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GESTATIONAL DIABETES MELLITUS: A DETAIL REVIEW

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ABSTRACT

Gestational diabetes mellitus (GDM) is commonly defined as glucose intolerance first recognized during pregnancy. Diagnostic criteria for GDM have changed over the decades. Perinatal and postpartum complications associated with GDM include preterm delivery, shoulder dystocia, stillbirths, clinical neonatal hypoglycemia, hyperbilirubinemia, cesarean deliveries, obesity and cardiovascular disease in the mothers. Management strategies increasingly emphasize optimal management of fetal growth and weight. Monitoring of glucose and fetal weight through ultrasound combined with maternal weight management, medical nutritional therapy, physical activity, and pharmacotherapy can decrease co morbidities associated with GDM. Consensus is lacking on ideal glucose targets, degree of caloric restriction and content, algorithms for pharmacotherapy, and in particular, the use of oral medications and insulin analogs in lieu of human insulin. Postpartum glucose screening and initiation of healthy lifestyle behaviors, including exercise, adequate fruit and vegetable intake, breastfeeding, and contraception, are encouraged to decrease rates of future glucose intolerance in mothers and offspring.

KEYWORDS

Glucose intolerance, Pregnancy and Perinatal complications.

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INTRODUCTON

Gestational diabetes mellitus (GDM) is defined by the World Health Organization (WHO) as carbohydrate intolerance with onset or first recognition during pregnancy. Gestational diabetes mellitus is not clearly type 1 or 2 diabetes. The International Diabetes Federation indicates that 1 in 6 infants are born to mothers with some form of hyperglycemia during pregnancy[1,2].

Globally the prevalence of GDM ranges from 1-14% depending upon the screening method, diagnostic criteria and population screened. High

prevalence of GDM around 18% has been reported in India of which south India has its major contribution. The WHO estimate of the prevalence of gestational diabetes mellitus in India is around 40.9 million in 2006 and is expected to rise to 69.9 million by 2025. The estimated prevalence in the US was 7% while it was reported to be 25.0% in the South-East Asia Region and 10.4% in the North America and Caribbean Region[3-6].

According to Diabetes in pregnancy study group in India (DIPSI) criteria, Out of 225 Women 22 women (9.7%) were diagnosed as having GDM and among risk factors, higher BMI was shown to be significant association ($p<0.05$)[5]. Higher prevalence was observed in the higher age group, higher gravidity, higher BMI, and those with hypertension and family history of diabetes. The history of abortion, neonatal death and stillbirth were found higher among GDM mothers than non-GDM mothers[7]. Patient with GDM are at higher risk for excessive weight gain, preeclampsia, and cesarean sections. Infants born to mothers with GDM are at higher risk for macrosomia, birth trauma, shoulder dystocia, jaundice and still birth. After delivery, these infants have a higher risk of developing hypoglycemia, hypocalcemia, hyperbilirubinemia, respiratory distress syndrome, polycythemia and subsequent obesity and type 2 diabetes[8-9]. Those women with undiagnosed or poorly managed GDM as well as their infants are at increased risk of developing T2DM and other cardio metabolic diseases including obesity, hypertension and coronary artery diseases[7].

Pregnant women without known diabetes mellitus should be screened for GDM after 24 weeks of gestation. Treatment of GDM results in a statistically significant decrease in the incidence of preeclampsia, shoulder dystocia, and macrosomia. Initial management includes glucose monitoring and lifestyle modifications. If glucose levels remain above target values, pharmacologic therapy with metformin, glyburide, or insulin should begin. Antenatal testing is customary for women requiring medications. Induction of labor should not occur before 39 weeks in women with GDM, unless glycemic control is poor or another indication for delivery is present. Unless otherwise indicated, scheduled cesarean delivery should be considered only in women with an estimated fetal weight greater than 4,500 g. These patients should be screened 6 to 12 weeks postpartum for persistently abnormal glucose metabolism, and should undergo screening for diabetes every three years thereafter[10].

Appropriate knowledge and positive attitude with reference to disease, is highly related to prevent the complications of disease by proper management of disease, which permits people to live better with their diseased condition. Health care professionals' strategies and abilities can influence positive behavioral changes in diabetic patients so as to adhere to diet, exercise, and blood glucose monitoring, which results is adequate metabolic control[9]. Low socio-economic condition, social discrimination, lack of adequate nutritional knowledge, myths and misbelieves related to diabetes with pregnancy and lack of knowledge related to proper pregnancy planning and care were the possible barriers to effective pregnancy outcomes for women with diabetes[7]. A successful pharmacist can counsel a gestational diabetes patient[6].

For those reasons it is important to pay rigorous attention to GDM and the purpose of this review is therefore to cover a wide range of clinical issues related to GDM, including the challenges of epidemiology, diagnostic criteria and screening, the pathophysiology of GDM, the treatment and prevention of GDM and the long and short term consequences of GDM for both mother and child.

Historic Evolution

The history of GDM dated back to 1964 when O'Sullivan proposed specific criteria to interpret the glucose tolerance level in pregnancy to identify women at a higher risk for developing diabetes after delivery. The criteria were later modified by the National Diabetes Data Group (NDDG) in 1979. In 2008, the result of "Hyperglycemia and Adverse Pregnancy Outcomes (HAPO)" study was published. This major observational study provided us valuable information regarding the risks of adverse outcomes associated with various degrees of maternal glucose intolerance[11].

Epidemiology

The prevalence of GDM in India varied from 3.8 to 21% in different parts of the country, depending on the geographical locations and diagnostic methods

used. GDM has been found to be more prevalent in urban areas than in rural areas. For a given population and ethnicity, the prevalence of GDM corresponds to the prevalence of Impaired Glucose Tolerance [IGT, in non-pregnant adult] within that given population[12]. The prevalence of GDM in Iran has been estimated at 3.4% ranged from 1.3% to 18.6% while in Northern Europe it ranges from 0.6% in The Netherlands to 3.6% in Denmark. It is higher in Italy 6.3%. In the USA, 7% of all pregnancies are complicated by GDM. GDM prevalence was 2.4 times higher using the most recent International Association of Diabetes in Pregnancy Study Group (IADPSG) criteria compared to the World Health Organization (WHO) 1999 criteria. Using the new criteria, GDM prevalence ranged between 9 and 26% in the 15 centers that participated in the hyperglycemia and adverse pregnancy outcome (HAPO) study, a large international observational study[3,13].

Pathophysiology

Pregnancy is a condition characterised by progressive insulin resistance that begins near mild pregnancy and progressive through the third trimester. In late pregnancy, insulin sensitivity is fallen by ~ 50%. Two main contributors to insulin resistance include increased maternal adiposity and insulin desensitising effects of hormones produced by the placenta. The fact that insulin resistance rapidly decreases post-delivery suggests that the major contributors are placental hormones.

The placenta produces human chorionic somato-mammotrophs (HCS, formerly called human placental lactogen), bound and frees cortisol, estrogen, and progesterone. HCS stimulates pancreatic secretion of insulin in the fetus and inhibits peripheral uptake of glucose in the mother. As the pregnancy progresses and the size of the placenta increases, so does the production of the hormones, leading to a more insulin–resistant state. In nondiabetic pregnant women, the first and second phase insulin responses compensate for this reduction in insulin sensitivity, and this is associated with beta-cell hypertrophy and hyperplasia. However, women have a deficit in this additional insulin secretory capacity develop GDM. Beta-cell dysfunction in women diagnosed with GDM may fall into one of three major categories: (1) Autoimmune, (2) monogenic, or occurring on a background of insulin resistance (as is most common)[8].

Risk Factors

1. The age increased risk with increasing age (>35 years)
2. Ethnicity
   - Highest risk-Native Americans, Hispanic, Asian decent
   - Moderate risk-African women
   - Lowest risk-Non-Hispanic white women 3
3. Obesity (BMI > 30 kg/m2)
4. Family history (1st degree relative or sister with GDM)
5. Past obstetric history
   - Women who have previously delivered a stillbirth baby, anomalous baby, macrosomic baby (birth weight >4500g or >90th percentile) or multiple miscarriages
   - Women with a history of previous GDM
6. Previously elevated blood glucose level
7. Shoulder dystocia
8. Polycystic ovarian syndrome
9. Other medical conditions
   - Recurrent urinary tract infection or fungal infection during pregnancy
   - polyhydramnios with an unknown cause
   - polyuria, polydipsia or glycosuria for possible GDM that remained unnoticed
   - IUMF
   - Hypertensive disorders – gestational hypertension, chronic hypertension, pre-eclampsia, and eclampsia.
   - Hypoglycemia in the newborn
   - Hyperbilirubinemia
   - Preterm delivery
   - Cesarean delivery
10. Medications: corticosteroids, antipsychotics[8,14-17].

DIAGNOSIS AND SCREENING

Currently, there are a number of different diagnostic criteria for GDM, which makes comparison of the epidemiology and outcomes across different countries difficult (Table No.1). Because there is no

clear threshold glucose level above which the risk of adverse pregnancy outcome increases, it is hard to reach consensus on the diagnostic glucose cut-off levels for GDM. GDM can be diagnosed by using the same criteria used to diagnose type 1 and type 2 diabetes mellitus. Most diagnostic tests use the 2-hour 75gram oral glucose tolerance test (OGTT), but in United States, the National Diabetes Diagnostic Group (NDDG) had favored the use of the 3-hour 100 g OGTT. Following the HAPO Study, the IADPSG had advocated using 75 g OGTT, with GDM diagnosed by at least of the criteria: fasting glucose level ≤ 5.1, 1-hour glucose level ≤ 10.0 mmol/l or 2-hour glucose level ≤ 8.5 mmol/l. The strategies of screening for GDM during pregnancy vary between different countries, and this may be related to the prevalence of diabetes in the region and the resources available. In some countries such as Australia, universal screening is recommended. In that country, women who are considered at high risk for GDM may be recommended to undergo OGTT after the first an-tenatal visit in first trimester. This is to exclude women who may already have pre-existing diabetes at the time of pregnancy. If found to be negative for GDM, the OGTT can be repeated between 24 and 28 weeks of gestation. Performing OGTT on all pregnant women is labor intensive and takes up substantial amount of time and resources for midwives, obstetrician as well as pathology services. Furthermore, some women may not tolerate the glucose loading well, especially for those with persisting morning sickness during pregnancy. In one study, the failure rate of OGTT can be as high as 10%. It was proposed that women who are low-risk may not need screening, and women of average risk may be tested at 24-28 week of gestation. The 1-hour 50g glucose challenge test (GCT) has also been advocated for the screening of GDM. This test is more convenient for the women as it can be done at any time of the day and does not involve overnight fasting. Women with glucose level above 7.8 mmol/l following the 50 g GCT will proceed to the 75 g OGTT. In a retrospective analysis of women who underwent 50 g GCT during pregnancy, at a glucose cut-off value of 11 mmol/l, the positive predictive value for GDM was 85.3%, based on the subsequent OGTT. However, for women with GCT above 7.8 mmol/l, only 45% of the women actually had GDM on the OGTT. In a systematic review, the sensitivity of the GCT was only 0.74 while the specificity was 0.77, at the glucose cut-off level of 7.8 mmol/l. As a result, the GCT cannot replace the 75 g OGTT and is gradually being phased out in many centers[13].

Complications

GDM has a wide range of complications which include maternal complications, obstetric complications, perinatal complications and incidence of developing lifestyle–related diseases in off springs of mothers with GDM[8].

PREVENTION AND MANAGEMENT OF GDM

A team approach is ideal for prevention and management of GDM. The team would usually comprise an obstetrician, diabetes physician, a diabetes educator, dietitian, midwife and pediatrician[12].

PLANNING AND PREPARATION BEFORE PREGNANCY

There are some countries with high burden of diabetes, and the age at onset of T2DM among women is decreasing. Furthermore, women of reproductive age usually do not receive regular physical examination or know their blood glucose levels. Thus, sometimes, hyperglycemia is already present at conception. Studies have shown that hyperglycemia during organogenesis can markedly increase the risk of spontaneous abortions and congenital anomalies, while satisfactory glycemic control could reduce these risks. Thus, all women, especially women with diabetes, impaired glucose tolerance, impaired fasting glucose, and a history of GDM need to plan for pregnancy and seek pre-pregnancy counseling early. They should also have their blood glucose levels evaluated as early as possible to determine their glucose metabolism conditions; before pregnancy is the ideal time, but if this is difficult, evaluation should be done at least in the first prenatal visit. Women with diabetes who are planning pregnancy and those using insulin should control their hemoglobin A1c (HbA1c) levels at <6.5% and <7.0%, respectively, to prevent hyperglycemia. All women are encouraged to adopt

good dietary and lifestyle habits before pregnancy, especially those who are underweight or overweight/obese. As a woman's body mass index (BMI) prior to pregnancy is of high importance, both low and high BMIs are closely related to poor pregnancy outcomes. However, these are modifiable risk factors. Adherence to a low-risk lifestyle (healthy body weight, healthy diet, regular exercise, and non-smoking) before pregnancy is associated with a low risk of GDM[2].

Non-Pharmacologic

The first-line management option for GDM is diet and regular physical activity. The main goals of nutritional therapy include preventing ketosis, achieving normoglycaemia, improving fetal well-being and achieving adequate weight gain (ACOG, 2013). Nutritional therapy modifications are based on individual preferences, ethical considerations, weight changes and blood glucose monitoring. Many programmes involve carbohydrates and calorie counting and exchange systems (National Institute of Child Health and Human Development, 2006; Serlin and Lash, 2009). The latest recommendations include reducing carbohydrate intake so that the composition of calories consumed is 33–40%from carbohydrates, 20% from protein and 40%from fat (ACOG, 2013). Complex carbohydrates are preferred because their consumption leads to less postprandial hyperglycaemia than simple carbohydrates (ACOG, 2013). During calorie restriction, however, pregnant women with GDM should be carefully monitored for ketone formation because calorie restriction in such women may cause mental and psychomotor deviation in the unborn child. Women with GDM should also take regular moderate physical activity, such as walking, because physical activity enhances the work of insulin in maintaining blood glucose levels (ACOG, 2013). Thirty minutes of physical activity is considered the best type of exercise for pregnant women (Whitelaw and Gayle, 2010). Women are also encouraged to breastfeed because this promotes weight loss, thus decreasing the risk of glucose intolerance and reducing the chance of developing diabetes later in life (Gunderson, 2007)[19].

MEDICAL NUTRITION THERAPY (MNT)

All women with GDM should receive nutritional counselling. MNT is the cornerstone of therapy for women with GDM. The purpose of such treatment is to supply food for the mother and the embryos, control glucose levels and prevent from Keto-acidosis resulted from food deprivation (fasting). The food plan should be designed preferably by a dietician so as to fulfil minimum nutrient requirements for pregnancy and to achieve glycemic goals without inducing weight loss or excessive weight gain. MNT is a self-management therapy. Education, support, and follow-up are required to assist the women in making lifestyle changes Excellence for pregnant women with GDM suggest that that pre-pregnancy BMI is greater than 27 kg/m2should restrict their energy intakes to 105kJ/kg per day or less and combine this with moderate exercise of at least 30 min duration per day. Essential to successful nutrition therapy.

To satisfy the various needs, the following dietary principles have been suggested as suitable for someone with GDM: (i) eating regular small meals of slowly absorbed carbohydrate to maintain blood glucose concentrations; (ii) taking similar portions of carbohydrate at meals daily (especially if the GDM is not treated by insulin); (iii) allowing the consumption of a moderate amount of sugar-containing foods as long as it neither promotes hyperglycemia nor excessive weight gain; (iv) eating at least five portions of fruits and vegetables per day; (v) eating low-fat dairy foods and attempting to drink a pint of milk or its equivalent every day and meat/fish/poultry or alternatives; (vi) attempting to eat two portions of oily fish per week. In addition the recently revised guidelines of the UK National Institute for Health and Clinica[18,20].

Exercise

For vast majority of pregnant women with gestational diabetes, exercise will be beneficial and recommended. Exercise decreases peripheral insulin resistance and is an appropriate adjunctive therapy to diet for the GDM patient. Patients are encouraged to participate in exercise 30 min several times weekly. In women with relative contraindications, appropriate assessment and counselling it may be possible to allow exercise in pregnancy. With appropriate caution, women with chronic

respiratory conditions, obesity and previous sedentary lifestyle can be introduced to an appropriate exercise programme during pregnancy that may motivate them to continue exercise after pregnancy.

Pregnant women frequently require modifications of their exercise regimen because of musculoskeletal or mechanical symptoms such as pubic symphysis dysfunction or back pain. The prescription of an upper body exercise program, for example, cycle ergometry or water based exercise programs can overcome these limitations. By including specific exercise advice in the management plan for gestational diabetes, it may help validate the women's request for the support in both the workplace and home to allow her to meet these recommendations. As gestational diabetes is a relatively common complication, it may be practical to offer supervised group exercise such as walking groups, antenatal exercise classes or aqua aerobics[8]. Higher levels of physical activity before pregnancy or in early pregnancy are associated with a significantly lower risk of developing GDM[21].

COMBINED DIETARY INTERVENTION AND PHYSICAL ACTIVITY DURING PREGNANCY FOR MANAGING GDM

Some interventions may involve a combination of dietary and physical activity modalities. Regular physical activity may help normalise maternal blood glucose for pregnant women with gestational diabetes and in combination with dietary interventions may reduce the need for oral anti-diabetic agents or insulin. As women with gestational diabetes are at increased risk of developing type 2 diabetes in the future, regular physical activity may also help reduce the risk of this long-term complications[22].

Other Interventions during Pregnancy for Managing GDM

There may be other interventions, including psychological approaches that could be used independently or alongside physical activity or dietary modalities such as mindfulness eating, yoga or spiritual support[22].

Patient Education

The importance of educating women with GDM (and their partners) about the condition and its management cannot be over emphasized.

The compliance with the treatment plan depends on the patient's understanding of:

- The implications of GDM for her baby and herself
- The dietary and exercise recommendations
- Self-monitoring of blood glucose - Self-monitoring between four and seven times per day (including fasting and post-prandial measurements) can contribute to improved maternal and perinatal outcomes, and is likely to be most effective when combined with effective treatment.
- Self-administration of insulin and adjustment of insulin doses
- Identification and treatment of hypoglycemia (patient and family members)
- Incorporate safe physical activity (walking at usual pace/arm exercise)
- Development of techniques to reduce stress and cope with the denial.

Care should be taken to minimize the anxiety of the women[12,22].

Pharmacologic Treatment

Drug therapy is introduced when diet and exercise have little effect in controlling GDM. Traditionally, insulin has been the first-line drug therapy in treating GDM because it does not cross the placental barrier however, insulin therapy can be potentially challenging to use in pregnant women because of possible additional weight gain, risk of hypoglycaemia, and need for multiple injection sites. Some of these disadvantages related to insulin have prompted research into the use of oral hypoglycaemic agents as a pragmatic alternative treatment for GDM[19].

Insulin Therapy

When dietary and lifestyle intervention fail to maintain glucose levels within the specified targets as discussed above (upper targets for fasting BGL 5.3-5.8 mmol/l; upper targets for 2-hour post-prandial BGL 6.7-7.2 mmol/l), insulin is the pharmacologic therapy of choice. Insulin does not cross the placental barrier, and has consistently been

shown to reduce fetal morbidities when added to MNT. The women are usually started on a small dose, and SMBG is essential to guide the titration of the insulin doses.

The proportion of women with GDM requiring insulin therapy varied between different studies, ranging between 20% and 50%. Factors that predict requirement of insulin therapy included elevated BMI, high fasting glucose level on OGTT, and history of previous GDM. Offspring of women on insulin therapy had higher birth weight and birth-weight percentile than those of women on MNT, but there was no difference in neonatal morbidity including APGAR scores or need for neonatal intensive care support. The need for insulin therapy also varied between different ethnic groups.

The choice of the type of insulin will depend on the woman's glycaemic profile. For women with elevated fasting BGL, night-time basal insulin (intermediate-acting insulin such as Isophane insulin) is usually initiated. For women whose post-prandial BGLs are elevated, regular insulin (short-acting) is appropriate. The combination of night-time basal insulin and meal time short-acting insulin is referred to basal-bolus regimen. In addition to basal-bolus regimen, twice daily pre-mixed insulin (combination of short and intermediate-acting insulin) is sometimes used. A study comparing basal-bolus regimen with pre-mixed insulin demonstrated that basal-bolus insulin regimen resulted in a lower rate of overall neonatal morbidity than the twice daily pre-mixed insulin regimen, and the relative risk for hyper-bilirubinaemia and hypoglycaemia was lower.

Human insulin is safe to be used during pregnancy, but in the last 10 years, there has been more widespread use of rapid-acting insulin analogues such as Insulin Lispro and Insulin Aspart. Studies had shown that these rapid-acting insulin analogues are safe to be used in pregnancy with no evidence of increase adverse pregnancy outcomes. On the other hand, the safety profiles of the more long-acting insulin analogues such as Insulin Glargine and Insulin Detemir have not been fully validated for use in pregnancy. Emerging evidence suggests that the use of these long-acting analogues does not result in adverse maternal or fetal outcomes. For women with pre-existing type 1 diabetes, it may be appropriate to continue these basal insulin analogues during pregnancy, since changing insulin therapy during pregnancy can result in a period of glycometabolic instability. These long-acting insulin analogues may also be considered if the woman develops an allergic reaction to Isophane insulin[4].

ORAL HYPOGLYCAEMIC AGENTS FOR GDM

Many researchers have been exploring the use of oral hypoglycaemic agents, such as glibenclamide (glyburide) and metformin, as a safe and effective alternative to insulin for the treatment of GDM[19].

Metformin

Metformin belongs to the biguanide class, and is classified by the Food and Drug Administration (FDA) in the US as a category B drug in pregnancy. In the UK, NICE (2008) recommend that metformin is used as an adjunct or alternative to insulin in the preconception period and during pregnancy, when the likely benefits from improved glycaemic control outweigh the potential for harm. Metformin works to lower glucose levels by decreasing peripheral insulin resistance, intestinal absorption and hepatic production of glucose, and decreasing peripheral uptake and utilisation of glucose. In addition, the drug does not stimulate insulin secretion, cause hypoglycaemia, or stimulate the fetal pancreas to over secrete insulin. Metformin, unlike insulin, does cross the placental barrier, which previously caused concern for its use in pregnant women. Research has since demonstrated, however, that transfer of metformin across the placenta does not have negative effects on the fetus. The starting dose for metformin is 500 mg for the first day and titrated up to 2500 mg as tolerated, depending on the mother's glucose level (Menato *et al,* 2008; Medicines and Healthcare Products Regulatory Agency, 2007)[19].

Glyburide

This sulfonylurea has been identified in the past several years as an alternative to insulin therapy for the treatment of GDM. Its primary action is to enhance insulin secretion. Glyburide does not significantly cross the placenta. Several studies have found that glyburide serves as a suitable alternative to insulin for treatment of GDM with similar perinatal outcomes. A survey performed by

the American colleges of Obstetricians and gynaecologists found that 13% of Obstetricians and maternal–fetal medicine specialists were using glyburide as a first–line agent in the treatment of women with GDM who failed to achieve glucose control with diet.

Glyburide is a category C medication in pregnancy. Hypoglycemia may occur with all sulfonylureas, and glyburide is no exception. The incidence of hypoglycemia with glyburide ranges from 1 to 5%. The most common adverse effects are gastrointestinal and (nausea, vomiting, dyspepsia) and dermatologic (pruritis, urticaria, erythema, and maculopapular eruptions). Elevations of liver function testes have been reported, but jaundice is rare. The overall incidence of adverse effects ranges from 3.2 to 4.1 %.

Identifying those women who might fail glyburide therapy in pregnancy is important when deciding medical therapy for the treatment of gestational diabetes. Conway in an observational trial to examine factors predicting failure of glyburide treatment in gestational diabetes found that among women with high FPG levels greater than or equal to 110 mg/dl, 24% failed to respond to glyburide. Studies focusing on the transfer of glyburide into the milk of lactating mother have been performed. Breastfeeding is safe in women receiving glyburide. However, the drug has not been endorsed by any decision-making body for routine use in GDM[8].

Acarbose

Acarbose reduce intestinal carbohydrate absorption by inhibiting the cleavage of disaccharides and oligosaccharides to monosaccharides in the small intestine and reduce post-prandial hyperglycemia. Due to less than 2% absorption in the maternal circulation, these agents may have potential benefits in pregnancy. There are only scanty data of its use in human pregnancy because of the lack of human pregnancy safety data[23].

Management Post-Partum

There are particular benefits in encouraging breastfeeding in women who have had GDM. Evidence suggests there are weight advantages to mother and infant, both of whom are at increased risk of overweight. All women diagnosed with GDM should have a 75 g OGTT at 6–12 weeks post-partum. As women with GDM have a 50% risk of developing type 2 DM within 20 years, they need to be tested regularly for DM. While an OGTT is currently considered the gold standard, HbA1c is easier to perform and is likely to be used for post-GDM testing in the future[16].

Monitoring Glycemic Control

The success of the treatment for a woman with GDM depends on the glycemic control maintained with meal plan or pharmacological intervention. Studies suggest 1, 1 ½ and 2 hour post meal for monitoring glycemic control. They should be advised to perform self-monitoring of blood glucose (SMBG) on a daily basis, failing which, at least weekly monitoring should be encouraged. If self-monitoring is not possible, laboratory venous plasma glucose has to be estimated for adjusting the dose of insulin[12].

Pharmacist's Role

A diagnosis of GDM implies that the patient and baby will have an increased chance of complication before, during and after delivery and that future pregnancies are also more likely to be complicated by diabetes or GDM. It is important for women with GDM to be proactively treated and followed after delivery to prevent or minimize unfavourable outcomes. Pharmacists can help educate the patient regarding the various pharmacotherapy options available to her. A diagnosis of GDM is understandably an additional complication when so much is already happening to the patient's body. The women will need guidance in blood glucose testing. It is important that we as pharmacists encourage the women with GDM to be compliant with recommendations for her diet, exercise, blood glucose monitoring and medications she needs to be taking. Well controlled glycemia is important for preventing serious medical problems for the mother and the fetus[8].

Importance to Do This Review

GDM affects a significant proportion of pregnant women and the prevalence is increasing worldwide. GDM is associated with an increased risk of a range of adverse pregnancy outcomes and these adverse health outcomes repeat across generations, which has important implications for the future. Providing dietary and lifestyle advice is usually recommended as the primary therapeutic strategy for women with GDM.

Table No.1: Different diagnostic criteria for gestational diabetes[4]

S.No		IADPSG	ADA - NDDG	ADIPS	WHO
1	Glucose load for glucose tolerance test	75g	100g	75g	75g
2	Fasting glucose (mmol/l)	≥5.1	≥5.3	≥5.5	≥7.0
3	1-hour glucose level (mmol/l)	≥10	≥10.0	-	-
4	2-hour glucose level (mmol/l)	≥8.5	≥8.6	≥8.0	≥11.1
5	3-hour glucose level (mmol/l)	-	≥7.8	-	-
6	To diagnose GDM, abnormal result in:	1 or more	2 or more	1 or more	1 or more

ADA = American Diabetes Association; ADIPS = Australian Diabetes in Pregnancy Society; IADPSG = International Association of Diabetes and Pregnancy Study Group; NDDG = National Diabetes Diagnostic Group; WHO = World Health Organization.

Table No.2: Maternal and fetal complications in pregnancies with carbohydrate intolerance[18]

S.No	Maternal complications	Fetal complications
1	**Diabetes complications** Diabetic ketoacidosis Deterioration of diabetic retinopathy Deterioration of diabetic nephropathy Hypoglycemia (when using insulin) **Obstetric complications** Spontaneous abortion Premature birth Pregnancy-induced hypertension Hydramnios Shoulder dystocia	**Perinatal complications** Fetal distress/fetal death Congenital malformations Macrosomia hypoglycemia Neonatal hyperbilirubinemia Neonatal hypocalcemia Neonatal polycythemia Newborn respiratory distress syndrome Hypertrophic cardiomyopathy Offspring's complications Obesity/diabetes

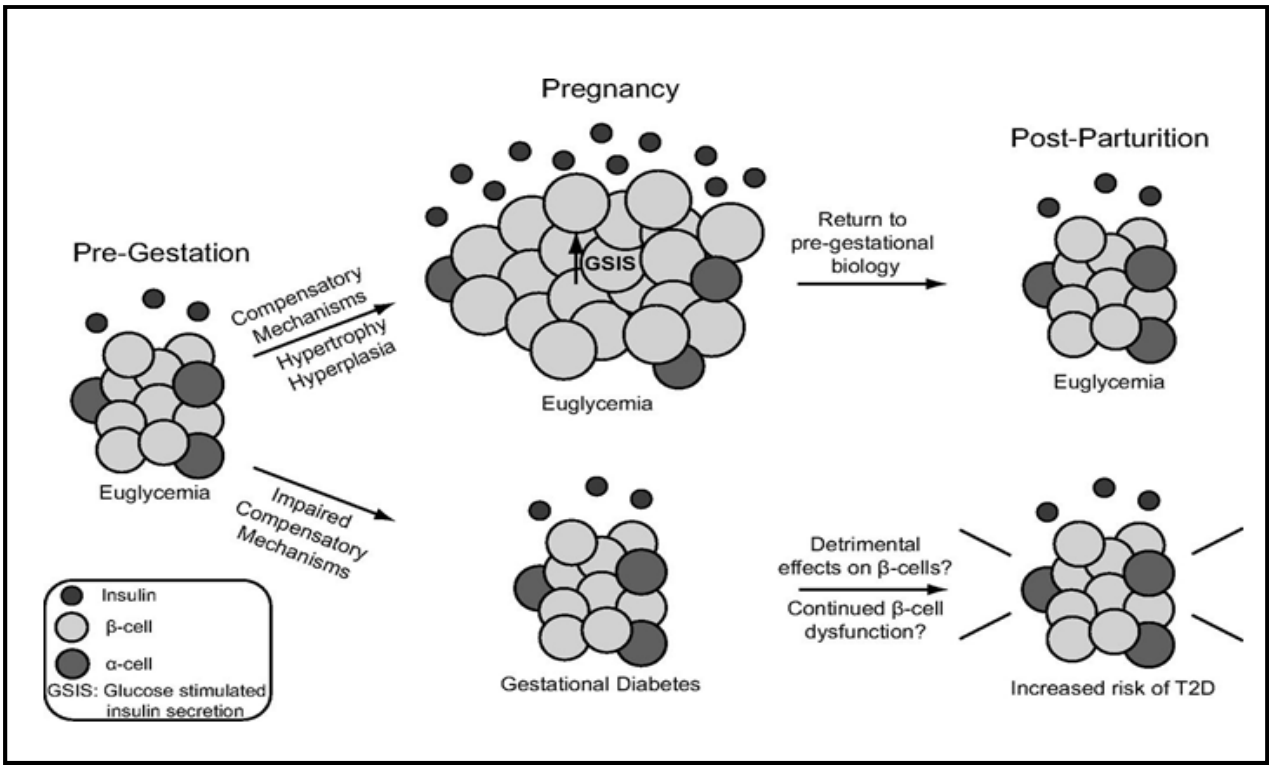

Figure No.1: Pathophysiology of gestational diabetes mellitus

Note: Source - Google

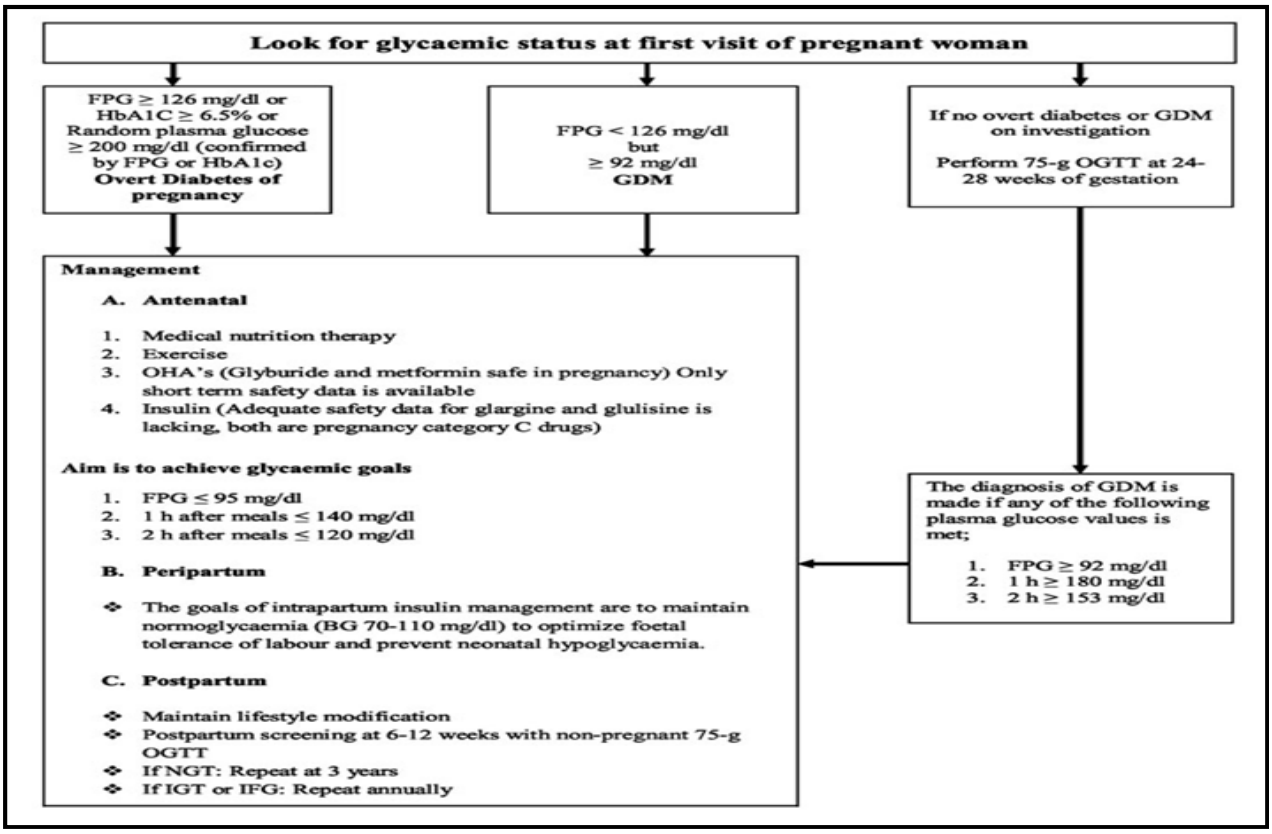

Figure No.2: Flow diagram to approach to a woman during pregnancy for glycaemicsatus

Note: source – Google

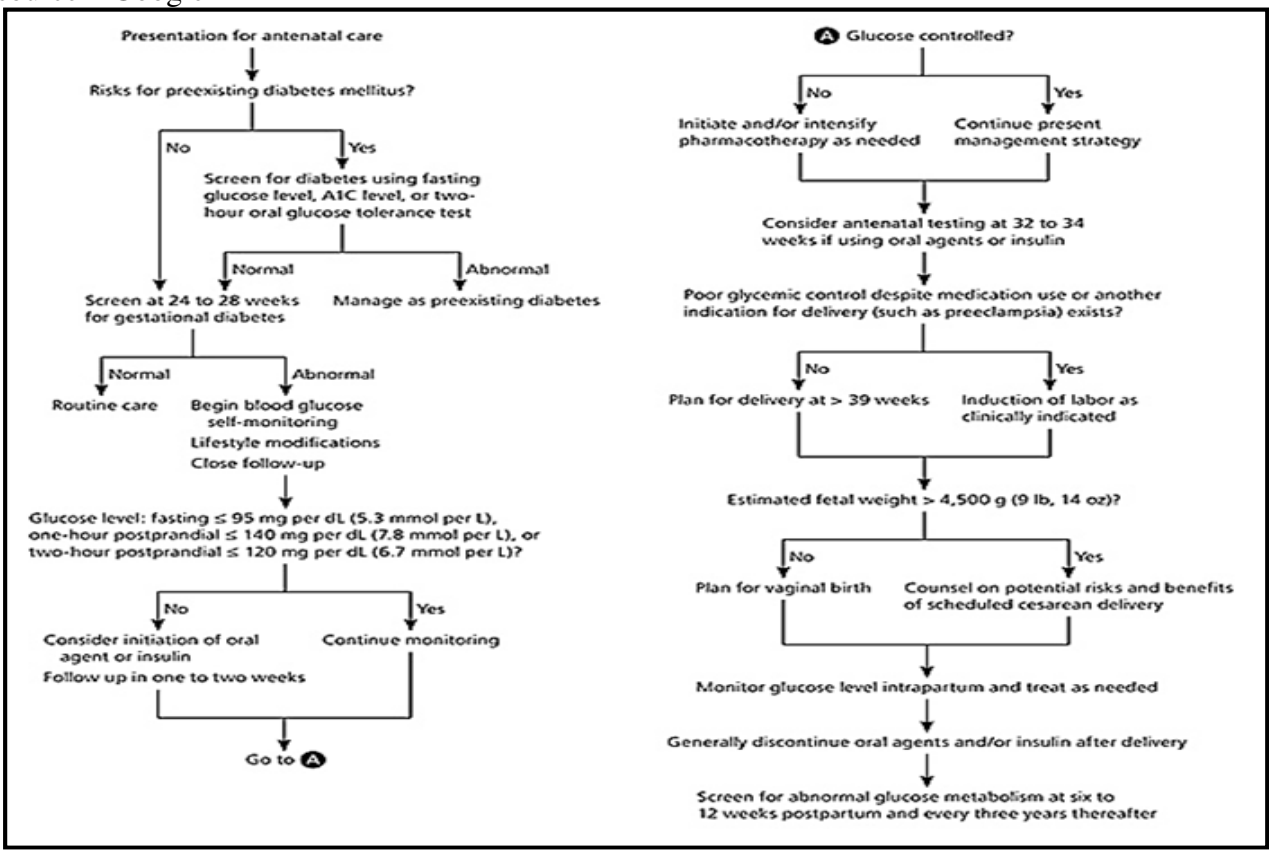

Figure No.3: Treatment Algorithm For GDM[10]

CONCLUSION

In conclusion, GDM is associated with a higher risk of adverse health outcomes for both mothers and offspring, not only during the perinatal phase but also in the long term. Thus, the prevention and management of GDM must be given enough importance throughout pregnancy, that is, prior to pregnancy, during pregnancy, and postpartum. Nutrition counseling and physical activity should be the primary and major strategies. If lifestyle modification alone fails to maintain normoglycemia, oral hypoglycemic drugs and insulin should be considered. Optimal management of women with GDM is important in ensuring good pregnancy outcomes Postpartum care should not be overlooked, as it plays a critical role in the prevention of future chronic non-communicable diseases.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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