



Gestational Diabetes Mellitus: A Growing Concern

GDM, the leading cause of diabetes in pregnancy, affected about 21 million live births¹

- One in seven births is affected by gestational diabetes mellitus (GDM)
- Proportion of women with GDM is 85.1%
- Proportion of women with diabetes first detected in pregnancy is 7.4%
- Proportion of women with diabetes detected prior to pregnancy is 7.5%



Untreated GDM are associated with short- and long-term complications

- Macrosomia which is common in GDM women who is not diagnosed and treated affects around 15–45% of newborns²
- GDM is associated with a fourfold increased risk of stillbirth and death in the first week of life³
- Women with GDM are at an increased risk of pre-eclampsia³
- Hyperglycaemia in GDM increases the risk of early labour and delivery³
- About 50% of women with GDM develop type 2 diabetes within 5 years of pregnancy⁴
- Children born to women with GDM are at eightfold increased risk of developing type 2 diabetes in their early childhood or adolescence⁴
- Children born to women with GDM are at increased risk of hypoglycaemia, respiratory distress syndrome and other complications⁵

Universal screening for GDM

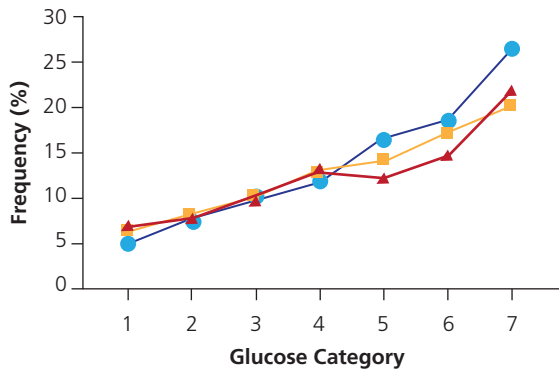
- Hyperglycemia and Adverse Pregnancy Outcome (HAPO), an international prospective cohort study, which involved ~25,000 pregnant women who underwent a 75 g oral glucose tolerance test (OGTT) and assessed the perinatal outcome measures, demonstrated the risk of adverse pregnancy outcomes increased continuously with glucose levels⁶
 - With increasing maternal glucose levels, the frequency of each primary outcome including birth weight above the 90th percentile, primary cesarean section, clinical neonatal hypoglycemia and cord-blood serum C-peptide level above the 90th percentile increased, however, it is less for clinical neonatal hypoglycemia as compared with the other outcome measures
 - The fasting plasma glucose level frequencies in the lowest and highest categories, respectively, were 5.3% and 26.3% for birth weight above the 90th percentile, 13.3% and 27.9% for primary cesarean section, 2.1% and 4.6% for clinical neonatal hypoglycemia and 3.7% and 32.4% for cord-blood serum C-peptide level above the 90th percentile.

Women with GDM and children born to women with GDM are at an increased risk of type 2 diabetes mellitus

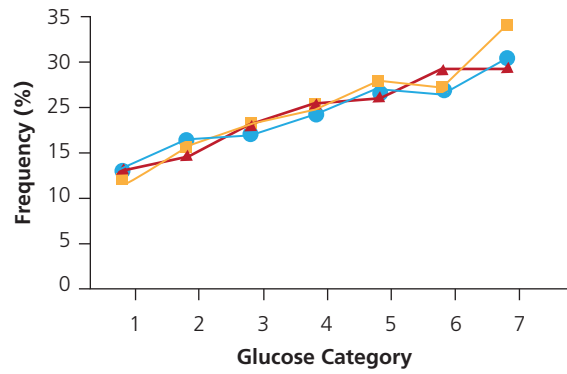
Glycaemic targets in pregnancy^{7,8}

- Stringent glycaemic control can be considered in pre-gestational diabetic women

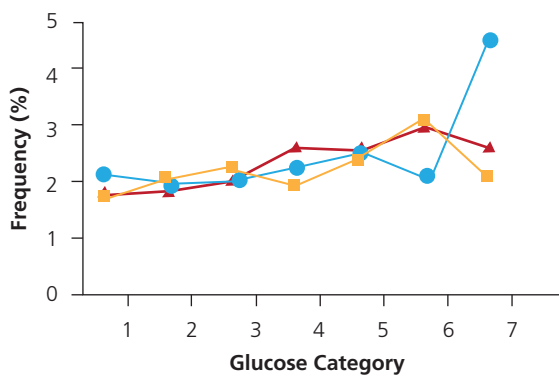
A Birth Weight >90th Percentile



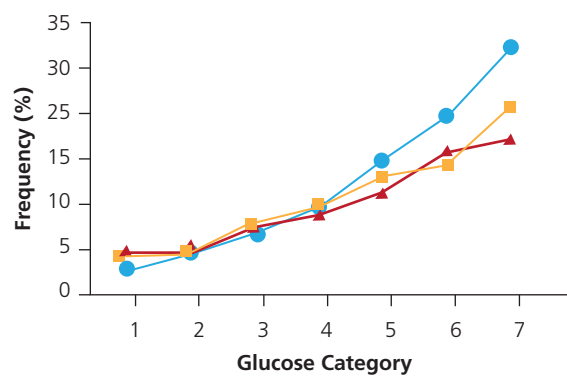
B Primary Cesarean Section



C Clinical Neonatal hypoglycemia



D Cord-Blood Serum C Peptide >90th Percentile



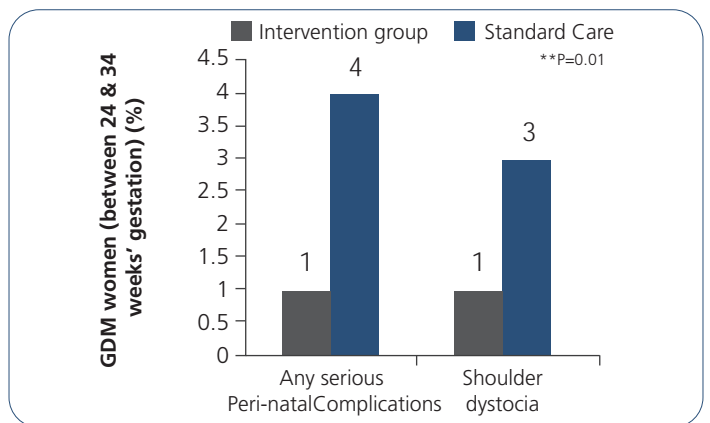
Based on the HAPO study results, many guidelines including IDF and IADPSG advocated universal screening for GDM at 24-28 weeks' gestation

- The primary measure used for assessing glucose levels during pregnancy is self-monitoring of blood glucose (SMBG)
- The recommended targets for SMBG are shown on-screen
- A1C should be used as the secondary measure. The recommended A1C target in pregnancy is, <6% if this can be achieved without hypoglycaemia

Strict glycaemic control improve maternal and neonatal outcomes

- Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) trial, a multicenter trial, evaluated the effects of treatment on peri-natal complications and maternal outcome⁹

- A total of 1000 women who were between 24 and 34 weeks' gestation and had GDM were randomized into the intervention group that received dietary advice, glucose monitoring and insulin as needed, and the other group received routine standard care practiced at the centre
- The trial demonstrated that the rate of serious perinatal complications was significantly lower among the infants of the intervention group than among the infants of the routine-care group.



Guidelines	Fasting	Pre-meal	1-h postprandial (mmol/L)	2-h postprandial (mmol/L)
ADA: Pre-gestational diabetes		60-69 mg/dL (3.3 - 5.4 mmol/L)	100-129 mg/dL	(3.4-7.1 mmol/L)**
ADA: GDM	≤95 mg/dL (5.3 mmol/L)		≤140 mg/dL (7.8 mmol/L)	≤120 mg/dL (6.7 mmol/L)
ACOG: GDM	≤90 mg/dL (5 mmol/L)	≤105 mg/dL (5.8 mmol/L)	≤140 mg/dL (7.8 mmol/L)	≤120 mg/dL (6.7 mmol/L)

** Peak postprandial glucose

- Although both the groups had comparable rates of caesarean delivery, women in intervention group had consistent improved health status at 3 months post-partum

Treating pregnant women with mild GDM reduces the perinatal complications

Majority of GDM can be managed by lifestyle modifications alone

- Once diagnosed, all patients should receive extensive diet and exercise counseling
- It has been estimated that 70–85% of GDM can be managed with lifestyle modifications alone¹⁰
- If treatment targets are not met, usually within 1–2 weeks, pharmacotherapy should be initiated
- As per the ADA and ACOG guideline recommendation, initiation of insulin therapy is to be based on measures of maternal glycaemia^{7,8}
- Glyburide and metformin are considered safe and effective; however, long-term safety data are inadequate.

ADA

- Initiation of insulin therapy to be based on assessment of maternal glycaemia with or without monitoring the foetal growth characteristics

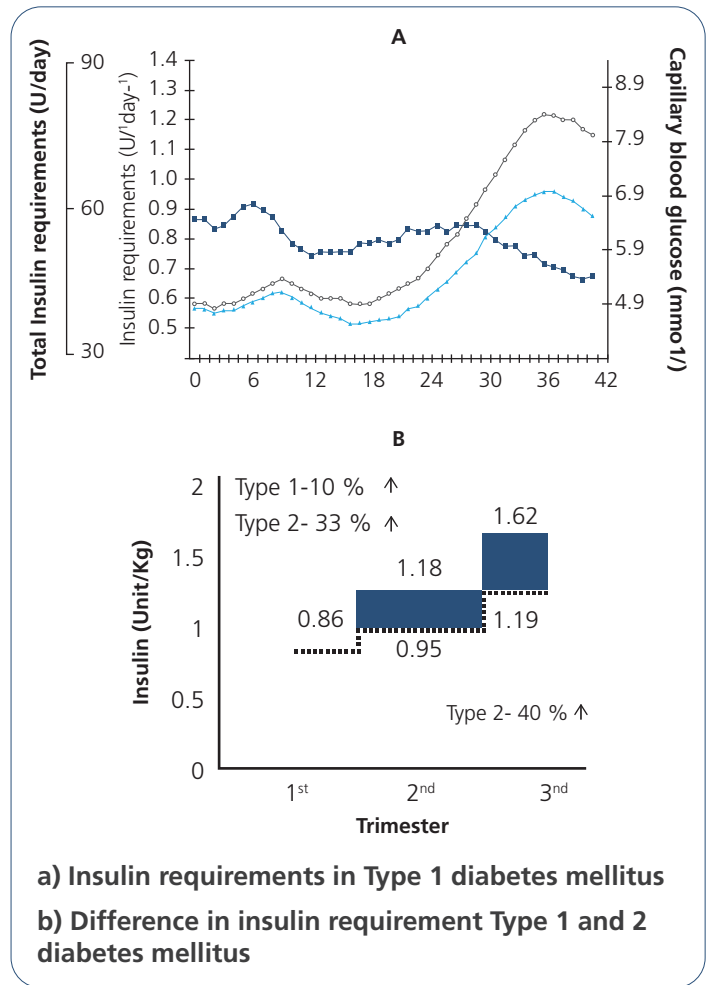
ACOG

- Insulin therapy is based on the assessment of maternal glycaemia, fasting, 1 hour and 2 hour plasma glucose levels
- Glyburide and metformin can be considered

Insulin requirement vary during pregnancy¹¹

- In a pregestational type-1 diabetes woman, during the 10–14 weeks' gestation, the requirement of insulin may decrease due to increased insulin sensitivity
 - During the later half of pregnancy, insulin requirement increases due to the increased concentration of circulating placental hormones (see Figure a)
- As compared to type 1 diabetes, type 2 diabetes women require a significantly higher dose of insulin during each trimester (as shown in Figure b)
- Although there is no difference in insulin requirement between type 1 and type 2 diabetes women during the first trimester, the insulin requirement significantly increases during the second trimester with type 2 diabetes (33%) as compared with type 1 diabetes (10%)
- In the third trimester, the insulin requirement continues to increase reaching a total increment of 40% in patients with type 2 diabetes
- This leads to the sudden increase in body mass and heightened insulin resistance in type 2 diabetes women during pregnancy
- As a result, constant insulin adjustment is necessary to keep up with the increasing insulin requirement of pregnancy

- With the available efficacy and safety evidence with the various insulin products, it is reasonable to utilize any of the insulin products (regular, NPH, or one of the analogs) in the management of GDM¹²



- Providers can select a product and delivery form (pen or vial and syringe) based on the patient's needs³
- It is vital for patients to be screened for type 2 diabetes between 6 weeks and 6 months postpartum³
- If treatment is required, the safety of pharmacotherapy during breastfeeding must be considered³

- Lifestyle modifications are quintessential in the management of GDM along with the pharmacotherapy
- Maintaining optimized glycaemic control can reduce perinatal complications

1. International Diabetes Federation. Diabetes Atlas. 2015. Available from <http://www.diabetesatlas.org/>. Accessed on 27th Oct 2016. 2.
2. Kc K, Shakya S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. *Annals of nutrition & metabolism*. 2015;66 Suppl 2:14–20.
3. Kim C. Gestational diabetes: risks, management, and treatment options. *International Journal of Womens Health*. 2010;2:339-351
4. Kim C, Newton KM, Knopp RH. Gestational Diabetes and the Incidence of Type 2 Diabetes: A Systematic Review, *Diabetes Care* 25, 2002.
5. Clausen TD, Mathiesen ER, Hansen T, et al. High prevalence of type 2 diabetes and pre-diabetes in adult offspring of women with gestational diabetes mellitus or type 1 diabetes the role of intrauterine hyperglycemia. *Diabetes care*. 2008;31(2):340–346
6. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2008;358(19):1991–2002.
7. American Diabetes Association. Standards of Medical Care in Diabetes-2016. *Diabetes care*. 2016;34(1):S1-S112.
8. Simmons D, McElduff A, McIntyre H, Elrishi M. Gestational Diabetes Mellitus: NICE for the U.S.? A Comparison of the American Diabetes Association and the American College of Obstetricians and Gynecologists Guidelines With the U.K. National Institute for Health and Clinical Excellence Guidelines: Response to Holt et al. *Diabetes Care*. 2010;33(3):e48-e48.
9. Crowther C, Hiller J, Moss J, McPhee A, Jeffries W, Robinson J. Effect of Treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes. *New England Journal of Medicine*. 2005;352(24):2477-2486.
10. American Diabetes Association. Management of diabetes in pregnancy. Standards of medical care in diabetes—2015. *Diabetes Care* 2015;38(1):S77–9. <http://dx.doi.org/10.2337/dc15-S015>
11. Balaji V, Seshiah V. Management of diabetes in pregnancy. *J Assoc Physicians India*. 2011;59 Suppl:33-6.
12. [Accessdata.fda.gov/Drugs@FDA: FDA Approved Drug Products \[Internet\]](http://www.accessdata.fda.gov/Drugs@FDA: FDA Approved Drug Products [Internet].). 2015 Available from: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>