because of an increased risk for thrombosis, cardiovascular disease, and the progression of albuminuria. Progesterone-only preparations, including oral contraceptives and implantable and intrauterine devices are preferred[30]. In general, pregnancy outcome is favorable in women with modest elevations in serum creatinine (below 1.4 mg/dl), proteinuria less than 1 g/24 h, and a normal blood pressure[31,32]. In contrast, serum creatinine above 2 mg/dl, severe hypertension, proteinuria in the nephrotic range (≥ 3 g/24 h), and/or pre-existing cardiovascular disease are associated with a high risk of poor maternal and fetal outcomes[31].

Women who are taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker should discontinue the medication before conception[11]. However, in case of severe renal dysfunction, the patients should be informed about the possible loss of the renal protective properties if the medication is discontinued and the risk of teratogenesis if it is continued. In case ACE inhibitors or angiotensin-receptor blockers have been continued up to the time of conception, the medication should be withdrawn immediately upon confirmation of pregnancy[8,11,30].

Intensive glucose control and blood pressure control should be done. The risk of hypoglycemia is higher, therefore inulin analogues, CGMS and insulin pumps may be considered for such cases. Monitoring needs to be intensive and follow up should be frequent. Serum creatinine and albumin-creatinine ratios should be checked at least every 4 weeks till 32 weeks and

at least 2 weekly starting from 32 weeks gestation[30]. Thromboprophylaxis may have to be considered if there is high risk of thrombosis[30].

Autonomic Neuropathy

The most relevant manifestations of diabetic neuropathy during pregnancy are cardiovascular autonomic neuropathy (CAN), gastroparesis diabeticorum and hypoglycemia unawareness[33]. Airaksinen et al. studied 100 consecutive pregnancies complicated by T1DM and compared pregnancy outcomes between 23 and 77 gestations with and without autonomic neuropathy respectively. Patients with neuropathy had a significantly increased risk of adverse outcomes, from 23 to 52% ($p<0.01$)[34]. Impaired hypoglycemia awareness is a risk factor for severe hypoglycemia during pregnancy[16]. The Clarke Hypoglycemia Awareness Questionnaire can help in identifying women with hypoglycemia unawareness[18]. These can benefit from advanced technology such as sensor-augmented insulin pump, use of continuous glucose monitoring system, approved insulin analogues and frequent blood glucose monitoring. Pregnancy has not been a risk factor for the progression of diabetic neuropathy. Neuropathic changes of pregnancy when they are found are physiological, transient and resolve in a short time post-partum[35,36].

Cardiovascular disease

The frequency of myocardial infarction is 1 in 350 women with T1DM. Preconception optimization of risk factors such as blood glucose and blood pressure control, weight control for overweight/obese and cessation of smoking are important. Screening studies for CAD should be undertaken, women who are older and have longer duration of disease along with multiple cardiovascular risk factors[11]. Inpatients with CAD, good glycemic control is important. Hypoglycemia should be avoided since tachycardia secondary to catecholamine release increases myocardial demand. There is not enough evidence to make solid recommendations on the mode of delivery. Some suggestions are for instrumental delivery to avoid the Valsalva maneuver, (in case the patient is going for vaginal delivery) do continuous cardiac monitoring, and to treat labor pains aggressively with early epidural analgesia to decrease pain related stress and the subsequent cardiovascular response[33].

Psychological evaluation and social support

Depression, anxiety and stress are as such common in patients with T1DM[36].With the additional pressure of getting pregnant and challenges during pregnancy, these can increase. Health professionals should promote a positive transition to motherhood by proactively supporting women with T1DM in informed decision-making, by facilitating communication within the health care team and coordinating care for women with T1DM transitioning to motherhood[38]. Therefore, psychological assessment and referral to psychiatrist/psychologist if required should also be a part of preconception to postpartum care.

Postpartum care

The insulin requirement declines by 30-40% immediately after delivery, owing to lack of placental hormonal influence. Insulin requirements gradually increase over the next weeks, and usually return to pre-pregnancy levels in 2 to 4 months. The insulin-dose requirement is around 10% lower compared top reconception requirement in those who are breastfeeding[2]. Women should be advised to have a meal or snack before or during breastfeeding to decrease the risk of hypoglycemia[6].