Consensus on Use of Insulins in Gestational Diabetes

NIS-2016 Expert Group: Kalyan Kumar Gangopadhyay¹, JJ Mukherjee², RK Sahay³

Abstract

Introduction: Gestational Diabetes Mellitus (GDM), diabetes diagnosed during pregnancy is associated with maternal (caesarean delivery, hypoglycaemia, hyperbilirubinaemia, shoulder dystocia, pre-term delivery and birth trauma) and fetal (Hyperbilirubinaemia in offspring, Neonatal hypoglycaemia, Macrosomia) complications. Despite, insulin being the standard treatment for GDM cases, there is no existing comprehensive consensus update on use of insulin in Indian patients with GDM.

Objective: To provide simple and easily implementable guidelines to healthcare physicians on use of insulin in GDM.

Methods: Each consensus based on indications, choice of insulin regimen, titration and insulin therapy during intrapartum and postpartum was presented based on established guidelines and published scientific literature. These evaluations were then factored into the national context based on the expert committee representatives’ patient-physician experience in their clinical practice and common therapeutic practices followed in India for successful GDM management.

Results: Recommendations based on use of insulin in GDM has been developed. The key recommendations are: to monitor fasting plasma glucose (FPG) and 2-hour post prandial glucose PPG levels and the glycaemic targets are: FPG < 95 mg/dL and 2-hour PPG < 120 mg/dL, short- and intermediate acting human insulin are the first choice of insulin regimens, rapid-acting (Insulin Aspart or Lispro) may be considered, use basal/intermediate acting insulin at bedtime, if FPG>110 mg/dL. During intrapartum, start IV insulin infusion with hourly glucose monitoring. Those women who require insulin < 20 U over 24 hours prior to labor may not need interpartum use of insulin infusion and Insulin dosing is stopped after birth and capillary glucose monitoring for 24-48 hours.

Conclusion: We hope that the consensus based recommendations mentioned in this paper will be a useful reference tool for healthcare practitioners to achieve glycaemic targets in GDM patients.

Introduction

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. It is generally diagnosed at 24-48 weeks of gestational period. As per global estimates of hyperglycaemia in pregnancy, 20.9 million or 16.2% of live births to women were expected to have some form of hyperglycaemia during pregnancy; 85.1% of these cases were estimated to be due to GDM, 7.4% cases due to other types of diabetes first detected in pregnancy and 7.5% cases due to diabetes detected prior to pregnancy. Approximately 88% of hyperglycaemia cases in pregnancy have been reported from low and middle income countries; highest prevalence of hyperglycaemia in pregnancy aged 20-49 years were reported from South-East Asia region (24.2%) and the least prevalence from Africa (10.5%). In the US, there was a higher prevalence rate of GDM for African American, Hispanic, American Indian and Asian women in comparison to white population and have affected up to 8.7% of all pregnancies. In India, GDM has been estimated to affect over 4 million pregnant women. The prevalence of GDM has been reported to vary from 3.8% to 41% across different states of India; Kashmir (3.8%), Mysore (6.2%), Western India (9.5%), Tamil Nadu (17.9%), Punjab (35%) Lucknow (41%).

There are several risk factors, which steadily increases the prevalence of GDM in pregnant women; the most common factor was a history of macrosomia, type II diabetes mellitus (T2DM), spontaneous abortions and unexplained stillbirths, hypertension, GDM in previous pregnancy, obesity, sedentary lifestyle, increased caloric intake, ethnicity and age >25 years. Women with GDM have a high risk of gestational hypertensive disorders, including pre-eclampsia, eclampsia, gestational hypertension, primary caesarean section, preterm labor and also have an increased risk of developing T2DM later in life. They are also associated with an increased insulin resistance (due to alterations in growth hormones, reduced levels of estrogen and progesterone, decreased cortisol, human placental lactogen and insulinase secretion.

¹Consultant Endocrinologist, Fortis Hospital, Kolkata, West Bengal; ²Consultant Endocrinologist, Department of Endocrinology and Diabetes, Apollo Gleneagles, Kolkata, West Bengal; ³Professor, Department of Endocrinology, Osmania Medical College, Hyderabad, Telangana
Better patient outcomes.14 related complications and have reduce the prevalence of any GDM-control throughout pregnancy.9-13 But tight glycaemic and islet autoantibodies) during pregnancy (due to impaired beta cell function and impaired insulin secretion (pre-partum, intra-partum and birth trauma). Long-term neonatal complications include obesity, diabetes, delayed motor development, premenopausal breast cancer.15-17

Maternal hyperglycaemia in pregnancy can also cause perinatal complications like macrosomic babies (>4,500 g), still birth, hypoglycaemia, hyperbilirubinaemia, shoulder dystocia, pre-term delivery and birth trauma. Long-term neonatal complications include obesity, diabetes, delayed motor development, premenopausal breast cancer.15-17 In the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study, a positive correlation was reported between maternal hyperglycaemia and neonatal complications.18

Insulin is considered as the standard treatment for GDM cases when patients fail to achieve adequate glycaemic levels even after two weeks of medical nutrition therapy (MNT).1,19 It is added to MNT, if fasting blood glucose (FBG) ≤95 mg/dL, 1-hour and 2-hour post-meal glucose ≤140 and ≤120 mg/dL, respectively. It is very important to frequently monitor glycaemic levels during pregnancy and accurate and timely adjustments are made based on blood glucose (fasting, preprandial, 1-hour and 2-hour prandial, bedtime glucose) levels and the type of insulin used. Insulins which does not cross placenta for achieving tight glycaemic control throughout gestational period. The summary of available insulins and its classification as per FDA, European medicines agency (EMA) and Indian label is provided in Table 1.

**Table 1: Available insulins in GDM patients and classification as per FDA, EMA and Indian label guidance**

<table>
<thead>
<tr>
<th>Type of insulin</th>
<th>Time of onset</th>
<th>Peak time</th>
<th>Duration</th>
<th>FDA classification</th>
<th>EMA guidance</th>
<th>Indian label guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular insulin</td>
<td>30 min (U-100 &amp; U-500)</td>
<td>3 hours (U-100 &amp; U-500)</td>
<td>8hrs (U-100) Up to 24hrs (U-500)</td>
<td>B</td>
<td>Can be used</td>
<td>Can be used</td>
</tr>
<tr>
<td>Insulin Aspart</td>
<td>10-15 min</td>
<td>40-50 min</td>
<td>3-5 hours</td>
<td>B</td>
<td>Can be used</td>
<td>Can be used</td>
</tr>
<tr>
<td>Insulin Lispro</td>
<td>10-15 min (U-100 &amp; U-200)</td>
<td>30-90 min (U-100 &amp; U-200)</td>
<td>3-5 hours (U-100 B &amp; U-200)</td>
<td>B</td>
<td>Can be used</td>
<td>Can be used</td>
</tr>
<tr>
<td>Insulin Glulisine</td>
<td>10-15 min</td>
<td>55 min</td>
<td>3-5 hours</td>
<td>C</td>
<td>No clinical data</td>
<td>No adequate data</td>
</tr>
<tr>
<td>Insulin Detemir</td>
<td>1-2 hours</td>
<td>None</td>
<td>24 hours</td>
<td>B</td>
<td>Can be used</td>
<td>Can be considered</td>
</tr>
<tr>
<td>Insulin Degludec</td>
<td>1 hour (U-100 &amp; U-200)</td>
<td>None</td>
<td>24 hours (U-100 &amp; U-200)</td>
<td>C</td>
<td>No clinical data</td>
<td>No clinical experience</td>
</tr>
<tr>
<td>Insulin Glargine</td>
<td>1-2 hours (U-100) &gt;6hours (U-300)</td>
<td>42 hours at steady state (U-100&amp;U-300)</td>
<td>No human pregnancy data (previously C)</td>
<td>No clinical data</td>
<td>No clinical data</td>
<td></td>
</tr>
<tr>
<td>NPH insulin</td>
<td>1-2 hours</td>
<td>4-8 hours</td>
<td>10-20 hours</td>
<td>B</td>
<td>Can be used</td>
<td>Can be used</td>
</tr>
</tbody>
</table>

**FDA category not used after 30 June 2015.**

and increased maternal adiposity) and impaired insulin secretion (due to impaired beta cell function and islet autoantibodies) during pregnancy.9-13 But tight glycaemic control throughout pregnancy could reduce the prevalence of any GDM-related complications and have better patient outcomes.14

Though, there are multiple methods to initiate insulin like weight-dosing method (0.7-1 U/kg daily in divided doses), trimester plus weight based dosing (1st trimester, 2nd trimester, and 3rd trimester 0.7,0.8 and 0.9-1U/Kg, respectively) or single dose for all regimen (NPH 20U in morning and 20U bedtime; Aspart or lispro: 10U each at breakfast and dinner), there is no existing comprehensive consensus update on use of insulin in Indian patients with GDM. The proposed consensus plans to provide simple & easily implementable guidelines to health care physicians on use of insulin in GDM patients. To address this concern, a group of experts from across India held a consensus meeting in Delhi, India on 20 August 2016. The idea of consensus on use of insulin in GDM in current clinical practice was initiated by National Insulin Summit (NIS) group and was supported by Novo Nordisk India. The objectives of the meeting were to:

1. Evaluate the available guidelines on use of insulin in GDM
2. Examine the existing evidence on dosing and titration of insulin in GDM
3. Evolve consensus recommendations on use of insulin therapy in GDM (indications, choice of regimens and titrations) and on practicalities of insulin therapy (pre-partum, intra-partum and...
Methods

During the consensus meeting on use of insulin in GDM, the expert group committee proposed recommendations by consensus: Consensus 1 on use of insulin therapy in GDM (indications, choice of insulin regimen and titration) and Consensus 2 on practicalities of insulin therapy (pre-partum, intra-partum and post-partum) (Figure 1).

The consensus was proposed based on established guidelines (from globally recognised professional bodies as well as those published within India), prescribing information or summary of product characteristics for each insulin type and published scientific literature. These evaluations were then factored into the national context based on the expert committee representatives’ patient-physician experience in their clinical practice and common therapeutic practices followed in India. The evaluations were debated and discussed within the expert group committee. The final proposed consensus-based recommendations were proposed and collectively recorded in easily implementable steps, without any bias and in an as much possible unambiguous language.

The global and national guidelines and widely accepted and evaluated consensus statements (evaluated by the expert group) include: The American College of Obstetricians and Gynaecologists (written hence forth as ACOG 2013)\(^8\), American Diabetes Association Standard of Care 2016 (written hence forth as ADA 2016)\(^22\), consensus statement by AACE/ACE on the comprehensive T2DM management algorithm 2011 Executive Summary (written hence forth as AACE/ACE Consensus statement 2011)\(^23\), Global guideline for T2DM International Diabetes Federation (written hence forth as IDF 2015)\(^24\), NICE UK: Clinical Guidelines on Type 2 diabetes (written henceforth as NICE UK 2015)\(^25\), Canadian Diabetes Association guidelines (written hence forth as CDA-, 2013)\(^26\), Diabetes in Pregnancy Study Group (written hence forth as DIPSI 2006)\(^19\), South Australian (written hence forth as SA, 2015)\(^27\) and Queensland guidelines (written hence forth as Queensland, 2015)\(^28\).

Consensus 1 on Insulin Therapy in GDM; Indications, Choice of Insulin Regimen and Titration

Current place in guidelines

ADA, ACOG and AACE/ACE guidelines are in support of providing stringent glycaemic targets in pregnancy and recommended FBG levels ≤95 mg/dL (5.3 mmol/L) and 1-hour and 2-hour postprandial glucose concentration to be ≤140 mg/dL (7.8 mmol/L) and ≤120 mg/dL (6.7 mmol/L) respectively (ADA 2016; AACE/ACE 2011; ACOG 2013 22,23,8). All the guidelines, including ACOG, IDF, NICE and DIPSI recommended rapid-acting insulins (Lispro and Aspart) to be safe and effective in achieving targeted post prandial glucose (PPG) values during pregnancy since they do not cross the placenta.\(^8\),\(^22\),\(^23\),\(^25\)

According to ACOG 2013, the insulin is often added with nutrition therapy with the starting total dosage of 0.7–1.0 U/kg daily (in divided doses) when fasting plasma glucose (FPG) levels are persistently >95 mg/dL (5.3 mmol/L) and 1-hour and 2-hour postprandial glucose level are persistently ≥140 mg/dL (7.8 mmol/L) and ≥120 mg/dL (6.7 mmol/L), respectively. If both fasting and postprandial hyperglycaemia are present, multiple injections of intermediate- and short-acting insulins are administered. Regardless of the starting dosage, the dosage adjustments should be based on the blood glucose levels at particular times of the day.\(^8\)

IDF guidelines recommends initiation of insulin, if FPG ≥90 mg/dL (5 mmol/L) or postprandial plasma glucose (PPPG) ≥140 mg/dL (7.8 mmol/L) in 1-hour or ≥120 mg/dL (6.7 mmol/L) in 2-hours after 2 weeks of medical nutrition therapy and exercise. The usual recommendation is to use NPH or IDet as basal insulin. Besides rapid-acting insulins, premix insulin’s have been considered as convenient alternatives but lacked flexibility. The insulin doses were adjusted so as to address the elevated blood glucose levels; the doses were adjusted based on weekly self-monitoring of blood glucose (SMBG) and FPG and PPPG measurement every two weeks.\(^2\)

NICE guideline recommends individualised target for SMBG with due consideration of the risk of hypoglycaemia. The guideline recommended to maintain capillary plasma glucose (CPG) fasting level
Recommondations

NIS Expert Group Consensus Recommendations on use of insulin therapy in GDM: indications, choice of insulin regimen and titration

Recommendations on Targets
- Fasting < 95 mg/dL
- 2 hour postprandial < 120 mg/dL

Recommendations on Indication to Start Insulin?
- Known Type 1 (continue the insulin regimen) and Type 2 (shift to insulin)
- MNT to be initiated and glycaemic status reassessed after 2 weeks with the exception below.

2 hr FPG mg/dL Recommendations
- >200 mg/dL Initiate Insulin
- 160 – 200 mg/dL in 1st and 2nd trimester Consider MNT for 1 week. Insulin can be initiated if MNT fails
- >160 mg/dL in the 3rd trimester To start insulin immediately

Recommendations on Dosing Regimen
- Fasting and 2-hour post meals values are to be used for monitoring the glycaemic control
- It is advisable to monitor twice a day (vary time of monitoring) throughout the pregnancy
- Once targets are maintained for 2 weeks, consider monitoring on alternate days (ideally daily)

Recommendations on Choice of Insulin Regimen
- Preferable to start with prandial insulin (targeting the meal at which PP excursions exceed the target). Starting dose 4 units
- If FPG> 110 mg/dL, preferable to use basal /intermediate acting insulin at bed time
- In those patients where basal bolus regimen is not convenient for the patient, premix regimen may be considered keeping in mind the limitations of titration with premix insulin

Recommendations: Which Type of Insulin?
- Human Insulin remains the first choice – short acting and intermediate acting
- Rapid acting insulin analogues can be considered keeping convenience and affordability in mind

Recommendations on Titration of Basal and Bolus Insulins

<table>
<thead>
<tr>
<th>FPG * (mg/dL)</th>
<th>Dose adjustment (Units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal insulin</td>
<td></td>
</tr>
<tr>
<td>&lt; 70</td>
<td>-2</td>
</tr>
<tr>
<td>71–95</td>
<td>0</td>
</tr>
<tr>
<td>95–110</td>
<td>+2</td>
</tr>
<tr>
<td>110-140</td>
<td>+4</td>
</tr>
<tr>
<td>&gt; 140</td>
<td>+6</td>
</tr>
<tr>
<td>Bolus insulin</td>
<td></td>
</tr>
<tr>
<td>2 hr PPG*(mg/dL)</td>
<td>Dose adjustment (Units)</td>
</tr>
<tr>
<td>&lt; 99</td>
<td>-2</td>
</tr>
<tr>
<td>100-120</td>
<td>0</td>
</tr>
<tr>
<td>120-140</td>
<td>+2</td>
</tr>
<tr>
<td>140-160</td>
<td>+4</td>
</tr>
<tr>
<td>&gt; 160</td>
<td>+6</td>
</tr>
</tbody>
</table>

*Needs an individualized approach (hypoglycaemia, GI problems)

as 96 mg/dL (5.3 mmol/L) and 1-hour and 2-hour postprandial CPG as 140 mg/dL and 116 mg/dL (7.8 mmol/L and 6.4 mmol/L) respectively. For GDM patients who were on insulin or glibenclamide, CPG level should be maintained > 72 mg/dL (4 mmol/L). 25

The Indian DIPSI guidelines recommends insulin initiation after MNT, for 2 weeks, has failed to achieve the glycaemic control and FPG level ≥ 90 mg/dL (5 mmol/L) and/or 1 ½ hour PPG ≥ 120 mg/dL (6.7 mmol/L). The mean plasma glucose level should be maintained at ~105 mg/dL (5.8275 mmol/L) [ideal for good fetal outcome] and it is possible if FPG and PP peaks are around 90 mg/dL (5 mmol/L) and 120 mg/dL (6.7 mmol/L) respectively. Few GDM patients may require a combination of short-acting and intermediate-acting insulins in the morning and evening. 25

Published scientific literature

Choice of insulin regimen

Insulin analogues are preferred over NPH in the management of GDM as the former are unable to cross placenta, have a rapid onset of action, less maternal hypoglycaemia and early loss and skeletal defects than other regular insulins. 26 In 2007, Mathiesen et al reported statistically significantly greater reduction in PPG when Aspart as compared with NPH in pregnant women with T1DM (In visit 1=6.82 Vs.6.82 mmol/L, p=0.044, Visit 2=6.96 Vs.7.10 mmol/L, p=0.0007, Vist 3 6.23 Vs. 6.58, p=0.153). 27

In 2008, Hod et al compared insulin Lispro with regular insulin in a randomized parallel group study where insulin Lispro, against regular insulin, was associated with near-normalization of 1-hour PPG and normal anthropometric characteristics. 28 In 2 randomized trials, IDet was compared with NPH in GDM patients and IDet was associated with significantly greater reduction in FPG and hypoglycaemic events when compared to NPH.[31,32] In another randomized, open-label, parallel group trial, to acess the efficacy and safety of biphasic insulin Aspart (BIAsp 30) including 323 women with GDM which were randomly assigned to receive 6 U of either BIAsp 30 or biphasic human insulin (BHI 30) in a 1:1 ratio, the trial reported that the incidence of macrosomia was found to be lower with the use of 6 U of BIAsp 30 (6.3%) against BHI 30 (6.9%) in GDM patients; however the difference was not statistically significant pregnant women. Additinally, BIAsp 30 offered greater treat-to-target potential for pregnant women. 29

Titration of Insulin

In cases of FPG > 90 mg/dL (5 mmol/L), NPH/IDet/IGlar should be given and the bed time doses should be adjusted depending upon the FPG
levels; the dose is reduced by 2U if FPG is < 75.6 mg/dL (4.2 mmol/L); no dose change if FPG is 75.6-88.2 mg/dL (4.2-4.9); dose increased by 1U, 2U, 4 U and 6 U, if the FPG level is 90-95.4 mg/dL (5.0-5.3 mmol/L), 97.2-108 mg/dL (5.4-6.6 mmol/L), 109.8-144 mg/dL (6.1-8 mmol/L) and > 144 mg/dL (8 mmol/L), respectively.

If the PPG > 140.4 mg/dL (7.8 mmol/L), then regular insulin/rapid-acting insulin analogs should be given before meals. If 1-hour PPG is 99 mg/dL (5.5 mmol/L), then pre-meal insulin dose should be decreased by 2 U, no change in present pre-meal dose if PPG is 100.8-129.6 mg/dL (5.6-7.2 mmol/L); pre-meal dose is increased by 1U and 2 U, if 1-hour PPG is 129.6-180 mg/dL (7.2-10.0 mmol/L) and 180 mg/dL (10 mmol/L), respectively.

Consensus 2 on Practicalities of Insulin Therapy; Pre-Partum, Intra-Partum and Post-Partum

Pre-partum

The SMBG, both fasting and postprandially, should be performed to achieve glycemic targets and improve pregnancy outcomes. If women with GDM do not achieve glycemic targets within 2 weeks from nutritional therapy alone, insulin therapy should be initiated. Insulin therapy in the form of multiple injections should be used and strive for target glucose values: FPG < 96 mg/dL (5.3 mmol/L) 1-hour and 2-hour postprandial < 140 mg/dL (7.8 mmol/L) and < 120 mg/dL (6.7 mmol/L), respectively. Rapid-acting bolus analogue insulin may be used over regular insulin for PPG control, although perinatal outcomes are similar.

Intrapartum

Intrapartum is the period from onset of labor to end of 3rd stage of labor. During the latent phase of labor, the requirement of insulin is stable as the hepatic glucose supply is sufficient but during the active phase, the hepatic glucose supply and insulin requirement declines. During peripartum period (starts from last month of gestation to first few months after delivery), the main aim is to avoid maternal hyperglycaemia as it further increases the incidence of neonatal hypoglycaemia and fetal academia. Continuous monitoring of blood glucose during labor has shown to improve clinical outcomes of both mother and baby. Short or rapidly acting insulin analogues are preferred in GDM as they prevent postprandial excursions and cause less incidence of hypoglycaemia. The insulin requirement is directly proportional to the patient’s current glycaemic levels; a higher dose of insulin is required during labor in cases of uncontrolled sugars during pregnancy and a lower dose if the patient has a good glycaemic control during pregnancy. In clinical practice, 6-8 U of insulin along with 5% dextrose solution is given according to a patient’s requirement. In cases where GDM is controlled by lifestyle modification, blood glucose should be monitored once in every 6-8 hours during labor and every 1-2 hourly in cases which were on insulin; in both cases the blood glucose levels (BGL) should be maintained between 80 and 110 mg/dL (4.4-6.1 mmol/L).

Current place in guidelines

Both ACOG and ACE guidelines recommend maintenance of blood glucose between 70 and 110 mg/dL (3.9-6.1 mmol/L) during labor.

The South Australian Guidelines has set up the management procedure for obtaining and maintaining physiological blood glucose during labour and birth and for caesarean section (peri-operatively) of women with Type 1 or Type 2 diabetes. If blood glucose is ≥ 144 mg/dL (10 mmol/L), it is recommended to set up an infusion of 5% glucose (has to be taken on opposite arm of the infusion) and infuse it at the rate of 100 mL/hour. The insulin (short-acting insulin) infusion pump is set at the rate of 2U per hour (2 mL/hour), which would gradually bring blood glucose within the physiological range. The blood glucose should be checked hourly or two hourly and units of insulin/hour may need to be changed (between 1 and 3 U) based on BGL.

CDA 2013 recommends that women should be closely monitored during labour and delivery, and maternal BGL should be kept between 72-126 mg/dL (4.0-7.0 mmol/L) in order to minimize the risk of neonatal hypoglycaemia. Additionally, they should receive adequate glucose during labour in order to meet their high-energy requirements and monitored hourly or two hourly to titrate insulin infusion rate accordingly.

Published scientific literature

Metzer and Alsayari developed a protocol where the initial insulin infusion rate was based on patient’s TDD. On the morning of induction or Caesarean section, 5g/hour of glucose was infused in the form of dextrose 10% at 50 mL/hour. If BGL was more than 81 mg/dL (4.5 mmol/L), insulin infusion was initiated. The insulin dose is adjusted hourly; if BGL < 72 mg/dL (4 mmol/L), the insulin dose is reduced quickly and at 54 mg/dL (3 mmol/L), the insulin was stopped. Women who delivered during 2004-2006 and were treated with an insulin dose ≥ 30 units/day prior to labour and were managed with an intra-partum protocol were included in the study. Out of 86 pregnancies, 80 women were evaluated. They received glucose infusion at a rate of 5g/hour as 10% dextrose in water and an insulin infusion using ½ of the TDD/24 as the initial hourly rate, if the CBGM≥101 mg/dL (5.5 mmol/L) and adjusted to maintain glucose level between 81-99 mg/dL (4.5-5.5 mmol/L). Insulin infusion was stopped at placental delivery and glucose was increased to 10g/hour until glucose was >99 mg/dL (5.5 mmol/L). The results of the study report that this simple protocol was able to safely maintain the glycaemic levels in GDM patients with minimal hypo- or hyper-glycaemic risk to mother and offspring.
sugar levels between 4-8 mmol/L (72 and 144 mg/dl). Hence, there should be a stringent blood glucose monitoring for tight glycaemic regulation.38

**Postpartum**

A postpartum period or postnatal period is the period beginning immediately after the birth of a child and extending for about six weeks. During child’s birth, there may be a rapid increase in the placental hormones like glucagon, growth hormone, epinephrine, which causes insulin resistance and hyperglycaemia. Hence, BGL should be continuously monitored during postpartum period and accordingly the insulin dose needs to be adjusted [Kalra and Anakal 2013 35]. Approximately 10-15% of women develop diabetes within 5 years of delivery.39 After delivery, patient should be advised for lifestyle modification and should have oral glucose tolerance test (OGTT) test after 6 weeks of delivery to see the glycaemic level.

**Current place in guidelines**

The Queensland 2015 guideline recommend to cease metformin and/or insulin immediately after child’s birth. It is recommended to monitor BGL four times (preprandial and before bed) in first 24 hours after birth. If PPG is between 72-126 mg/dL (4-7 mmol/L), further BGL monitoring is not required. If BGL < 72 mg/dL (4 mmol/L) or has intolerability in diet, the patient should seek medical review and consider IV fluid 12 hourly. If PPG > 126 mg/dL (7 mmol/L), the patient should seek medical review and continue blood glucose monitoring. A lower dose of insulin (against the dose prescribed in pregnancy) may be prescribed, if indicated. If BGL is ≥72 mg/dL (4.0 mmol/L) and diet is tolerated, then cease mainline IV fluids after birth.28

The medical review and BGL monitoring need to be continued, If BGL>126 mg/dL (7.0 mmol/L) and if insulin therapy is required recommended dosing is lower than prescribed in pregnancy.

**CDA 2013 recommends** that women with GDM should be encouraged to breastfeed immediately after delivery in order to avoid neonatal hypoglycemia and to continue for at least 3 months postpartum in order to prevent childhood obesity and reduce risk of maternal hyperglycemia. Women should also be screened with a 75 g OGTT between 6 weeks and 6 months postpartum to detect prediabetes and diabetest.26

**IDF recommends to initiate insulin treatment if the patient has** FPG ≥126 mg/dL (7.0 mmol/L), 2-hour PPG ≥200 mg/dL (11.1 mmol/L) and random blood glucose ≥ 200 mg/dL (11.1mmol) and repeat OGTT after 6-8 weeks, in case of normal sugar levels.24

**Published scientific literature**

There is a strident decline in insulin after delivery and BGL monitoring should be continued to see the sugar levels in the postpartum period. About 15% of GDM cases develop T2DM in the postpartum period; hence both FPG and PPG should be checked to diagnose T2DM. The dose of insulin should be adjusted during lactation due to a higher risk of hypoglycaemia.25

**Recommendations**

<table>
<thead>
<tr>
<th>NIS Expert Group Consensus Recommendations on Practicalities of Insulin in GDM; Intra-Partum and Post-Partum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-partum</strong></td>
</tr>
<tr>
<td>• At the time of admission, it is recommended to stop Metformin.</td>
</tr>
<tr>
<td>• At the time of labor, DNS or 5% dextrose at 100 mL/hr to be infused (type of fluid and rate of infusion can be individualized based on patient profile).</td>
</tr>
<tr>
<td>• In the ideal situation, start IV insulin infusion with hourly glucose monitoring based on IV sliding scale.</td>
</tr>
<tr>
<td>• If continuous IV insulin infusion is not feasible, add insulin in 500 ml of 5% dextrose/ DNS (each bag of 500 ml over 5 hours to have ¼ of the total subcut insulin dose requirement at the time of admission).</td>
</tr>
<tr>
<td>• Monitor capillary glucose 2 hourly and adjust insulin accordingly.</td>
</tr>
<tr>
<td>• Those requiring &lt; 20 U over 24 hrs prior to labor may not need intrapartum use of Insulin infusion.</td>
</tr>
</tbody>
</table>

**Post-partum**

- Stop insulin after delivery
- Monitor capillary glucose for 24-48 hours.
- In patients with T1DM and T2DM, start insulin at a lesser dose than their previous requirement and titrate depending on monitored values.

**Conclusion**

GDM represents a global health burden effecting a significant number of live births. The adequate glycaemic control is essential in GDM as maternal hypoglycaemic levels can cause neonatal complications. Insulin remains a standard treatment option for management of GDM when patients fail to achieve adequate glycaemic levels even after two weeks of MNT. The consensus based recommendations mentioned in this paper are based on the existing guidelines on insulin regimen in GDM and published literature. Collated review of the recommendations presented in this consensus on use of insulin therapy in GDM can be further simplified as follows:

- FPG and 2-hour PPG levels should be monitored and the glycaemic targets are: FPG < 95 mg/dL (5.2725 mmol/L) and 2-hour PPG < 120 mg/dL (6.66 mmol/L)
- Short-and intermediate acting human insulin is the first choice of insulin regimen. Rapid-acting (IAsp or Lispro) may be considered
- Use basal/intermediate acting insulin at bedtime, if FPG>110 mg/dL (6.105 mmol/L)
- During intrapartum, start IV insulin infusion with hourly glucose monitoring. Those women who require insulin < 20 U over 24 hours prior to labor may not need interpartum use of insulin infusion
- Insulin dosing is stopped after birth and capillary glucose monitoring for 24-48 hours

The strength of the current consensus is that it has been developed with due considerations
to national context based on experience and common therapy practices in India while drawing on recommendations from globally acceptable guidelines and relevant clinically published evidence. The final proposed consensus-based recommendations were collectively recorded in easily implementable steps, without any bias and in an as much possible unambiguous language. We hope that these consensus recommendations will be a useful reference tool for physicians and that their impact will be validated through observational research in real-life practice, involving large number of physicians and in the setting of routine outpatient care of GDM in India.

Acknowledgement

The authors thank the following members of the expert group committee for their comments and suggestions during the workshop: Dr PV Rao, Dr VG Nadagouda, Dr R Mahendran, Dr BN Ravi Kumar, Dr Yogeesh R, Dr Ajay Rotte, Dr Prahalad Kelavkar, Dr Sonali Patange, Dr Deepak Raisingani, Dr Khel Shankar Bharadwaj, Dr Parikshit Goswami, Dr Rahul Arora, Dr Hiranmoy Paul, Dr Saumya Sen Gupta, Dr Mohamed Raneesh P, Dr Sivabalamarugan, Dr Rajiv Gupta, Dr Lily Khosa.

The authors thank Novo Nordisk India Pvt Ltd for supporting the conduct of the consensus meeting & providing writing assistance in the development of this manuscript.

References