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Chapter

A Clinical Insight into Gestational Diabetes

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Abstract

Pregnancy is a diabetogenic state manifested by insulin resistance and hyperglycaemia. The age group at risk of getting gestational diabetes is between 20 and 39 years in 96.8% of cases. Gestational diabetes is the development of symptoms and signs of diabetes mellitus during pregnancy and the glucose level reverting to normal during puerperium. Depending on the type of population and the diagnostic criteria used, gestational diabetes is said to complicate 1–16% of all pregnancies. Many researchers in American, European and Asian surveys have reported 3–6% of prevalence. Compared with white European women, the prevalence rate for GD is increased approximately elevenfold in women from the Indian subcontinent, eightfold in South East Asia, sixfold and threefold in Arab and black Afro-Caribbean women, respectively. Such figures draw a potent clinical interest towards gestational diabetes (GD), and this chapter attempts to highlight some major aspects of GD in respect to both the mother and the foetus or the newborn specially emphasizing on its management as per the World Health Organization (WHO) and International Federation of Gynaecology and Obstetrics (FIGO).

Keywords: antenatal care, hyperinsulinaemia, impaired glucose tolerance, International Federation of gynaecology and obstetrics, medical nutrition therapy

1. Introduction

Gestational diabetes (GD) is characterised with impaired glucose tolerance (IGT) whose first recognition or onset is during pregnancy. International statistics claim that out of 10 pregnancies, at least 1 is associated with diabetes, most of which are GD. Lack 0f diagnosis or treatment of GD can lead to significant maternal and foetal complications. Moreover, women with GD and their offsprings are comparatively at higher risk of developing type 2 diabetes later [1–10].

The incidence of GD is expected to increase at an expedited rate in the near future, amounting to one in every five pregnant women suffering from GD. According to a field study conducted in one of the Indian states under the 'Diabetes in Pregnancy'—Awareness and Prevention project, in most of the pregnant women screened in urban, semiurban and rural areas, respectively, the prevalence of GD was reported to be 17.8% in the urban, 13.8% in the semiurban and 9.9% in the rural areas [11–16].

GD may result in development of many pregnancy-associated disorders like polyhydramnios, pre-eclampsia, prolonged labour, obstructed labour, caesarean section, uterine atony, postpartum haemorrhage, infection and progression of retinopathy which are the leading global causes of maternal morbidity and mortality.

Moreover, GD could also pose foetal risks including spontaneous abortion, intrauterine death, stillbirth, congenital malformation, birth injuries, neonatal hypoglycaemia and infant respiratory distress syndrome.

Long-term clinical effects of GD are important contributors to the burden of non-communicable diseases in many countries [17, 18].

2. Aetiology and pathophysiology of GD

During normal pregnancy, resistance to insulin action increases. In most pregnancies, the pancreas is able to meet the increased insulin demands, and normal blood glucose level is maintained. On the contrary, women who develop GD have impaired beta-cell response resulting in insufficient insulin secretion to meet the increased insulin demands. The following factors tend to enhance the chances of developing GD:

- Age: Due to age-related decreased pancreatic beta-cell reserve.
- Obesity: Leads to increased insulin resistance, which is further compounded by pregnancy.
- Smoking: Increases insulin resistance and decreases insulin secretion.
- Polycystic ovarian syndrome: Associated with insulin resistance and obesity.
- Nonwhite ancestry.
- Family history of type 2 diabetes.
- Intake of diet with low-fibre and high-glycaemic index.
- Weight gain.
- Lack of physical activity: Exercise increases insulin sensitivity.
- Prior GD: GD recurs in as many as 80% of subsequent pregnancies.

Products of the placenta, including tumour necrosis factor-alpha (TNF-α) and human chorionic somatomammotropin, are considered to play pathological roles in inducing maternal insulin resistance. Insulin resistance is observed at peak levels in the third trimester of pregnancy. Women who develop GD have pathologically impaired beta-cell function that leaves them with inability of adapting to pregnancy. In GD, as in type 2 diabetes, the deficit in beta-cell function is usually multifactorial and polygenetic. However, unmasked by the increased insulin needs of pregnancy, autoimmune diabetes and maturity-onset diabetes of youth (MODY) may occasionally be first recognised as GD. Hyperglycaemia in late pregnancy is associated with macrosomia and neonatal hypoglycaemia, hyperbilirubinemia and hypocalcaemia, as well as adverse maternal outcomes, including gestational hypertension, pre-eclampsia and caesarean delivery [19–35].

3. Strategical diagnosis of GD

Profound international evidences and standard protocols suggest definite guidelines for screening pregnant women for GD.

The American and Canadian guidelines recommend universal screening by two-step approach. This includes a screening with 50-g 1-hour blood glucose test (>140 mg/dL taken as screen positive). Women who screen positive are subjected to 100-g oral glucose tolerance test (OGTT), and those with 2 or more abnormal values of blood glucose are diagnosed with gestational diabetes.

Similarly, the National Institute for Health and Care Excellence (NICE), UK, and Australian guidelines recommend a slightly different risk-based screening. It recommends a 75-g 2-hour OGTT. Women with fasting blood glucose ≥126 mg/dL and postprandial (PP) blood glucose ≥140 mg/dL are diagnosed with GD [36, 37].

The WHO and International Federation of Gynaecology and Obstetrics (FIGO) endorse universal screening for GD at 24–28 weeks of gestation using the 75-g 2-hour blood sugar (fasting ≥126 mg/dL and PP ≥140 mg/dL).

Almost all guidelines agree to the management of GD using medical nutrition therapy (MNT) which is a standard diet plan for GD-diagnosed mothers and insulin therapy if required. Recently, global evidences have also concluded that the traditional biguanide—metformin—is safe and effective for GD management after 20 weeks of gestation if blood glucose level is not controlled alone by MNT [38–42].

GD pregnant women should be managed by medical nutrition therapy (MNT) and metformin or insulin therapy as required. In the postpartum period, OGTT must be repeated at 6 weeks post delivery; if blood glucose is <140 mg/dL, then women should be referred for postprandial blood glucose (PPBS) testing annually [43, 44].

3.1 Testing and management of GD

Ideally, all pregnant women should be screened for gestational diabetes, especially those who have one or more risk factors discussed above.

Trained human resources are required to manage the cases after diagnosis. Testing for GD is recommended twice during ante natal care (ANC).

The first testing should be done during the first antenatal contact as early as possible in pregnancy. If the first test result is negative, the test must be repeated between the second and third trimester of pregnancy. It is important to conduct a second test as most pregnant women develop blood glucose intolerance during this period (24–28 weeks). Mostly, one third of all GD-positive women are diagnosed during the first trimester. Hence, the test is repeated after the second trimester.

There should be at least a gap of 4 weeks between the two tests. The test should be conducted for all pregnant women even if she comes late in pregnancy for ANC. However, if the woman is over 28 weeks of pregnancy, only one test should be conducted if it is her first visit for ANC [45–51].

3.2 Methodology for diagnosis

The following stepwise protocol complies with the WHO guidelines for screening of pregnant women:

- The test is conducted with intake of 75 g of oral glucose dissolved in approximately 300 mL of water, irrespective of whether the pregnant woman comes in fasting or non-fasting state, followed by measuring the blood glucose level by a plasma-standardised glucometer after 2 hours of ingestion (postprandial blood glucose).

- If within 30 minutes of oral glucose intake the mother vomits, the test has to be repeated the next day. If vomiting occurs after 30 minutes, the test continues.

- The threshold blood glucose level of ≥140 mg/dL is considered as limit for diagnosis of GD [52–61].

4. Internationally acceptable guidelines for management of GD

4.1 Guiding principles

All pregnant women who screen positive for GD in the first test are subjected to medical nutrition therapy (MNT) and physical exercise for 2 weeks. The woman is advised to walk or exercise for at least 30 minutes a day.

After 2 weeks on MNT and physical exercise, a 2-hour PPBS (post meal) should be done. All standardised protocols for management of GD suggest initial management with MNT and physical exercise strictly. If diabetes is not controlled with MNT (lifestyle changes) alone, metformin or insulin therapy is recommended.

If 2-hour PPBS is <120 mg/dL, the test is to be repeated as per high-risk pregnancy protocol, i.e. to undertake eight tests (four regular tests and four additional). It is recommended to conduct at least one test every month during the second and third trimester. More follow-up tests can be done as recommended by the gynaecologist. If 2-hour PPBS is ≥120 mg/dL, medical management (metformin or insulin therapy) has to be started as per guidelines (**Figure 1**) [62–66].

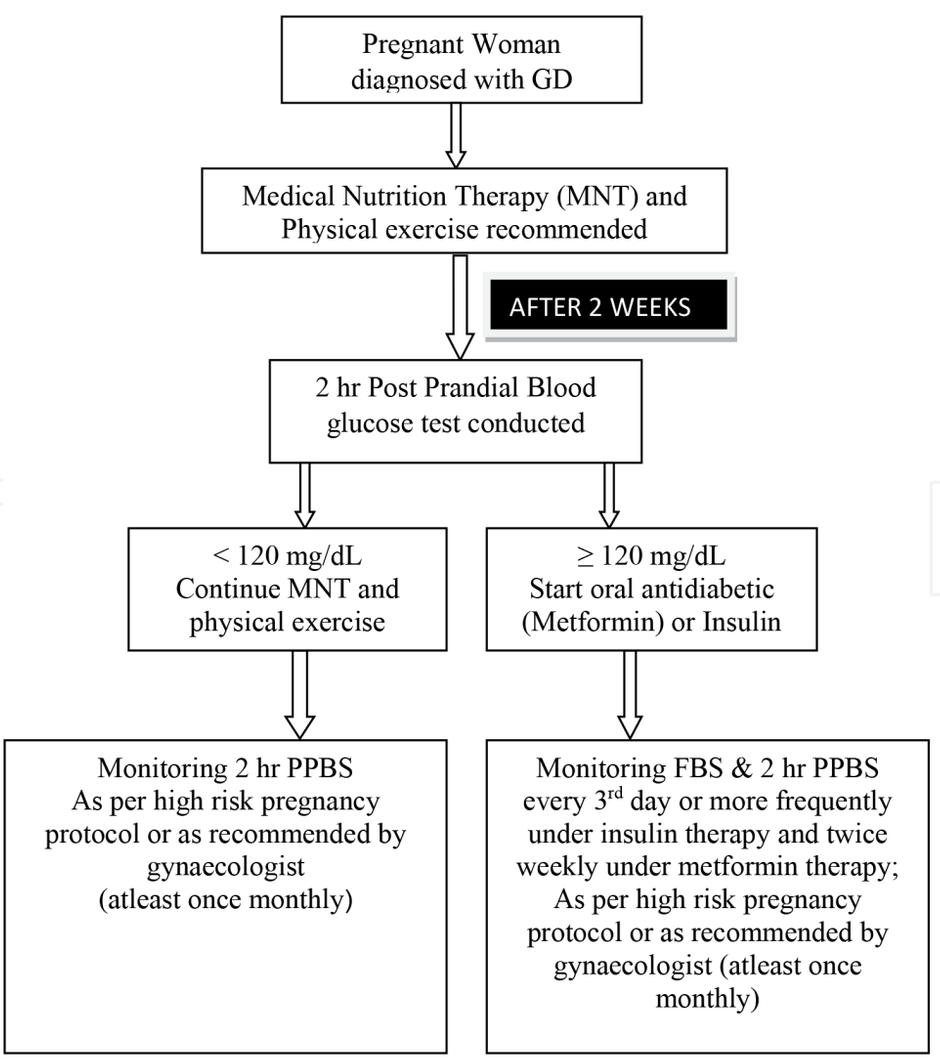

Figure 1.
Standard health management protocol for pregnant women with GD.

4.2 Medical nutrition therapy (MNT)

4.2.1 Healthy eating during pregnancy

All pregnant women with GD should get medical nutrition therapy (MNT) as soon as diagnosis is made. MNT for GD primarily involves a carbohydrate-controlled balanced meal plan which promotes:

- Optimal nutrition for maternal and foetal health
- Adequate energy for appropriate gestational weight gain
- Achievement and maintenance of normoglycaemia [67, 68]

4.3 The significance of the individualised nutrition plan assessment in GD

Assessment of diet or nutrition plan in GD is an important criterion for diagnosis and subsequent follow-up on mother's and foetus' development. The nutrition plan must be individualised from patient to patient so that accurate appraisal of the woman's nutritional status could be assessed. This assessment includes defining her body mass index (BMI) or percentage of desirable weight during pre-pregnancy to the optimal weight gain during the entire tenure of pregnancy [24, 69].

4.4 Monitoring calorie intake in GD

The energy demand of the body during pregnancy increases many times than that in a nonpregnant state. Individualization of nutritional requirement proves to be very helpful in determining the energy requirement and making amendments in the diet plan based on weight change patterns.

Normally calorie monitoring is not a point of concern in the first trimester unless a woman is underweight. It becomes more significant during the second and third trimester to monitor the energy requirements. Calorie intake should suffice the appropriate weight gain during gestation.

Ideally, for an average woman, weight gain of 10–12 kg is considered normal during pregnancy; an additional 350 kcal/day intake to the adult requirement is recommended during the second and third trimester.

Severe caloric restriction is strictly prohibited as it may cause ketonaemia and ketonuria in the mother as well as impair physical and mental growth in the offspring (**Tables 1** and **2**) [70–72].

Energy requirement can be calculated as follows:

$$\text{Energy requirement (kcal/day)} = \text{BMR} \times \text{PAL} \quad (1)$$

*BMR = basal metabolic rate; *PAL = physical activity level.

where the basal metabolic rate (BMR) for an adult female in the age group of 18–30 years is calculated as 14 × BW (kg) + 471 and similarly BMR for adult females of age group 30–60 years as 8.3 × BW (kg) + 788 (**BW = body weight)*.

4.4.1 Daily intake of carbohydrates

Carbohydrates are essential for both the mother and the baby. They are the ultimate source of glucose in the blood. Hence, the nature, quantity and frequency of carbohydrate intake influence greatly the blood glucose level.

S. no.	Nature of lifestyle	Energy requirement during pregnancy	Total energy requirement (kcal/day)
1.	Sedentary	1900 + 350	2250
2.	Moderately active	2230 + 350	2580
3.	Highly active	2850 + 350	3200

Table 1.
Energy requirement in relation to nature of lifestyle.

S. no.	Body mass index	Calorie requirement
1.	<18.5 (underweight)	Calorie requirement as per activity + 500 kcal/day
2.	18.5–22.9 (normal)	Calorie requirement as per activity
3.	23–24.9 (overweight)	Calorie requirement as per activity
4.	>25 (obese)	Calorie requirement as per activity—500 kcal/day

Table 2.
Calorie requirement according to body mass index (BMI).

The carbohydrates must be evenly distributed through the daily food chart foods in order to avoid high blood glucose level. It is better to spread carbohydrate foods over three small meals and two to three snacks each day than taking three large meals [8, 73–78].

Complex carbohydrates (like whole-grain cereals like oats, vegetables and fruits) should be preferred over simple carbohydrates like food with lots of added sugar or honey. Also keeping a record of the number of carbohydrate serves that a mother eats during the day helps her to eat the right amount of carbohydrates [79].

4.4.2 Daily intake of fats

Overall fat intake by a pregnant woman should be planned in a manner that saturated fat such as butter, coconut oil, palm oil, red meat, organ meat and full cream milk amounts to less than 10% of total calories. The dietary cholesterol must be less than 300 mg/dL. In obese and overweight patients, a lower-fat diet overall can help slow the rate of weight gain [80].

4.4.3 Daily intake of proteins

Proteins are a very important dietary element for the growth and health of the foetus.

At least three servings of protein foods are recommended every day to meet the increased demand. Milk and milk products, egg, fish, chicken, pulses, nuts, etc. are all rich sources of protein that a mother can take during her pregnancy [80].

5. Pharmacotherapy of GD with metformin and insulin

The widely accepted treatment protocol for gestational diabetes advocates metformin or insulin therapy for clinical management of pregnant women diagnosed with GD that is not well controlled with MNT alone. Insulin is the first drug of choice for GD mothers.

The advantage of insulin therapy over metformin is that it can be started any time during pregnancy for GD management. If the gestation is less than 20 weeks,

and medical nutrition therapy (MNT) is not effective in controlling blood glucose levels, insulin should be started, but metformin can be considered only after 20 weeks of gestation for clinical management of GD.

Metformin therapy can be started at 20 weeks of pregnancy, if MNT has not been able to control blood glucose alone. In the cases where the woman's blood glucose is not controlled even with the maximum dose of metformin and MNT, the therapy must be switched to insulin therapy. The dose of metformin is 500 mg BID orally up to a maximum dose up to 2 g/day.

The incidence of hypoglycaemia and weight gain with metformin is less than insulin. If insulin is required in high doses, metformin may be added to the treatment. Any pregnant women on insulin therapy should be instructed to keep sugar/glucose powder handy at home to treat hypoglycaemia if it occurs [81–84].

5.1 Common side effects with metformin

- Diarrhoea
- Nausea
- Stomach pain
- Heartburn
- Lactic acidosis
- Low blood glucose

5.2 Types of insulins

Unlike the nonpregnant patients with diabetes who have a plethora of choices to achieve glucose control, the pregnant cases with GD offer a big challenge to the clinicians when it comes to the choice of drugs for its management. In the recent years, we have come across a variety in new insulins, novel delivery systems and additional concentrations of existing insulins. With an alarming increase in the gestational diabetic population, the demands of the newer insulins will be ever increasing; hence, understanding these insulins becomes crucial. Additional pharmacokinetic and pharmacodynamic studies of these insulins in pregnancy are also required [85].

5.2.1 Short-acting insulin and rapid-acting insulin analogues

5.2.1.1 Regular (U-100) insulin

It is identical to human insulin and is synthesised in *Escherichia coli* bacteria. It is used before meal to compensate for heavy carbohydrates. The onset of action is around 30 minutes but can range from 10 to 75 minutes. The peak action is achieved at 3 hours (range 20 minutes to 7 hours), and the overall duration of action is ~8 hours. U-100 vials can stay at room temperature for 31 days [86].

5.2.1.2 Regular (U-500) insulin

It is identical to human insulin but more concentrated than the U-100 formulation; its pharmacokinetic profile differs from U-100 as well. The onset is ~30 minutes, but the duration of action can last up to 24 hours. Severe hypoglycaemia may occur 24 hours

after the initial dose, although there are clinical reports suggesting that in pregnancy, severe hypoglycaemia is rare with U-500 insulin. Two to three injections daily are required, and a U-500 vial is good for 40 days at room temperature while in use [87–89].

5.2.1.3 Insulin aspartate

It is produced in a type of yeast, *Saccharomyces cerevisiae*, and is homologous to human insulin. It should be taken 5–10 minutes prior to meals. It can be administered as injections or in an insulin pump. The time of peak concentration ranges between 40 and 50 minutes, and the duration of action is 3–5 hours. It is also available in the forms of pens, penfills and vials that retain their pharmacological potency for at least 28 days at room temperature while in use. The risk of developing hypoglycaemia with insulin aspartate is less than regular insulin, although patients allergic to yeast must avoid it as this could potentially cause a site reaction [90].

5.2.1.4 Insulin lispro (U-100 and U-200)

It is an analogue produced in *Escherichia coli*. Its onset of action is 10–15 minutes, peak action is attained in 30–90 minutes and the duration of action is 3–4 hours. Intraperitoneal injections are preferred for the maximum absorption and shortest duration of action. It can be used in the form of insulin pumps or as multiple daily injections. The U-100 and U-200 formulations are bioequivalent, having the same pharmacokinetics. Insulin lispro U-200 is only available in pens to avoid administration errors. Pens, penfills and vials can be stored for 28 days at room temperature while in use [91].

5.2.2 Intermediate insulin and long-acting insulin analogues

5.2.2.1 Insulin isophane (NPH)

It is a U-100, intermediate-acting insulin. It is produced in *Escherichia coli* and is identical to human insulin available as a suspension. The onset of action is 1–2 hours, with an average peak action of 4 hours (range, 4–8 hours). Duration of action lasts for 10–20 hours. Vials remain usable for 31 days at room temperature, whereas pens can be used for 14 days [92].

5.2.2.2 Insulin detemir (U-100)

This is a long-acting analogue of insulin produced in *S. cerevisiae*. One of the setbacks with this formulation is that it can potentially cause a reaction in patients who are allergic to yeast. Detemir lacks a defined peak of action, but the pharmacological action lasts for up to 20 hours. The time to onset of action ranges between 1 and 2 hours. The pen and vial can be used up to 42 days at room temperature while in use. The chances of developing hypoglycaemia with detemir are less than NPH in pregnant women [93].

5.2.2.3 Insulin glargine (U-100)

It is a long-acting analogue produced in *Escherichia coli*. It differs from other contemporaries in terms of its distribution in plasma; the acidic solution is neutralised in subcutaneous tissue to form microprecipitates. These microprecipitates slowly release glargine over a duration of 24 hours, resulting in no well-defined peak. Its onset of action is 1–2 hours. Vials and pens are reusable for 28 days at room temperature.

5.2.2.4 Insulin degludec U-100 and U-200

They are long-acting analogues approved by the US Food and Drug Administration (FDA) in September 2015. The U-100 and the U-200 are considered bioequivalent. Insulin degludec is extracted by means of recombinant DNA technology implemented in *S. cerevisiae*, to avoid potential reaction to the yeast, if allergic. Insulin degludec's slow absorption into blood and prolonged action are attributed to the formation of soluble multi-hexamers. Its onset of action is ~1 hour and takes 8 days to reach steady state, and, once achieved, its duration of action lasts for 42 hours. It is usually administered once daily at any time of the day due to its long duration of action. Noncompliant patients may inject their dose at intervals of 8–40 hours without significant decreases in glycosylated haemoglobin (HbA1C) compared to taking it at the same time every day. U-100 degludec and U-200 degludec are only dispensed in pens to decrease administration errors. Pens are good for up to 56 days at room temperature while in use [93].

5.3 Novel drug delivery system for insulin

Insulin in the form of inhalational powder is a newer form of insulin introduced in recent years. Human insulin inhalation powder was approved by the FDA in 2014. Inhaled human insulin is produced in *Escherichia coli* and is adsorbed onto fumaryl diketopiperazine and polysorbate 80 carrier particles. Inhalation powder is equivalent unit for unit to insulin lispro. Its onset is 12–15 minutes, and it takes ~57 minutes to reach peak levels in plasma. The duration of action is ~2 hours. Inhaled human insulin is contraindicated in patients with chronic pulmonary obstructive disease as it may precipitate chronic bronchospasm. Sealed blister cards at room temperature must be discarded after 10 days. If kept in the refrigerator, they are good for use up to 1 month (**Figure 2**) [94, 95].

5.4 Glyburides-new hypoglycaemic drugs

A new advent in the field of glucose-lowering agents is glyburides. It is an oral hypoglycaemic class of drugs used for the management of type-II diabetes mellitus. Pharmacologically it belongs to sulphonylurea class of insulin secretagogues. These agents stimulate β cells of the pancreas to release insulin. The members of this class have different binding sites on their target pancreatic β-cell receptor. Their dose, rate of absorption, duration of action and route of elimination also differ from the conventional hypoglycaemic agents. Apart from lowering the blood glucose level directly, glyburide also increases peripheral glucose utilisation, decreases hepatic gluconeogenesis and may increase the number and sensitivity of insulin receptors. Glyburides proved to be advantageous over insulin because weight gain associated with it is less than in the case of insulin. However, one of its fallacies is that it may cause hypoglycaemia and require consistent food intake to decrease this risk. The risk of hypoglycaemia is increased in elderly, debilitated and malnourished individuals. Glyburide has been shown to decrease fasting plasma glucose, postprandial blood glucose and glycosylated haemoglobin (HbA1c) levels. It is metabolised in the liver. Its metabolites are excreted in urine and faeces in approximately equal proportions [96].

5.4.1 Indication

It is prescribed to be taken at meal time to lower the blood glucose level in patients with non-insulin-dependent diabetes mellitus where hyperglycaemia cannot be controlled by diet alone.

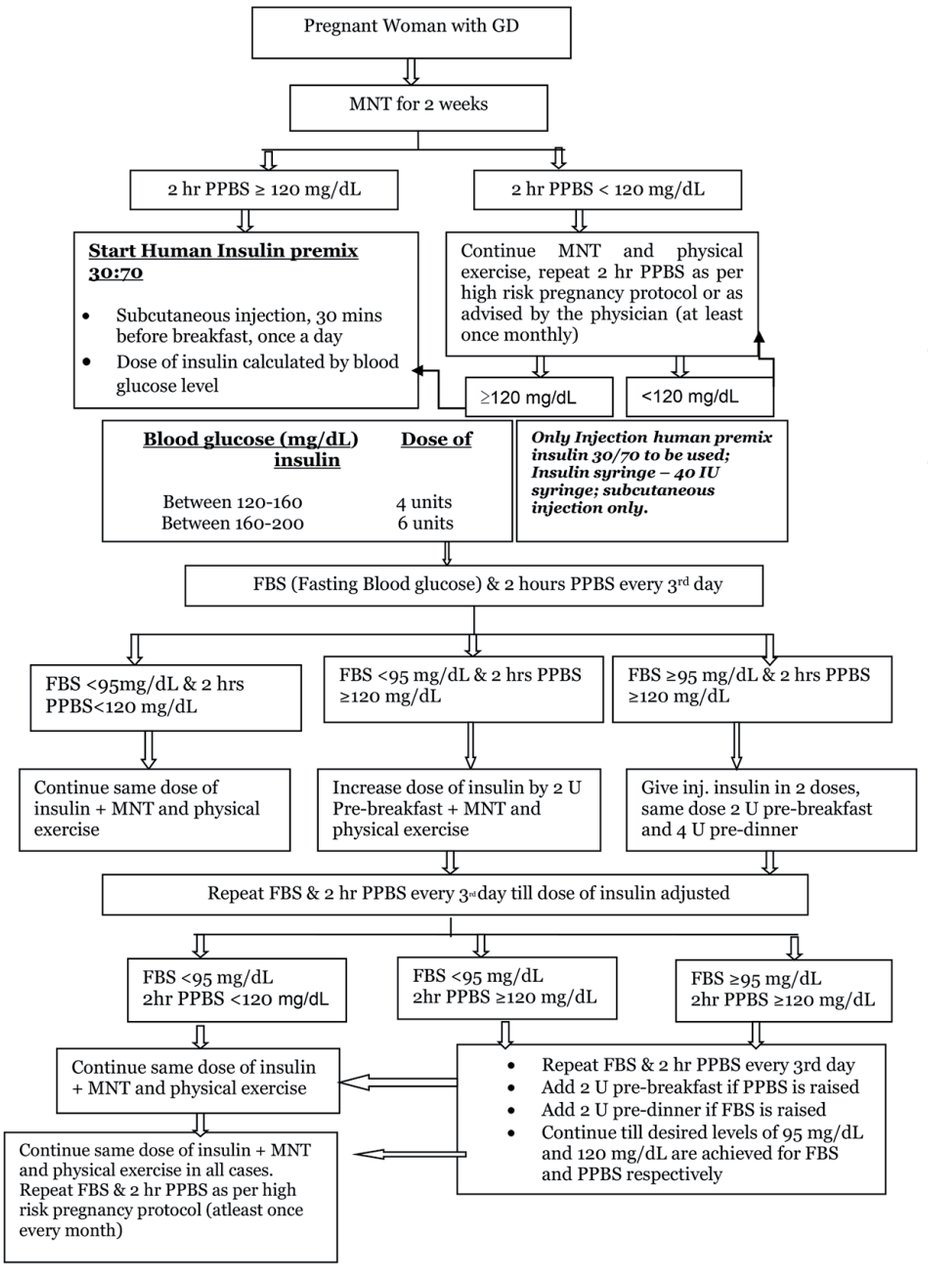

Figure 2.
Insulin therapy for GD.*

5.4.2 Half-life (t 1/2) and duration of action

The half-life of unchanged drug lies between 1 and 2 hours and its metabolites have an extended half-life of 10 hours. Duration of action is 12–24 hours.

5.4.3 Side effects

Nausea, heartburn, stomach fullness and weight gain may occur.

5.4.4 Precautions

- Contraindicated in hypersensitive patients.

- Given the high risk of hypoglycaemia associated with it. Patients must be counselled to avoid driving, the use of machinery or any activity that requires alertness or clear vision as low blood glucose levels may cause drowsiness, fatigue and blurred vision.

- Alcohol intake must be avoided under its medication as it aggravates hypoglycaemia and may cause disulfiram-like reaction.

- Older adults may be more sensitive to the side effects of this drug, especially low blood sugar.

- During pregnancy, this medication should be used only when clearly needed. Pregnancy may cause or worsen diabetes.

Hypoglycaemia	**Considerations**
Criteria	• *Mild hypoglycaemia:* Blood glucose level is <4.0 mmol/L and may or may not be associated with symptoms of a low blood glucose level • *Severe hypoglycaemia:* Blood glucose level is very low, generally <3.0 mmol/L, and is associated with confusion and potential loss of consciousness. The woman requires third-party assistance to manage the episode
Causes	• Extensive physical activity • Insulin overdose • Lack or inadequate carbohydrate in meal • Alcohol consumption (decreases blood glucose)
Symptoms	• Hunger • Light headedness/headache • Sweating/shaking/weakness • Tingling around the lips • Irritability • Blurred vision • Severe hypoglycaemia (when unable to self-treat) can lead to confusion and loss of consciousness and requires urgent medical treatment
Treatment	• Consume one 15-g serve of fast-acting carbohydrates (one of the following) • 5–7 glucose candies • Glass of soft drink rich in calories • Three-heaped teaspoons of sugar or honey dissolved in water • If after 15 minutes symptoms persist or BGL is less than 4.0 mmol/L, repeat one serve of fast-acting carbohydrates • Do not overtreat with fast-acting carbohydrates as this may lead to rebound hyperglycaemia • When BGL is 4.0 mmol/L or above, eat longer-lasting carbohydrate • Eat a snack (e.g. sandwich or glass of milk) or usual meal if within 30 minutes • Avoid overtreatment of hypoglycaemia resulting in hyperglycaemia • Document BGL and time of hypoglycaemic episode
Lifestyle management	• Plan to eat regular meals with adequate carbohydrate serves • Be prepared and carry a food snack at all times (including while exercising) • Aim to take long- or intermediate-acting insulin at the same time each day • Identify causal factors of the hypoglycaemic episode and avoid/mitigate for the future • Carry blood glucose metre at all times so BGL can be checked if symptoms present

Table 3.
Aspects surrounding hypoglycaemia in women under oral hypoglycaemic drugs or insulin.

- If glyburide is used, it may be switched to insulin at least 2 weeks before the expected delivery date because of glyburide's risk of causing low blood sugar in your newborn.

- It is unknown if this medication passes into breast milk. However, similar drugs pass into breast milk [97].

5.5 Monitoring blood glucose levels in GD mothers

The blood glucose monitoring in gestational diabetic cases remains a bone of contention amongst clinicians worldwide. There have been various cohort studies propounding different procedures for blood glucose level monitoring. Some suggest the evaluation of HbA_{1C} levels as accurate parameter; others suggest ultrasonography and laboratory testing of postprandial blood glucose levels every 2 weeks. For women whose fasting blood glucose levels remain <105 md/dL are well managed alone with medical nutrition therapy, whereas for those whose blood glucose levels are >105 mg/dL require additional medical assistance including insulin therapy. The foetal abdominal circumference (AC) is also considered a pivotal parameter for monitoring the GD mothers. If the foetal AC is <70th percentile at 30 weeks, perinatal outcomes will be free from any complications with continued management on diet therapy and without glucose self-monitoring. The excess risk of macrosomia is attributed to women with a foetal AC >70th percentile at 30 weeks. Such pregnancies will benefit only from aggressive glucose lowering by insulin therapy. The fasting or preprandial glucose targets of 60–80 mg/dL have to be met in such cases to eliminate the excess risk of stillbirth [98–101].

5.6 Hypoglycaemia

Hypoglycaemia is uncommon in women with GD who are only on MNT; the risk of developing hypoglycaemia is however increased in women on pharmacotherapy, i.e. insulin or metformin. Hypoglycaemia incurs potent hazards to the health of the foetus. Hence, management of hypoglycaemia is also a crucial aspect in GD. If hypoglycaemia is asymptomatic, BGL results must be confirmed prior to starting the treatment (**Table 3**) [102].

6. Special obstetric care for pregnant women with GD

6.1 Antenatal care (ANC)

Antenatal care is defined as the procedure of regular check-ups that allow clinicians to treat and prevent potential health problems throughout the course of the pregnancy and to promote healthy lifestyles that benefit both the mother and child. In the case of pregnant women with GD, they must be closely monitored. GD women who are diagnosed before 20 weeks of pregnancy undergo foetal anatomical survey by means of ultrasonography within 18–20 weeks of pregnancy.

At 28–30 weeks of gestation, a foetal growth scan should be performed and repeated at 34–36 weeks of gestation. There should be at least 3-week gap between the two ultrasounds, and it should include foetal biometry and amniotic fluid estimation.

In GD women having uncontrolled blood glucose level or any other complication of pregnancy, the antenatal visits should be programmed at least once monthly as per the protocol for high-risk pregnancy.

Monitoring of abnormal foetal growth and amniotic fluid volume for growth restriction and polyhydramnios, respectively, at each ANC visit is clinically important. Pregnant women with GD should be diligently monitored for gestational hypertension, proteinuria and other obstetric complications.

Antenatal steroids in pregnant women with GD between 24 and 34 weeks of gestation requiring early delivery should be administered as per standardised guidelines. Most guidelines like FIGO suggest dexamethasone injection. More vigilant monitoring of blood glucose levels should be done for the next 72 hours following injection. In the case of raised blood glucose levels during this period, adjustment of insulin dose should be made as required [103–105].

6.2 Monitoring foetal health in pregnant women with GD

The rate of foetal morbidity in pregnant women with GD is more than the normal ones. This risk is further accelerated in pregnant women under drug management. Hence vigilant foetal surveillance is required that includes foetal heart rate monitoring by auscultation on each antenatal care visit [105, 106].

6.3 Management of parturition in the case of GD

Pregnant women with GD but well controlled of blood glucose (2-hour PPBS <120 mg/dL) levels may be delivered at their respective health facility just like any normal pregnant woman. However, pregnant women with GD on insulin therapy with uncontrolled blood glucose levels (2-hour PPBS ≥120 mg/dL) on MNT and physical exercise and metformin or insulin requirement >20 U/day should be referred at 34–36 weeks for delivery planning at Comprehensive Emergency Obstetric Care (CEmOC) centres under supervision of a gynaecologist [107].

6.4 Timing of delivery

Most GD pregnancies are associated with delayed lung maturity of the foetus; hence routine delivery prior to 39 weeks is not recommended. Such referred cases must get assured indoor admission or can be kept in a birth waiting home with round-the-clock availability of gynaecologist for monitoring.

Managing the delivery timing in GD mother is very crucial if pregnant women with GD and well-controlled blood glucose have not undergone parturition spontaneously; induction of labour should be scheduled at or after 39 weeks of pregnancy.

If pregnant women with GD present poor blood glucose levels, accompanied with risk factors like gestational hypertension, previous stillbirth and other complications, then the timing of delivery has to be individualised by the obstetrician accordingly.

Vaginal delivery is preferred, and lower segment caesarean section (LSCS) is done for obstetric indications only such as in the case of foetal macrosomia, a condition where the estimated foetal weight is >4 kg where vaginal delivery may cause shoulder dystocia in the newborn.

Regular blood glucose monitoring of the pregnant women with GD on metformin or insulin is required during labour. The morning dose of insulin/metformin is withheld on the day of induction of labour, and pregnant women are subjected to 2 hourly monitoring of blood glucose.

IV infusion with normal saline (NS) is to be started and regular insulin to be added according to blood glucose levels as per **Table 4** [105–108].

Blood glucose level	Amount of insulin to be added in 500 mL of NS	Rate of NS infusion
90–120 mg/dL	0	100 ml/hour (16 drops/min)
120–140 mg/dL	4 U	100 ml/hour (16 drops/min)
140–180 mg/dL	6 U	100 ml/hour (16 drops/min)
>180 mg/dL	8 U	100 ml/hour (16 drops/min)

Table 4.
Rate and amount of insulin-normal saline infusion in relation to blood glucose level.

6.4.1 Neonatal care for baby of a GD mother

Immediate and timely management of all neonates in a proper NICU facility emphasising on early breastfeeding is done on a priority basis to prevent hypoglycaemia. Under any emergency situations, the sick neonates must be immediately resuscitated as per standard guidelines.

Hypoglycaemia monitoring of the newborn is started within an hour of delivery and repeated every 4 hours (prior to next feed) until four stable glucose values are obtained.

The newborn with the normal birth weight and blood glucose level of <45 mg/dL is considered hypoglycaemic and requires immediate medical management. In the case of intrauterine growth restriction (IUGR), newborns' Blood Glucose level limit is <54 mg/dL [108].

6.4.2 Diagnosis of hypoglycaemia

The glucometers' testing method is not very reliable for diagnosis of hypoglycaemia as their precision decreases at lower blood glucose level. The most definite diagnosis of hypoglycaemia is by measurement of blood glucose using established laboratory methods such as glucose oxidase method by calorimeter. However, if laboratory facility is unavailable at the place of childbirth, then the treating physician can take a decision to send a blood glucose sample to the laboratory at the nearest location without delaying the next management step. However, under adverse circumstances, blood glucose values obtained by glucometers may be considered for all operational steps if it's the question of newborn's wellbeing.

6.4.3 Symptoms of hypoglycaemia

Symptoms of hypoglycaemia are difficult to observe as in most cases it is asymptomatic, variable and observed only in a smaller proportion of patients or newborns:

- Stupor or apathy
- Jitteriness or tremors
- Episodes of cyanosis
- Convulsions
- Intermittent apnoeic spells or tachypnoea
- Weak and high-pitched cry, limpness and lethargy

- Difficulty in feeding
- Eye rolling
- Episodes of sweating
- Any unexplained clinical feature in baby of diabetic mother

6.4.4 Management of hypoglycaemia in newborn

All cases of newborn with hypoglycaemia should be managed in the following manner:

6.4.4.1 Step 1

Whether there are any symptoms of hypoglycaemia or not, if a baby is born to a GD mother, its blood glucose level must be checked immediately between 1 and 2 hours after birth. If blood glucose values are <45 mg/dL, this should be considered as 'hypoglycaemia'. The primary management in such cases is that the newborn should be given breastfeed without any delay. Direct breastfeeding is the best management step for neonatal hypoglycaemia. If the infant is unable to suck, expressed breast milk from the mother should be given. If the mother is not in a position to give breastfeed or in the case of no breast milk secretion, the baby should be given any formula feed. If the lactation management centres (human milk banks) are available at the facility, then it can also be involved in feeding the baby.

After an hour of breastfeeding the newborn, blood glucose level must be monitored again. If it is found to be more than 45 mg/dL, 2 hourly feeding (breastfeeding if not available, formula feed can be given) should be ensured by explaining to the mother/relatives and supervised.

6.4.4.2 Step 2

If at any point of time the blood glucose level drops below 20 mg/dL, immediate intravenous bolus injection of 10% dextrose at 2 mL/kg body weight of baby should be given. This should be followed by intravenous infusion of 10% of dextrose at a rate of 100 mL/kg/day. Blood glucose should be checked 30 minutes after starting the infusion. If it is still less than 20 mg/dL, the infant should be referred to a higher centre where a paediatrician is available [109, 110].

6.4.5 Postdelivery follow-up of pregnant women with GD

Immediate postpartum care required for women with GD is a lot similar to that for women without GD, but these women are at high risk to develop type 2 diabetes mellitus in the future, although in 80% of cases, the glucose level usually returns to normal postdelivery.

Subsequently, ANC must be performed 75-g OGTT (fasting and 2-hour PP) at 6 weeks postpartum to evaluate glycaemic status of a woman. Cut-off for normal plasma and abnormal blood glucose levels in the fasting and 75-g OGTT values are [111–113]:

- Fasting blood glucose (≥126 mg/dL)
- 75-g OGTT (2-hour blood glucose)

- Normal (<140 mg/dL)
- IGT (140–199 mg/dL)
- Diabetes (≥200 mg/dL)

7. Conclusion

This chapter summarises all the clinical aspects surrounding gestational diabetes, ranging from its pathophysiology, aetiology right to its proper clinical management, for both the mother and the newborn, to a GD mother. Pregnancy affects both the maternal and foetal metabolisms, and even the nondiabetic woman exerts a diabetogenic effect. Amongst pregnant women, 2–17.8% develop GD. Metabolic changes in the normal pregnant women also have a degree of insulin resistance that shunts glucose preferentially to the foetus. To maintain blood glucose levels within a tight range, the normal pregnant woman must increase her insulin secretion up to fourfold. When the pancreas is not able to compensate for the increased insulin needs of pregnancy, GD occurs resulting in hyperglycaemia and hyperinsulinemia.

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Conflict of interest

The authors declare that there are no 'conflicts of interest' in regard to this chapter's contents.

Notes/thanks/other declarations

None.

List of abbreviations

ANC	antenatal care
BMI	body mass index
BMR	basal metabolic rate
CEmOC	comprehensive emergency obstetric care
GD	gestational diabetes
IGT	impaired glucose tolerance
IUGR	intrauterine growth restriction
LSCS	lower segment caesarean section
MNT	medical nutrition therapy
NCD	non-communicable diseases
OGTT	oral glucose tolerance test
PPBS	postprandial blood sugar

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