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REVIEW ARTICLE

Diagnosis and management of gestational diabetes mellitus guidelines by DIPSI (Revised)

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Abstract

Gestational diabetes mellitus (GDM) is diabetes that appears during pregnancy, presenting an opportunity for early testing and care to prevent non-communicable diseases (NCDs). GDM has short-term impacts on both mother and offspring and increases the risk of future diabetes, including type-2 diabetes, due to possible epigenetic changes. Therefore, it is crucial to screen all pregnant women for glucose intolerance with an economical and reliable test recommended by DIPSI and approved by the Ministry of Health & Family Welfare Government of India. Treatment to achieve euglycemia can prevent the epidemic of NCD. Post-partum follow-up is crucial to encourage weight management and lifestyle adjustments in mothers to prevent the onset of type 2 diabetes. Similarly, children of these mothers should adopt a healthy lifestyle to prevent future NCD risk.

Keywords Gestational diabetes mellitus · Gestational diabetes · GDM · Diabetes and pregnancy · Pregnancy and diabetes · Screening for gestational diabetes

Preamble The Ministry of Health Government of India has mandated screening all pregnant women for gestational diabetes mellitus (GDM) as part of the routine antenatal care, in line with 2014 national guidelines [1]. The Ministry of Health Government of India released national guidelines for diagnosing and managing GDM in February 2018 [2]. Comprehensive primary healthcare under the Ayushman Bharat – Health & Wellness Centres (AB-HWC) scheme has included the screening for gestational diabetes as a part of 4 antenatal checks, part of a 12 component check in "Care in pregnancy and childbirth" in 2022 [3]. However, operationalisation at the primary healthcare level is still suboptimal. One of the reasons for this inertia could be the incongruent opinion regarding the diagnosis and management of GDM among different healthcare providers in our country. It is time that clinicians review the Indian evidence and accept that the "Indian problem needs Indian solution" and there is universal acceptance of the DIPSI criteria.
Extended panel of experts (in alphabetical order)
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Introduction

The definition of gestational diabetes mellitus (GDM) is any degree of glucose intolerance with onset or first recognition during pregnancy [4]. GDM is dysglycaemia during pregnancy, while HIP encompasses any dysglycaemia in pregnancy, further classified as DIP and GDM. DIP can be pre-existing diabetes or first diagnosed during pregnancy, and is diagnosed when hyperglycaemia during pregnancy meets non-pregnant diagnostic criteria. Criteria include fasting plasma glucose (FPG) ≥ 7.0 mmol/L or 126 mg/dL, 2-h 75-g OGTT value ≥ 11.1 mmol/L or 200 mg/dL, or random plasma glucose (RPG) ≥ 11.1 mmol/L or 200 mg/dL with diabetes symptoms. A first-time diabetes diagnosis during pregnancy is likely type 2. DIP can be detected in the first trimester with proper testing, unlike GDM [4]. GDM is diagnosed when hyperglycaemia in pregnancy does not meet DIP criteria. Although it usually appears later in pregnancy with milder hyperglycaemia, GDM still increases risks of poor pregnancy outcomes and future diabetes and cardiovascular disease. [1] Worldwide, 85–90% of diabetes-related pregnancies are GDM. Undiagnosed or undertreated GDM can cause significant maternal and foetal problems, and both GDM-affected women and their offspring have higher risk for type 2 diabetes. GDM prevalence seems to be increasing

alongside overall diabetes prevalence. [5] Gestational diabetes risk factors include health conditions such as obesity, PCOS, high blood pressure, and pregnancy in advanced age, as well as lifestyle factors such as physical inactivity, overeating, and family history of diabetes and heart disease [6]. Untreated GDM poses risks to maternal and foetal health, such as pre-eclampsia, preterm labour, and delivery complications. Foetal complications might include macrosomia, neonatal jaundice, hypoglycaemia, hypocalcaemia, hyperbilirubinemia, and an increased risk of intrauterine foetal death.

Need for revision of the guidelines

Clinical practice guidelines (CPGs) offer recommendations to guide healthcare providers, patients, and stakeholders in making informed decisions. They are valuable tools for disseminating medical knowledge and have a significant impact on healthcare providers and patient outcomes. While international and western guidelines exist and are regularly updated, it is important to consider that these guidelines are primarily based on Caucasian data, making it challenging to apply them directly to the Indian population and resource settings. The DIPSI guidelines for gestational diabetes mellitus diagnosis and management were introduced in 2014 and underwent a revision in 2018. Given the emerging evidence in India and the need to update treatment strategies, it is crucial to evaluate the methodological soundness of these recommendations considering various factors. The purpose of these guidelines is to enhance care consistency, provide authoritative recommendations to support practitioners in their treatment decisions, challenge outdated practices, and offer clear guidance for clinicians facing the growing burden of GDM in India.

Epidemiology of GDM and its implications

According to the International Diabetes Federation (IDF 2021), there is a high and growing prevalence of diabetes worldwide, with a predicted increase from 536.6 million people to 783.2 million by 2045 [7]. In India, the burden of diabetes is equally high, with an estimated increase from 74.2 million people in 2021 to 124.9 million by 2045, and an additional 318 million estimated to have pre-diabetes, which is likely to increase to 481 million by 2040 [4]. A significant proportion of live births to women are affected by hyperglycaemia in pregnancy, with 80.3% [7] due to GDM, and a global prevalence of 14.7% for GDM [8], and 11.5% in Asia [9]. As a result, it is important to screen all women for GDM, even in the absence of symptoms, as GDM has become a major public health issue in India and other parts of the world [10, 11].

Studies conducted after 2021 in rural areas of central [12] and western [13] India showed a GDM prevalence of 1.9% and 12.7%, respectively, which is lower than previous studies in Vellore (Tamil Nadu)[14], Assam [15], Tiruvallur (Tamil Nadu)[16], and Gujarat that reported higher prevalence rates of 9.9 to 17.33% [17]. Conversely, urban areas have shown a higher prevalence of GDM in recent studies [18–21], with rates ranging from 6.6 to 27.2%. One study in Lucknow [22] reported a prevalence of 13.21%, while another in South Delhi reported 19.2% (Fig. 1) [23]. A meta-analysis reported a prevalence rate of 7.37% [21]. Public health campaigns are suggested to help reduce the prevalence of GDM [22].

Maternal complications and its implications

GDM contributes significantly to maternal morbidity and mortality globally through complications such as polyhydramnios, pre-eclampsia, protracted or obstructed labour, caesarean section, uterine atony, postpartum haemorrhage, infection, and retinopathy progression [1]. Additionally, GDM can cause immediate adverse effects on the mother, foetus, and neonate [13]. Furthermore, women with a history of GDM have an increased risk of developing type 2 diabetes in the future and can also transmit non-communicable diseases, including diabetes, to their offspring [24] (refer Table 1).

National evidence

A community-based screening program in Ahmedabad found that 12.7% of pregnant women had gestational diabetes mellitus (GDM) and required nutritional therapy or

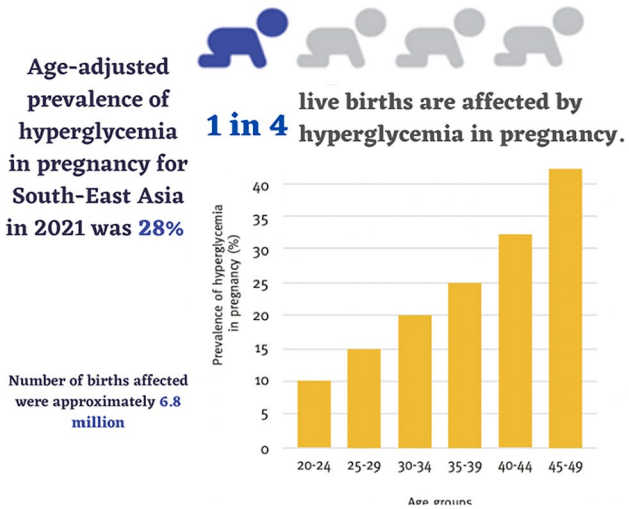


Fig. 1 Hyperglycaemia in pregnancy in women aged 20–49 years by IDF (2021)

Table 1 Maternal and foetal risks of GDM

Maternal risks	Foetal risks
- Abortion	- Spontaneous abortion
- Polyhydramnios	- Intra-uterine death
- Pre-eclampsia	- Stillbirth
- Pre-term labour	- Congenital malformation
- Premature rupture of membranes	- Shoulder dystocia
- Recurrent UTIs	- Neonatal hypoglycaemia
- Prolonged labour	- Infant respiratory distress syndrome
- Obstructed labour	- Hypothermia
- Caesarean section	- Hypocalcaemia
- Uterine atony	- Polycythemia
- Postpartum haemorrhage	- Hyperbilirubinemia
- Infection	- Hyper viscosity syndrome

medication [13]. Women with any abnormal glucose number were more likely to undergo a caesarean delivery and experienced cognitive dysfunction during pregnancy [25, 26]. In a study involving 644 pregnant women, 9% had GDM, and 60.3% needed insulin therapy to achieve glycemic control. The most common maternal and neonatal problems found were premature prelabour membrane rupture and jaundice [27]. In western Rajasthan, a study found that 6.6% of participants had GDM, and the GDM group experienced more foetal and maternal problems than the non-GDM group. The most common foetal complications were macrosomia and stillbirths, while the most common maternal issues were hypertension, vaginal candidiasis, and abruption placentae [18].

Foetal complications and their implications

Infants born to diabetic mothers are at a higher risk of neonatal complications due to exposure to high maternal blood glucose levels during foetal development. The severity of these complications, including metabolic and hematologic disorders, respiratory distress, cardiac disorders, and neurologic impairment, is influenced by maternal blood glucose levels. Macrosomia, which is a large birth weight, is a common consequence of maternal diabetes and can increase the risk of adverse neonatal outcomes. Neonatal hypoglycaemia, a prevalent metabolic disorder, should be prevented [28].

Women with pre gestational type 2 diabetes and maternal obesity have a significantly higher risk of perinatal death and birth defects. In developing countries with limited maternal and neonatal care and high rates of maternal hyperglycaemia, the burden of neonatal complications is even higher [29].

A study examining the impact of elevated blood glucose levels, nutrients, and psychosocial environments on childhood obesity found that 3.3% of children were small for gestational age, 10.8% were large for gestational age, and 9.7% were obese at birth [30]. Children born to mothers with gestational diabetes mellitus (GDM) have a higher risk of developing cardiovascular disease, childhood wheeze/asthma, high refractive error, attention deficit hyperactivity disorder, and psychiatric disorders. However, there is no evidence to suggest that they are more prone to allergy sensitisation [28].

Transgenerational effects and future NCD risk

Gestational programming is a distinctive process. The stimuli (like hyperglycaemia) or stresses that occur at critical or sensitive periods of foetal development ultimately lead to permanent changes in the structure, physiology, and metabolism of the growing foetus. This, in turn, predisposes these babies to increased NCD risk in their adult life. Manifestation of hyperglycaemia in pregnancy, i.e. GDM, represents the detection of chronic β cell dysfunction during pregnancy and is a stage in the evolution of type 2 DM. Women with a history of GDM are at increased risk of future diabetes, predominantly type 2 diabetes, as are their children, representing the "transgenerational transmission" [31].

Pathophysiology of GDM and its sequelae

Gestational diabetes mellitus (GDM) is caused by a complex combination of maternal, feto placental, genetic, and environmental factors [32]. In most cases, the pancreatic beta-cells cannot cope with a persistent fuel surplus, leading to insulin resistance, hyperglycaemia, and increased glucose supply to the developing foetus. Placental variables, adipose expandability, low-grade chronic inflammation, gluconeogenesis, and oxidative stress also contribute to the pathophysiology of GDM [33](Fig. 2).

A study by Filardi T. et al. also suggests that the expression of target genes can vary in the child as a result of the deregulation of ncRNAs (long noncoding RNA), which may be related to a harmful intrauterine environment. This might potentially contribute to the emergence of long-term GDM-related issues, such as metabolic and cardiovascular illnesses [34].

Public health policy

India's Ministry of Health and Family Welfare released "National guidelines on diagnosis and management of gestational diabetes mellitus" in 2014, mandating universal screening and management of GDM as part of the basic

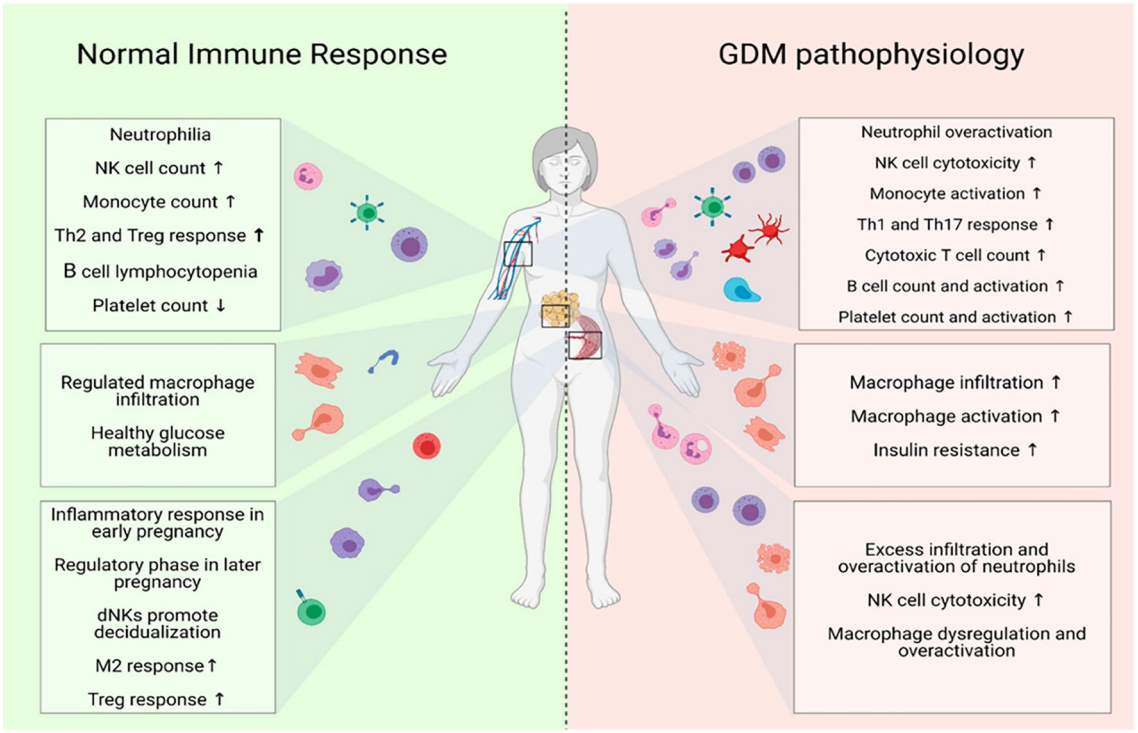


Fig. 2 Representation of the pathophysiology of GDM (adopted from McElwain et al.) [32]

prenatal package. The guidelines were implemented in the State of Madhya Pradesh's Hoshangabad district from November 2016 to October 2017, with assistance from the government, resulting in 84% of ANC clients being tested for GDM during the implementation period. Prevalence rates in urban and rural regions were 11% and 8%, respectively. Furthermore, GDM diagnostic and management services were launched in 11 additional Indian states, including Tamil Nadu, Karnataka, Gujarat, and others.[1, 3]

Universal screening

Previously, gestational diabetes was mostly diagnosed based on its association with the future risk of type 2 DM in the mother, rather than its perinatal outcomes. However, with Indian women having more than 11 times the risk of developing glucose intolerance during pregnancy than Caucasian women, universal early testing is now recommended.[35] This should start even before conception to rule out undiagnosed diabetes. The shift in approach is due to factors such as late marriage, delayed conception, and decreasing age of diabetes onset. The current recommendation is to screen for GDM in the early weeks of pregnancy, preferably at the first antenatal visit, to avoid false-negative results in the 2nd trimester. Foetal glucose steal phenomenon can make it difficult to detect GDM in the 2nd trimester, so if the initial screening is negative, repeat testing is necessary in the 2nd and 3rd trimesters [36] (Fig. 3).

Guidelines for diagnosing GDM

Women with diabetes planning to conceive should maintain normal blood sugar levels before and throughout pregnancy to prevent diabetic embryopathy, including congenital heart disease, renal anomalies, anencephaly, microcephaly, and caudal regression.[37] Observational studies have shown that high A1C levels during the first 10 weeks of pregnancy are directly proportional to these risks. Optimising glycaemia before conception is recommended as organogenesis occurs between 5 and 8 weeks of gestation.[38] An A1C level of less than 6.5% is associated with the lowest risk of congenital anomalies, preeclampsia, and preterm birth. Women of childbearing age with diabetes should be informed about the importance of maintaining normal blood sugar levels before pregnancy and throughout pregnancy. [37, 39–42]

DIPSI procedure

Studies in India have shown that GDM can be diagnosed with a single test where pregnant women are given 75 g oral glucose and 2 h PG $\geq$ 140 mg/dL is considered abnormal, regardless of fasting status.[43] This test has been approved

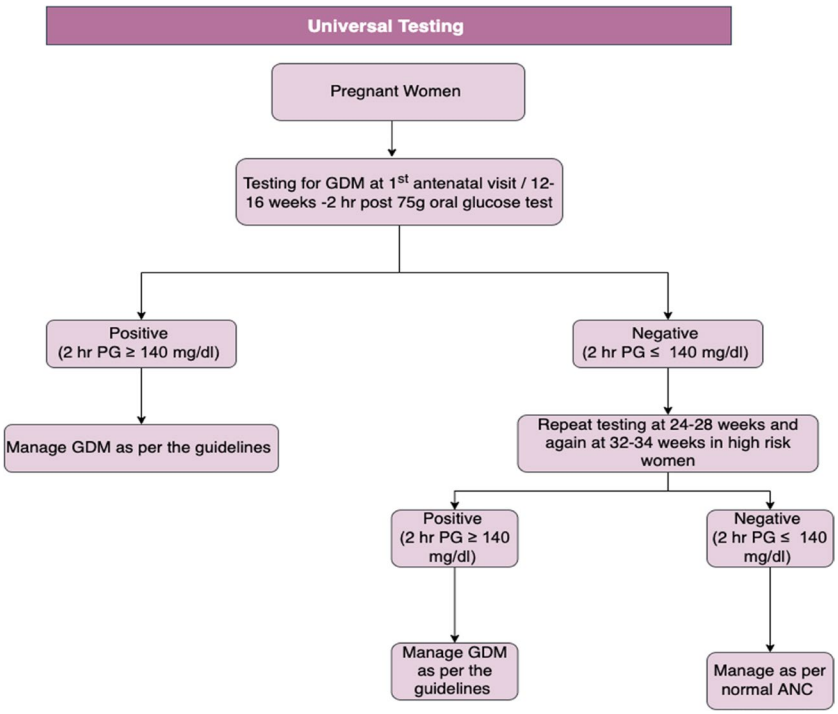


Fig. 3 Screening algorithm for GDM

by various organisations, including the Ministry of Health Government of India, WHO [44], IDF [6], and the International Federation of Gynaecologists and Obstetricians Society (FIGO) [45]. NICE guidelines also recommend 2 h PG > 140 mg/dL as diagnostic criteria for GDM based on a study in a multi-ethnic population in the UK.[46] A study by Saxena et al. in 2021 compared the diagnostic accuracy of three criteria for diagnosing GDM. A total of 1029 pregnant women underwent a 2-h 75 g OGTT in a non-fasting state. DIPSI was found to have high sensitivity (98.48% with CC, 99.89% with NDDG) and specificity (95.64% with CC, 92.38% with NDDG), with a diagnostic accuracy of 95.82% with CC and 95.52% with NDDG. The study concluded that DIPSI could be recommended due to its low cost, simplicity, and convenience.[47]

WHO observation

There is no high-quality evidence that women and their foetuses benefit from the treatment if only the fasting value is abnormal. Evidence from trials has shown benefit of treating GDM women identified primarily by post-load values [48].

Advantages of DIPSI procedure

The advantages of the procedure are given in Fig. 4 [49].

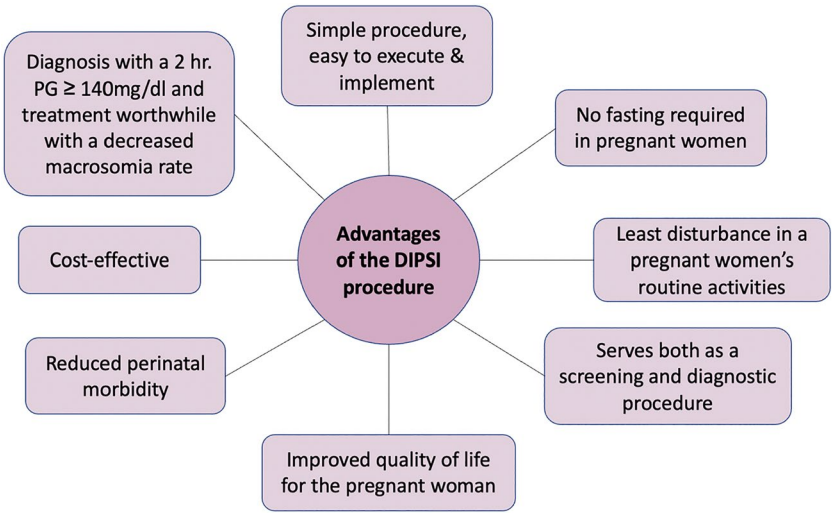


Fig. 4 Advantages of the single test procedure (DIPSI recommendation)

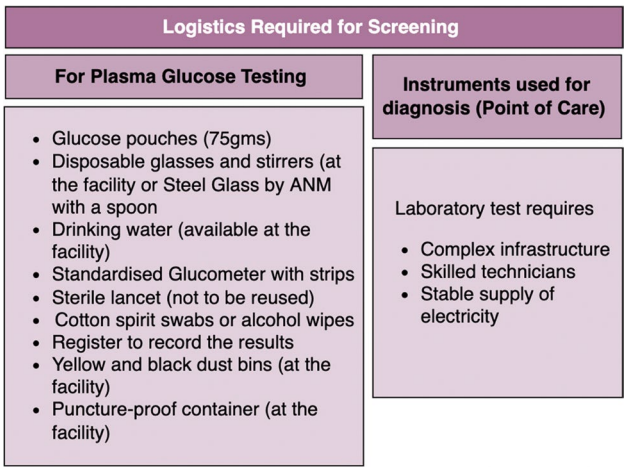


Fig. 5 Logistics required for screening

Methodology and procedure (DIPSI procedure)

A *single-test procedure* has been recommended by the Ministry of Health, Government of India (Fig. 5).

- Glucose (75 g) is to be given orally after dissolving in approximately 300 mL water, whether the pregnant woman comes in a fasting or non-fasting state, irrespective of the last meal timing. It is important that the intake of the solution is completed within 5–10 min.
- A standardised plasma-calibrated glucometer should be used to evaluate plasma glucose 2 h after the oral glucose load.
- If vomiting occurs within 30 min of oral glucose intake, the test has to be repeated the next day. If vomiting is post 30 min, then the test continues without disruption.
- The threshold plasma glucose level of ≥ 140 mg/ is taken as the cut-off for the diagnosis of GDM.

Testing for hyperglycaemia in pregnancy can result in delays in diagnosis due to long testing times in laboratories, causing women to leave before receiving a diagnosis. To avoid this, a portable blood glucose metre is recommended, allowing for immediate results and necessary advice to be given the same day. A glucometer should also be available in the labour room for close monitoring of GDM cases during labour. Non-fasting OGTT of all pregnant women should be done at Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA) sites, and at all other facilities up to the PHC level, an in-house arrangement of a glucometer and glucose pouches should be available for immediate testing and reporting. If a 75-g glucose pouch is not available, a 100-g glucose pouch can be procured and 5 teaspoons of glucose removed to obtain the 75 g required for the test. A survey conducted in rural areas found that less than 10% of pregnant women attending the AN Clinic were in a fasting state [50].

Technical guidelines on testing and management of GDM

Protocol for the investigation

Testing for GDM should be done during the first trimester or before 12 weeks and at 24–28 weeks of pregnancy if the first test is negative. There should be a gap of at least 4 weeks between the two tests. If the test is negative, repeat testing at 32–34 weeks is recommended. All pregnant women should be tested, even if they come late in pregnancy. If the woman presents beyond 28 weeks of pregnancy, only one test is to be done at the first point of contact. For planned pregnancies, screen for pre-pregnancy diabetes with an HbA1c test before conception. For normoglycemic women, follow Table 2 for subsequent screenings. For unplanned pregnancies, test at the first visit.

Evidence

In a study by Seshiah et al., a total of 4151 consecutive pregnant women, irrespective of gestational weeks attending antenatal health posts across Chennai city, underwent a 75-g OGTT recommended by WHO and diagnosed GDM if 2 h PG value > or = 140 mg/dL. Among the screened, 741 women (17.9%) had 2 h PG ≥ 140 mg/dL, and they were diagnosed with gestational diabetes mellitus. Observation in this study was that 38.7% developed gestational diabetes even prior to the 24th week of gestation. Of the 741 GDM women, 214 (28.9%) were diagnosed on repeat testing at subsequent visits. Thus, glucose intolerance occurs in the early weeks of gestation [48]. Hence, DIPSI recommends screening on the first visit, preferably in the first trimester, to avoid missing later due to foetal handling of maternal glucose.

Glycosylated haemoglobin (HbA1c)

There are very little data on the use of A1c to diagnose diabetes in pregnancy. Consequently, the 2013 WHO guideline

Table 2 Ideal screening times for GDM

Screening	Week of pregnancy
1st screening	To be done as early as on the first ANC visit for a check-up (if not done ideally at preconception)/ before 12 weeks
2nd screening	24–28 weeks
3rd screening	32–34 weeks

does not include A1c as a means of diagnosing diabetes in a pregnant woman and for monitoring [44]. The standardisation of A1c is impossible in countries like India, where all the laboratories need to possess equipment and standardisation is a problem. Moreover, false low and false high HbA1c secondary to different conditions such as anaemias and haemoglobinopathies further limits its value. At most, HbA1c in the first trimester helps establish pre-existing undiagnosed diabetes. In addition, due to the rapid turnover of RBCs in pregnancy, HbA1c changes rapidly and is not really of much value in assessing glycemic control.

Mild hyperglycaemia in pregnancy

A study from Tamil Nadu found adverse outcomes not only in women with gestational diabetes (GDM) but also in those with 2-h postprandial blood glucose (PGBG) levels between 121 and 139 mg% (termed gestational glucose intolerance or GGI) during any trimester [16]. Starting medical nutrition therapy (MNT) and drug therapy to achieve target glucose levels is necessary to avoid adverse outcomes. Another meta-analysis of 17 studies involving over 64,000 pregnant women found that those with mild GDM had a higher risk of several adverse maternal and neonatal outcomes, including caesarean section, pregnancy-induced hypertension, preeclampsia, macrosomia, and neonatal hypoglycaemia, among others. However, small for gestational age and neonatal death were not significantly different between the GDM and non-GDM groups (Table 3) [51].

Management of GDM

Managing gestational diabetes requires a coordinated approach to reduce the risk of complications and minimise maternal and neonatal morbidity. Glycemic control and a healthy diet are crucial, as women with GDM have a higher risk of developing diabetes 5–10 years after giving birth, and their children are at higher risk of developing type 2 diabetes and obesity. Treatment should aim to keep blood glucose levels normal and may involve special meal plans, regular physical activity, daily blood glucose testing, and pharmacotherapy. However, implementing expert guidelines can be challenging. Some obstacles are shown in Fig. 6.

Table 3 Categorisation of glucose intolerance during pregnancy

GDM	2 h PG > 140 mg/dL	Future type 2 DM
GGI (gestational glucose intolerance)	2 h PG > 120 mg/dL but < 140 mg/dL	Adverse pregnancy outcome future T2DM
Early gestational glucose intolerance (EGGI) 10th week	2 h PP ≥ 110 mg/dL	Prone to develop GDM-DM (foetus) IGT- DM (mother)[49]

Guidelines for management

The Diabetes in Pregnancy Study Group of India (DIPSI) criteria were used in guidelines on the diagnosis and management of gestational diabetes mellitus by the Government of India. As per DIPSI criteria, 2-h fasting or non-fasting OGTT ≥ 140 mg/dL is considered GDM,[13] which is similar to the NICE guidelines (Table 4).[50]

Medical nutrition therapy (MNT)

Lifestyle behavioural change is an essential component in the management of GDM.[50] All national and international guidelines suggest MNT, together with weight management and physical activity (PA), as the initial mainstay for the management of GDM [49].

A nutrition assessment based on the Dietary Reference Intakes (DRI) should guide the food plan for women with gestational diabetes. The DRI recommends a minimum of 175 g of carbohydrates, 71 g of protein, and 28 g of fibre for all pregnant women. The diet should focus on monounsaturated and polyunsaturated fats while limiting saturated and trans fats. The amount and type of carbohydrates will affect glucose levels, and the current recommended amount is 175 g or 50% of a 2000-cal diet. A diet with nutrient-dense carbohydrates can improve insulin action, vascular benefits, and control glucose levels. Fasting urine ketone testing may be useful to identify women who are restricting carbohydrates to control blood glucose. Simple carbohydrates can cause higher post-meal glucose levels. Substituting fat for carbohydrates can worsen insulin resistance and enhance lipolysis.

An easy method for the dietary guidelines for primary health care providers is given in Tables 5 and 6 (a and b).

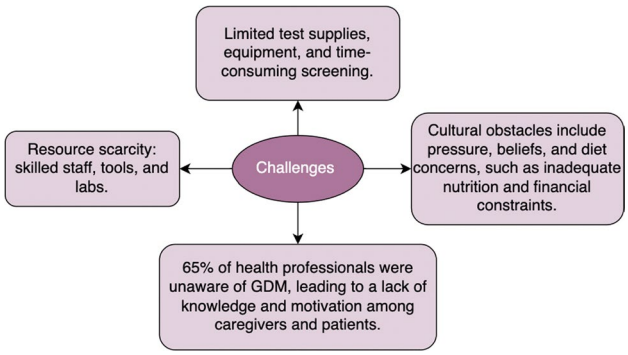


Fig. 6 Challenges of implementing expert guidelines

Table 4 Important therapies and recommendations

Therapy	Recommendation
Medical nutrition therapy (MNT) and physical therapy	Should be started for 2 weeks for all pregnant women who test positive for GDM for the first time
Insulin treatment or metformin (in limited situations)	Advised if 2 h post-prandial plasma glucose (PPPG) remains > 120 mg/dL despite MNT and lifestyle modifications
Insulin	Started immediately when the FBS > 126 mg/dL or 2 h PGBG > 200 mg/dL along with MNT

Meal plan for a plate of 10 in radius (Fig. 7; Tables 7 and 8)

- Half of the plate: green leafy vegetables, watery vegetables, traditional vegetables, and beans variety.
- A quarter of the plate: proteins-dhal and whole pulses for vegetarians.
- Egg or fish or chicken or mutton and dhal for non-vegetarians.
- A quarter of the plate cereals or whole grains or millets are preferred.
- Curd 200 mL for breakfast, lunch, and dinner.
- Snacks, preferably roasted/boiled Bengal gram and sprouts or salads.

Facilities

In places where nutritionists are not available for diet counselling, a readymade list of diet sheets containing the food items which can be taken in plenty and which should be avoided is made available.

Management of pregnant women with GDM (Fig. 8)

Pharmacotherapy/medical management

Standard care

- Insulin is the preferred medication for treating hyperglycaemia in pregnancy, including gestational diabetes mellitus.
- Metformin and glyburide should not be used as first-line agents, as both cross the placenta to the foetus. Other oral and noninsulin injectable glucose-lowering medications lack long-term safety data and are not recommended.
- Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester as studies show no benefits of continuing metformin in preventing GDM in such cases.
- Only when insulin is not possible or feasible or acceptable metformin may be used after 12 weeks of gestation after discussing the pros and cons of metformin in light of all emerging evidence.
- However, due to the potential for growth restriction or acidosis in the setting of placental insufficiency, metformin should not be used in women with hypertension, preeclampsia, or at risk for intrauterine growth restriction where insulin remains the drug of choice.[53]

Limited care

- Insulin is the first drug of choice and can be started at any time during pregnancy for GDM if medical nutrition therapy (MNT) fails.
- If a pregnant woman is not willing for insulin, or insulin use is not possible, metformin can be recommended after discussing its pros and cons, provided gestation is more than 12 weeks, and there are no contraindications to metformin use.[31]
- In Indian experience (what is good for conception should be good to continue during pregnancy), metformin may be continued throughout pregnancy.
- The initial dose of metformin is 500 mg twice daily with meals and is then titrated to higher doses gradually to avoid gastrointestinal side effects which are subsequently subtle. The maximum dose is 2 g/day. However, if blood sugar is not controlled with the maximum tolerated dose

Table 5 Energy requirements according to the levels of activity for pregnant women

Level of activity	Energy requirement during pregnancy	Total energy requirement (kcal/day)
Sedentary work	1900 + 350	2250
Moderate work	2230 + 350	2580
Heavy work	2850 + 350	3200

Table 6 Energy requirements according to each trimester

Trimester	Caloric intake (kcal/day)
1st trimester	1800
2nd trimester	2200
3rd trimester	2400

Fig. 7 Meal plan for a plate (10 in radius)

of metformin and MNT, insulin should be initiated without further delay.

- Hypoglycaemia and weight gain with metformin are less in comparison to insulin.
- However, the risk of prematurity is slightly increased with metformin.
- If insulin is required in high doses, metformin may be added to the treatment.

The contemporary and latest information on metformin in GDM

The MITy trial done in 2020 showed no major adverse events with metformin use in pregnancy. However, the study showed lower adiposity and infant size measurements, which resulted in fewer large infants but a higher proportion of small-for-gestational-age infants who were exposed to metformin in utero. It was highlighted that understanding the implications of these effects on infants will be important in the future to properly advise patients who are contemplating the use of metformin during pregnancy.[52]

The MiG TOFU trial revealed that metformin or insulin for GDM was associated with similar offspring total and abdominal body fat percent and metabolic measures at 7–9 years. Metformin-exposed children were larger at 9 years. Metformin might interact with foetal environmental factors to influence offspring outcomes.[53]

The Pregnancy Outcomes: Effects of Metformin (POEM) is an ongoing multicentre, open-label, randomised, controlled trial. The parameters that will be assessed include pregnancy-related hypertension, (pre-) eclampsia, large for gestational age baby (LGA) at delivery according validated guidelines, type and term of delivery, birth trauma, like fractures of clavicle and humerus, subdural/intracerebral haemorrhage, neonatal hypoglycaemia, and admission for neonatal intensive care.[54]

The obstetricians in India prefer to continue metformin even after the woman conceives based on their experience. Metformin may be used as a safe and effective oral hypoglycemic agent in GDM, especially in low-resource settings where cost, storage, and compliance are logistic issues and insulin cannot be used.[55] Metformin is routinely recommended by the National Guidelines in the Diagnosis and the Management of GDM (Ministry of Health Government of India) after 20 weeks of gestation.[56]

BMJ Open Diabetes Research and Care register-based cohort study found no increased long-term risk associated with pregnancy exposure to metformin (alone or in combination with insulin) compared with insulin.[44]

Recently in February 2022, a European study stated that metformin is safe for use throughout pregnancy. Glucophage (metformin) was approved as the first oral antidiabetic medicine to be used safely from conception to birth and also has a lower risk of pregnancy-induced hypertension and pre-eclampsia.[57]

NICE Guidelines state that the use metformin as an adjunct or alternative to insulin in the preconception period and during pregnancy when the likely benefit from improved blood glucose control outweighs the potential for harm.[50]

Monitoring glycemic control when on MNT or metformin

Standard care

- Frequent SMBG tracking with all 3 pre-meals and 2-h post-meal blood glucose is recommended.

Table 7 Recommendations for calorie intake and weight gain during pregnancy according to BMI

BMI (kg/m2)	Total weight gain (kg)	Rate of weight gain in second and third trimester (kg/week)	Approximate caloric intake
Underweight < 18.5	12.5–18	0.51 (0.44–0.58)	35–40 kcal/kg/day
Normal 18.5–22.9	11.5–16	0.42 (0.35–0.50)	30 kcal/kg/day
Over weight 23–24.9	7–11.5	0.28 (0.23–0.33)	22- 25 kcal/kg/day
Obese > 25	5–9	0.22 (0.17–0.27)	22- 25 kcal/kg/day

Table 8 Nutritional recommendation in pregnancy

Dietary component	Recommendations *(IDF MENA,2021)* [52]
Energy	Optimise growth and development of the foetus. Desirable maternal weight gain will vary according to pre-pregnancy and current weight Women with hyperglycaemia-induced pregnancy (HIP) should consume adequate calories and gain weight as recommended • Weight gain in the first trimester should be 0.5–2 kg • No increase in caloric intake is recommended during the first trimester • An additional 340 kcal/day is recommended during the second trimester • An additional 452 kcal/day is recommended during the third trimester • In women with polycystic ovarian disease (PCOS), weight monitoring should be fortnightly as these women are likely to gain excessive weight
Carbohydrates	• Carbohydrates minimum 175 g/day (35–45% of TEI)
Fibre	• Fibre 28 g/day (same as required before pregnancy)
Protein	• Proteins minimum 71 g/day (20–25% of TEI)
Fat	• Fats (25–35% of TEI)
Sodium	No benefit in alleviating gestational hypertension, Sodium-rich foods to be avoided. Sodium 1500–2300 mg/day (same amount as non-pregnant individual)
Fluid	• The minimum fluid requirement is 2.3 L/day (10 cups of beverages to maintain adequate hydration)
Vitamins and minerals	• Ferrous iron 40 mg/day, folic acid 570 µg/day, zinc 14.5 mg/day, calcium 1000 mg/day, vitamin C 80 mg/day, vitamin B_{12} 2.75 µg/day, and magnesium requirement is increased 385 mg/day *(RDA, ICMR, 2020)* • Remember to space the calcium and calcium-rich foods and iron supplement by an hour at least • Prefer to consume vitamin C with iron supplement
Non-nutritive sweeteners (NNS)	• USFDA-approved sweeteners for pregnancy in moderation (i.e., sucralose). Saccharin is contraindicated • It is important to note that NNS can cause gut dysbiosis *(Diet Metrics 2019)* • Higher artificial sweetener consumption increases the cardiovascular and cerebrovascular disease risk in an individual *(BMJ 2022)*
Dietary adjuvant therapy	• In general, pregnant women should not take any herbs and botanical products due to inadequate evidence on their consumption and impact on foetal outcome
Caffeine	• Avoided *(IDF-MENA 2021)* • 200 mg/day *(JAMA 2022)* Drink — Average amount of caffeine (mg) *(JRD 2021)* Brewed coffee 220 mL — 135 (80–200) Instant coffee 220 mL — 75 Instant tea 220 mL — 26–36 Soft drinks (cola) 330 m — LAvoided
Alcohol	• Avoided *(IDF-MENA 2021; JAMA 2022)* • Alcohol is strictly prohibited (risk for foetal alcoholic syndrome) *(JDR 2021)*
Sugar-sweetened, sugar-free fizzy drinks	• Avoided *(IDF-MENA 2021)*
Omega 3 fatty acids	• Essential from dietary sources for visual cognitive development of the foetus *(IDF-MENA 2021)*
• In certain special conditions Covid -19/Co-morbidities /celiac disease/lactose intolerance, etc., kindly follow updated guidelines to customise nutrition prescription and menu plan accordingly	

Abbreviation: TEI-Total energy intake; USFDA, US Food Drug Administration

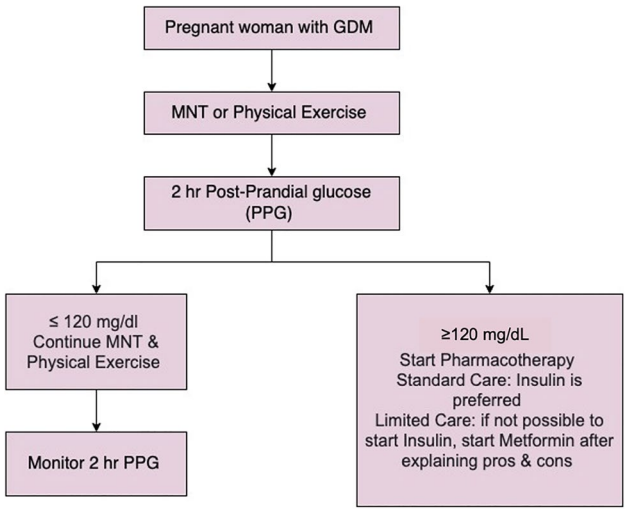


Fig. 8 Management algorithm for GDM

Limited care

After satisfactory glycemic control is achieved, monitoring at least once a month or more may be performed (in places with limited resources).

Monitoring glycemic control when on insulin

Women with GDM who are started on insulin to achieve tight glycemic control need to ideally do intensive self-monitoring of blood glucose with all 3 premeal and 2-h post-meal glucose tests. However, at least 4 glucose readings—daily fasting and 2 h after each meal—must be done for insulin dose titration to achieve optimal glycemic control. Continuous glucose monitoring (CGM) where available and affordable/acceptable may be used as an adjunct to SMBG to assess glycemic variability, which may be associated with macrosomia.[58]

Insulin therapy

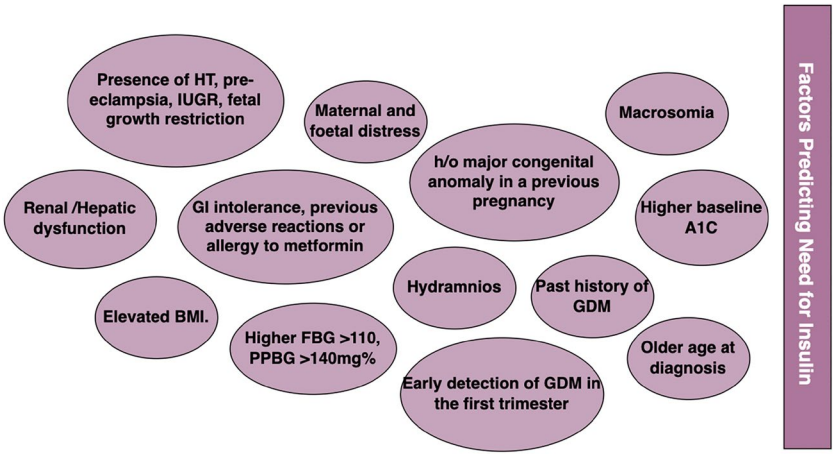
Standard care

Insulin remains the gold standard for all women with GDM who fail to achieve target glycemic control with MNT and exercise (Fig. 9).

Insulin: regime, type, and doses

- The insulin regime has to be individualised. No convincing evidence for the superiority of one insulin regimen over another.
- Most women with GDM present with postprandial hyperglycaemia, so it is best to start with prandial insulin. A starting dose of 4 units subcutaneously, titrated based on SMBG values, can be used until target is reached. In a study from India, 45.4% of 348 pregnant women with varying degrees of glucose intolerance required insulin to achieve euglycaemia. The lowest dose was needed during breakfast, higher during lunch, and the highest with dinner. The pre-dinner dose was almost double than that of pre-breakfast in all three groups, indicating the need to monitor and target glycemic goals after all three meals [59].
- If FPG > 110 mg/dL, use basal/intermediate-acting insulin at bedtime. Basal bolus insulin regime is preferred in pre-gestational DM. A study showed that insulin dose requirement in type 2 pre-gestational DM women increased significantly from 0.52 to 0.76 U/kg/day ($p < 0.0001$) during the 1st trimester. Insulin dose was positively correlated to fasting and 2 h postprandial plasma glucose at diagnosis [60].

Fig. 9 Factors predicting need for insulin



- Most insulins are safe during pregnancy, including short-acting and NPH insulins.
- Many insulin analogues are safe during pregnancy, such as aspart, FIASP, lispro, detemir, and degludec. Govt of India updated the insulin degludec label to allow its use during pregnancy if needed.[73]
- Insulin glargine can be continued during pregnancy if it was being used before pregnancy and discontinuing it may worsen glycemic control. Information on the use of glulisine during pregnancy is not available.
- Obese patients may need higher insulin dosages compared to non-obese individuals.
- Women with gestational diabetes mellitus (GDM) often do not need insulin after delivery, and a significant dose reduction of 20–40% may be seen in women with pre-GDM.
- Insulin pump therapy CSII can help control blood glucose levels and address hypoglycaemia or dawn phenomenon in patients who can afford it.

Limited care

- GDM is managed through medical nutrition therapy (MNT) along with physical activity, followed by subsequent 2-h postprandial blood sugar (PPBS) testing at 2 weeks. Two-hour PPBS level is maintained below < 120 mg/dL. If 2-h PPBS remains ≥ 120 mg/dL, medical therapy (insulin/metformin) is added to MNT as per the guidelines.
- Metformin (oral antidiabetic drug) or insulin therapy is the accepted medical management for GDM and can be started for treatment after mentioning its pros and cons to the patients, if availability of insulin in that setting is under question.
- Insulin therapy can be started anytime during pregnancy. However, if blood sugars are uncontrolled (2-h PPBS ≥ 120 mg/dL) with a maximum dose of metformin (2 g/day), insulin therapy is added.
- The dose of insulin/metformin is titrated as per blood sugar level and follow-up schedule. Monitoring fasting blood sugar (FBS) and 2-h PPBS is done every third day or more frequently for insulin and bi-weekly for metformin dose adjustment to maintain normal blood sugar levels.
- The recommended starting dose of insulin in GDM is 0.1 units/kg of body weight per day. The dose can be increased on follow-up until 2-h PG is around 120 mg/dL.
- Rarely, a GDM woman may require more than 20 units of insulin per day. If multiple doses of insulin are required, refer to a higher centre where a trained physician/diabetologist is available.
- Pre-GDM (type 1 and type 2 DM) may require pre-meal regular/rapid-acting insulin and bedtime basal insulin. However, premixed insulin twice a day may be an option in women with pre-existing type 2 DM, where a basal-bolus regime is not possible/acceptable. However, PHC is not expected to manage pre-GDM unless a trained physician/diabetologist is available to initiate and intensify such insulin regimes (Figs. 10 and 11).

Pregnancy monitoring

- GDM is considered a high-risk pregnancy, and women with GDM are monitored for potential complications, including abnormal foetal growth, polyhydramnios, hypertension, and proteinuria.
- Foetal heart sound is checked at every antenatal visit, and three ultrasound scans are performed during pregnancy for foetal assessment, including foetal biometry and amniotic fluid estimation.
- Women with GDM have regular follow-up visits to monitor blood sugar levels, including four additional antenatal visits and four routine visits before delivery and during the sixth week postpartum.
- Women with known diabetes are monitored for kidney and eye functions, and those with uncontrolled blood sugar or other danger signs are referred to higher centres with an obstetrician available.

Frequency of monitoring

- Women are advised to do frequent self-monitoring of blood glucose levels to maintain their glucose levels on target.
- Ideally 7-point testing with all 3 premeal and 2-h postmeal glucose tests along with bedtime glucose is recommended, especially for all GDM on intensive pharmacotherapy with insulin.
- However, at least 4 glucose readings—daily fasting and 2 h after each meal—must be done to achieve optimal glycemic control.
- In limited care settings or in GDM well controlled on MNT weekly fasting and 2 h post meals may be done if intensive self-monitoring is not possible.
- Continuous glucose monitoring (CGM) where available and affordable/acceptable may be used as an adjunct to SMBG to assess glycemic variability, which may be associated with macrosomia (58).

Target glycemic control

In pregnancies complicated by diabetes, the goal has been to achieve glycaemia similar to non-diabetic pregnancies (Table 9). Maintaining a fasting plasma glucose level below 90 mg/dL helps prevent adverse outcomes such as macrosomia and preeclampsia, and neonatal hypoglycaemia is

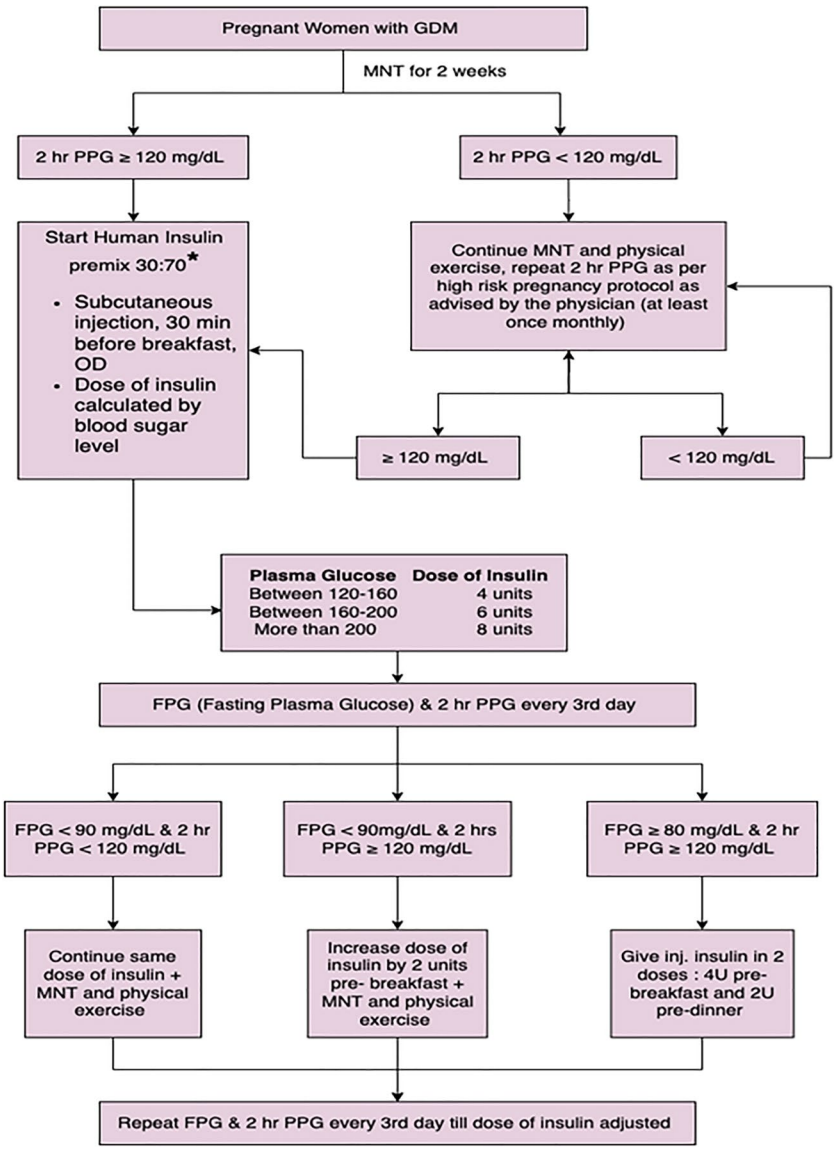


Fig. 10 Algorithm for insulin therapy in limited care setting. *Ideally in true GDM, it is the postprandial glucose levels that spike rather than fasting. These can be controlled with 1–3 doses of prandial insulin (short acting or rapid acting insulin) depending on the meal that needs to be targeted based on SMBG values. However, in limited resource or rural settings where analogue insulins are not feasible because of cost or availability, premix insulins may be initiated

not a concern in women with GDM.[61] Pregnant women are less likely to experience hypoglycaemia in response to insulin than non-pregnant individuals (Fig. 12).[62] The recommendation to maintain fasting plasma glucose at ≤ 95 mg/dL is not acceptable, but instead, the American College of Obstetrics and Gynaecology suggests fasting ≤ 90 mg/dL and 2-h postprandial glucose ≤ 120 mg/dL, which aligns with the DIPSI recommendation.[59]

Intrapartum care

Women with gestational diabetes who are undergoing medical management require close monitoring of their blood glucose levels during labour using a standardised glucometer. It is recommended that they deliver in a hospital setting vaginally if possible, unless there are obstetric complications or if the estimated foetal weight is greater than 4 kg, which may result in shoulder dystocia. However, early delivery prior to 39 weeks is not recommended due to the risk of delayed foetal lung maturity. If delivery is planned before 34 weeks and there is uncontrolled blood glucose or other obstetric indications, prophylactic corticosteroid therapy may be administered. Post-term pregnancy should be avoided. Women with uncontrolled blood glucose or those who require daily insulin doses of more than 20 U are referred to higher facilities for delivery planning. The insulin requirement may increase due to steroid therapy, which should be carefully monitored.

Immediate newborn care

Essential maternal and neonatal care is important for all GDM women (Fig. 13). All babies born to GDM mothers are evaluated for immediate hypoglycaemia (< 45 mg/dL) within the first hour of birth and at 4-h intervals using a glucometer until

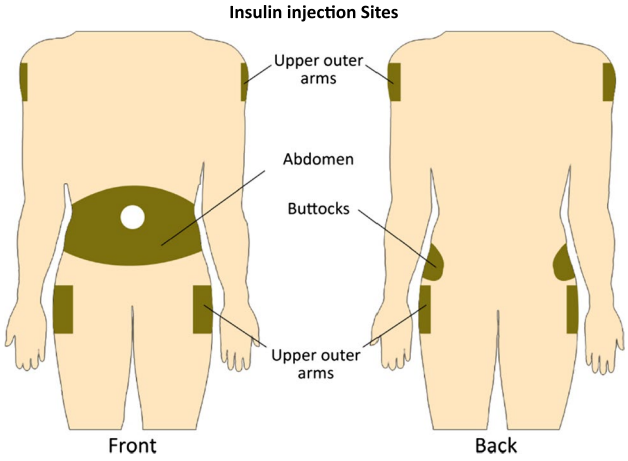


Fig. 11 Injection sites for insulin. In early pregnancy, they can inject anywhere in the abdomen. In late trimesters due to anxiety can inject insulin in the lateral aspect of abdomen

four stable readings of glucose values are achieved (≥ 45 mg/dL). In addition, newborns are monitored for respiratory distress, convulsions, and hyperbilirubinemia. Exclusive breastfeeding is promoted preferably by direct breastfeeding. In case blood sugar falls < 30 mg/dL, an infant is referred to a higher centre with 10% dextrose IV infusion drip (100 mL/kg/day) where a paediatrician is available.

Postpartum care

GDM mothers receive detailed clinical assessments and counselling about lifestyle modifications, future risks of T2DM, warning signs, exercise, and postpartum family planning before discharge. The guideline endorses GDM as part of the NCD program, and mothers are advised to have a postpartum follow-up test at 6 weeks to evaluate their glycemic status. Breastfeeding and lifestyle management are suggested for weight management and to avoid future risks of T2DM. Women with a history of GDM found to have prediabetes are encouraged to receive intensive lifestyle interventions and/or metformin. Postpartum care should also include psychosocial assessment and support for self-care. Regular annual follow-up screening for type 2 DM is recommended at various existing platforms, including NCD clinics, postpartum care clinics, and paediatric setups as per programmatic protocols.

Table 9 Target blood glucose level and birth weight

Target blood glucose levels should be that of normal pregnancy		
Fasting PG	*PPG*	*Mean PG level*
80 mg% ↑↓ 90 mg%	110 mg% ↑↓ 120 mg%	95 mg% ↑↓ 105 mg%

The goal is to obtain new-born babies' birth weight appropriate for gestational age between 2.5 and 3.5 kg (a step to prevent offspring developing diabetes in future)

Postpartum screening for glucose intolerance

Two-day postpartum glucose tolerance tests have similar diagnostic value as 4- to 12-week postpartum glucose tolerance tests in predicting impaired glucose metabolism and diabetes at 1 year after delivery and are associated with nearly 100% adherence to the test. Thus, changing the timing of the glucose tolerance test should be considered [60].

Management of complications of GDM

Gestational diabetes mellitus (GDM) during pregnancy results in high glucose levels that pose a minor but significant risk for poor outcomes and future obesity and glucose intolerance in children. Treatment focuses on nutrition, with medication like insulin or metformin if needed. Testing after delivery can assess future diabetes risk, and annual glucose and HbA1C testing can identify poor glycemic control that suggests future type 2 diabetes. Lifestyle changes are key to preventing or delaying diabetes, but drugs for diabetes prevention after GDM are debated. Family planning, breastfeeding, and healthy habits for children are recommended.[63]

Key points

- Early universal testing of all pregnant women for GDM.
- Testing is recommended thrice in pregnancy; at 1st antenatal visit/before 12 weeks and then at 24–28 weeks of gestation, and 32–34 weeks if needed.
- Single test procedure with 75 g GCT (glucose challenge test) to be performed.
- Pregnant women testing positive (2 h GCT ≥ 140 mg/dL) should be started on MNT for 2 weeks.
- If 2-h PPPG ≥ 120 mg/dL after MNT and physical exercise, medical management (= insulin therapy or metformin) of pregnant women is to be started as per guidelines.
- Pregnant women are be monitored by 2-h PPPG throughout pregnancy as per high-risk pregnancy protocol. Recommended 8 antenatal visits (4 additional visits) to be conducted during the pregnancy period (at least a monthly visit to be ensured).
- Pregnant women with GDM on insulin therapy with uncontrolled blood sugar levels (2-h PPPG ≥ 120 mg/dL) or insulin requirement > 20 IU/day should be referred for delivery to the centre, which has an obstetrician.
- GDM pregnancies are associated with a delay in lung maturity of the foetus, so routine delivery prior to 39 weeks is not recommended.

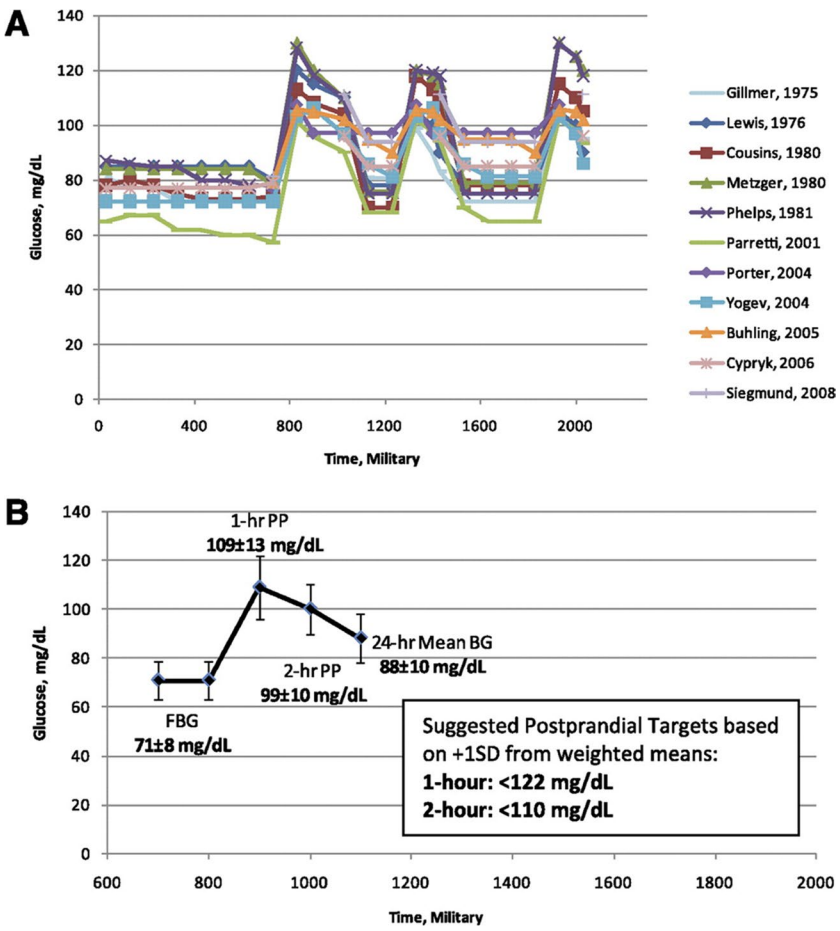


Fig. 12 **A**, **B** Pattern of glycaemia in normal pregnancy (adopted from Hernandez).[63]

- Early delivery with the administration of prophylactic corticosteroid therapy for foetal lung maturity is to be planned only if obstetrician and physician services are available.
- Vaginal delivery preferred, LSCS for only obstetric indications or foetal macrosomia—in the centre where obstetrician is available.
- Neonatal monitoring for hypoglycaemia and other complications.
- Postpartum evaluation of glycemic status by a 75-g OGTT at 6 weeks after delivery.

Conclusion

DIPSI is an accurate and practical tool for screening and diagnosing GDM, making it suitable for mass-scale testing in the community. Initiatives have been implemented to promote early diagnosis and treatment of GDM, ideally starting before conception and continuing throughout life. Women at risk for GDM should plan ahead of conception to minimise potential consequences. All women should be tested early in pregnancy and receive optimal care to ensure optimal glucose control throughout pregnancy.[52]

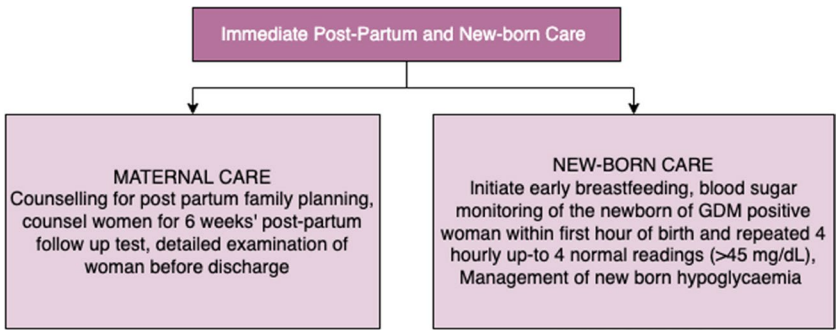


Fig. 13 Immediate post-partum and newborn care

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