OBSTETRIC MANAGEMENT

Antenatal management of pregnancy complicated by diabetes

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Abstract

The prevalance of Gestational Diabetes Mellitus (GDM) is increasing worldwide. It is estimated that 21 million women develop gestational diabetes out of which 1 in 7 births are affected. Women who have been previously diagnosed as GDM are at higher risk of developing diabetes in subsequent pregnancies and Type 2 Diabetes Mellitus (T2DM) later in life. Babies born to mothers with gestational diabetes also have a higher risk of developing type 2 diabetes in their teens or early adulthood. Instead of risk stratification universal screening is essential in all pregnant women. Tight glycaemic targets are required for optimal maternal and foetal outcome. This article outlines the importance of pre-pregnancy counseling, antenatal management, screening and treatment of Hyperglycaemia in Pregnancy (HIP).

Keywords: Pre-Pregnancy Counseling, Antenatal Care, Gestational Diabetes Mellitus, Blood Glucose Screening, Type 2 Diabetes, Lifestyle & Diet in Pregnancy.

Background

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[1] Hyperglycaemia in pregnancy may be classified as gestational diabetes mellitus, i.e. first detected during pregnancy or pre-diabetes diagnosed prior to pregnancy. It was first recognized clinically in 1824 in Germany.[2] About hundred years back (1916), Joslin reported a case of GDM which resolved with delivery, and reappeared later in life.[3] Later, an association of GDM with adverse perinatal outcome was recognized in early 1960's by Hoet,[4] First standardized criteria for GDM diagnosis was developed in Boston City Hospital by O'Sullivan. Later, this 100g OGTT test procedure continued in clinical use for four decades with some modifications.[5]

Prevalence of GDM

The incidence of GDM is increasing.[6-8] Globally 415 million people are affected by diabetes.[9] As the prevalence of this metabolic disorder is increasing in the younger generation, so more women are affected during pregnancy.[10] According to an estimate 21 million women or 16.2% of live births have some form of hyperglycaemia in pregnancy. Another 54 million women are affected by impaired glucose tolerance (IGT) with a potential to develop GDM if they become pregnant. Thus over 76 million women in the reproductive age are at risk of their pregnancy being complicated with pre gestational (existing) diabetes or gestational diabetes.[10] Sedentary lifestyle, stress of urbanization, bad eating habits, increasing age of marriage and high parity, contribute towards increasing prevalence of diabetes in pregnancy.[11] The highest raw and age adjusted prevalence from South East Asia (SEA) and Middle East North Africa (MENA) region is about 46% affecting 10.4 million live births.[9,10] Globally 88% of women who had high blood glucose during pregnancy were from low and middle income countries.[12] Despite the second highest prevalence of diabetes in MENA region, a total of only USD 17.1- 27.7 billion was spent on diabetes healthcare in 2015. This is equivalent to approximately 15% of the total health budget. Health expenditure on diabetes in this region accounts for just 2.5% of global spending on the disease.[10] This does not seem enough to adequately treat all people with the disease.

Importance of Screening During Gestational Diabetes

Universal screening (testing all pregnant women) is

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more relevant to Asian population including Pakistani women who are considered to be at high risk.[12] HIP usually is asymptomatic, women who are not screened for blood glucose estimation; will not be diagnosed and therefore will not be treated. This unrecognized and therefore untreated HIP can have foetal, neonatal and maternal complications in addition to the development of T2DM in the mother in later life and in the child in early adolescent life. So the diagnosis and management of hyperglycaemia in pregnancy may be done according to available resources as compared to no or poor care,[13] despite socioeconomic, cultural and health system constrains.

Screening for GDM

IADPSG Criteria

The global controversy continues about the best screening and diagnostic methods for GDM.[14] WHO (2013) and International Association of Diabetes and Pregnancy Study Group (IADPSG 2010) has approved single-step 75G OGTT criteria.[15] In IADPSG criteria venous blood sample is taken after 08 hours of overnight fasting. Thereafter 75G of anhydrous glucose dissolved in 250cc water is given to drink in 05 minutes. Venous blood samples are drawn at 1 and 2 hours after glucose load.[15]

The recommended blood glucose targets according to IADPSG for diagnosis of hyperglycaemia in pregnancy[14] are as under:

Fasting: 92 mg/dl

01 hr. post-prandial: 180 mg/dl

02 hours. post-prandial: 153 mg/dl

In IADPSG criteria an increased number of women up to 18 - 25% may be diagnosed as having GDM.[16] This is due to lower diagnostic levels of glucose thresholds and only a single abnormal value is recommended as conclusive for diagnosis.

DIPSI Criteria

Most women come to antenatal clinics in non-fasting state; they can be screened by Diabetes in pregnancy study group India, (DIPSI) method.[17] A non- fasting oral glucose tolerance test (OGTT) using 75 G glucose solution is given to drink irrespective of the last meal. A venous blood sample is tested 2 hours after the oral glucose load. In DIPSI method the cut off for screening and diagnostic level of blood glucose is 140 mg/dl.[15,17]

Frequency of Glucose Monitoring

The guidelines regarding frequency of blood glucose testing are equivocal. American Diabetes Association (ADA) encourages pre and postprandial monitoring of blood glucose but does not recommend a specific frequency of testing.[18] However, one fasting and three postprandial (two hours post meal) self-monitoring of blood glucose (SMBG) are recommended for women with hyperglycaemia in pregnancy (HIP) to prevent macrosomia.[19,20] In low resource settings one postprandial SMBG with documented relation to timing of meal can help in management of HIP.

Target Level of Blood Glucose in Pregnancy

It must be emphasized that diagnostic levels of blood glucose is not the same as the control levels of blood glucose (after the diagnosis of diabetes is confirmed). The aim of therapy is to achieve normoglyacemia without undergoing hypoglycaemic episodes during pregnancy.

Pathophysiology of GDM

In non-obese women insulin sensitivity decreases by 40% during normal pregnancy.[21] As a result insulin production is increased due to pancreatic beta cell hyperplasia. Increased insulin resistance during pregnancy is because of contra-insulin placental hormones like human placental lactogen, human chorionic somatotrophin and visceral adiposity. Normally blood glucose levels in pregnancy are lower due to continuous foetal consumption, increased glycogen storage and decreased hepatic glucose output.

Women who develop hyperglycaemia during pregnancy because of high insulin resistance and obesity, the compensatory mechanisms fail to meet the increasing demands with advancing gestation and result in manifestation of diabetes.

Risk associated with Hyperglycaemia in Pregnancy

Women who are not screened and thus remain undiagnosed for diabetes during pregnancy have greater risk of pregnancy complications like pregnancy induced hypertension (PIH), repeated vaginal candidal infections, polyhydramnios and increased risk of caesarean births but also run the risk of developing type 2 diabetes in later life.[11] The increased risk of foetal congenital anomalies, miscarriages, preterm births, macrosomia and iatrogenic prematurity are well known intra uterine complications. In newborns the risk of hypoglycaemia, hypocalcaemia, hyperbilirubinaemia can be reduced if mother is screened for diabetes during pregnancy and glycaemic control is appropriately instituted.

Pre-Pregnancy Care (PPC)

Despite the proven benefits of PPC the compliance is poor. PPC is the main principle of management for women with pre-existing hyperglycaemia or previous history of GDM. The aim is to optimize glycaemic control 03-06 months prior to planning next pregnancy. Attention to diet, exercise and counseling regarding weight reduction and normalizing BMI prior to conception may have beneficial effects on diabetes control and improve insulin resistance.

Medications like ACE inhibitors, ARBs and statins should be discontinued since these medications have known teratogenic effects. Instead Methyldopa is a safer antihypertensive in pregnancy. In women with long standing diabetes retinal, renal, neuropathic and cardio vascular complications need combined medical care.

Antenatal Management

Obstetric Management

Antenatal obstetric management should include frequent antenatal visits over and above which is required for a non-diabetic pregnancy. Frequent foetal ultrasound monitoring including second trimester anomaly scan to exclude cardiac, skeletal and neural tube defects. Third trimester growth scan are essential to rule out macrosomia or dysmaturity. Attention to blood pressure monitoring due to increased incidence of pre-eclampsia, urinalysis to exclude asymptomatic bacteuria, treatment of vaginal candidal infections. In view of iatrogenic prematurity and possibility of antenatal steroids (with increase in insulin dosage), an up titration of insulin with increasing gestation are few of the important antenatal management strategies. Strict glycaemic control throughout antenatal period with diet, lifestyle and or insulin is required. Decision regarding mode of delivery should be individualized according to estimated foetal weight (macrosomia), glycaemic control, medical and obstetrical history.

Life style modification

Lifestyle modification, diet, exercise and weight management are important pre-pregnancy and antenatal interventions. An individualized lifestyle intervention reduces the incidence of GDM by 39% in high risk pregnant women.[22]

Medical Nutritional Therapy

The overall goal of dietary intervention in pregnancy with diabetes is meant to reduce the risk of perinatal complications e.g. macrosomia associated with hyperglycaemia. To prevent excessive maternal weight gain, approx. 2000 - 2050 calories is required (irrespective of their BMI) to maintain euglycaemia, control maternal weight gain, and neonatal birth weight around 3.5 Kg.[23,24] Food having low glycaemic index (<70) helps in reducing glucose excursions.[25] High soluble fibre diets (up to 28 g/day) are recommended in pregnancy as it has low glycaemic index.[26] The dietary management can be achieved by using culturally appropriate model or color coding of food plate in low resource settings. Dietary regulations/ modifications and 30 minutes of physical activity may reduce glucose levels up to 23 mg/dl.[27]

Macronutrients and Micronutrients

An evidence-based recommendation for optimum nutritional intervention in pregnancy is scarce. A minimum of 175 grams of carbohydrates intake per day[28] or 40% of the carbohydrate are said to reduce hyperglycaemia.[29] It should be distributed throughout the day in three meals and three snacks.[30] Fish is a rich source of lean protein and contains three omega fatty acids. It also contains traces of mercury which readily crosses the placental barrier and is reported to damage foetal nervous system. However, shrimps, canned tuna, salmon have low levels of mercury and women can have approximately 250 - 300 grams a week (two average meals).[30]

For a positive impact on the metabolic goals of GDM,[31] in addition to macronutrients, some micronutrients such as vitamin D (400 - 1000 units/day), folate (400 micrograms up to 12 weeks of gestation to prevent foetal neural tube defects), B6, B12, calcium (800 units/day), iron (100-200 mg of oral elemental iron per day), zinc and omega 3 fatty acid are important for foetal development and to prevent maternal postpartum depression.[30] Extreme caloric restriction less than 1500 calories per day may increase the risk of ketonemia in pregnancy with Type 1 Diabetes Mellitus (T1DM).[13] An evening snack may prevent ketosis overnight.

Physical Therapy

Physical activity leads to increase glucose uptake into skeletal muscles,[32] improves insulin action and may change distribution of body fat and reduction in visceral fat.[33] Arm exercises while seated in a chair for 10 minutes after each meal is recommended in women with GDM.[32] Physical activity of moderate intensity of about 20 minutes per day, low caloric diet and weight loss may reduce the risk of progression to T2DM in women with history of GDM.[33-35] Each 5 kg increment of weight gain after GDM pregnancy is associated with a 27% higher risk

of future development of T2DM.[33]

Medical Therapy for HIP

When diet and physical activity are not sufficient to control hyperglycaemia in pregnancy, insulin is considered as gold standard of therapy. Requirement of insulin usually changes in each trimester. Short acting analogues Lispro and Aspart and long acting Detemir are considered safe to be used in pregnancy.[13]

In case of poor glycaemic control and non-compliance to medical therapy, HbA1c levels may be tested as per trimester-specific recommendations.[36]

Use of oral hypoglycaemic drugs (OHDs) like Metformin and Glyburide (Glibenclamide) are increasingly considered as a sole or adjuvant to insulin therapy. As a result, use of glyburide increased from about 7% to 65% in ten years period (from 2000 to 2011) since 2007.[26,37-39] According to a systematic review and meta-analysis published in BMJ 2015,[40] glyburide seems inferior to both Insulin and Metformin. While a combination of Insulin and Metformin performs slightly better than metformin alone.

Conclusion

Considering the high prevalence of hyperglycaemia in pregnancy, universal screening of all pregnant women should be recommended.[7] The importance of early diagnosis of hyperglycaemia in pregnancy is crucial to avoid fosetal and maternal complications and future development of Type 2 diabetes in both mother and child.

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