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Early Gestational Glucose Intolerance (EGGI) Diagnosis and Prevention of Diabetes

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The NIH recommends screening at the 10th week of pregnancy because the fetal beta cell begins insulin secretion at the 11th week of gestation. Abnormal prandial glycaemic levels may stimulate beta cell secretion. According to the pattern of glycemia in normal pregnancy, if the postprandial blood sugar (PPBS) in the 10th week is greater than 110 mg/dl, it predicts gestational diabetes mellitus (GDM)[1]. Therefore, it is important to bring blood glucose levels to less than 110 mg/dl, as fetal beta cells start secreting insulin around 10-11 weeks, which leads to changes in maternal metabolism[2]. Given this background, there is a need to lower the cut-off to detect glucose intolerance, especially in the early weeks of pregnancy. With this in mind, a practical sub-categorization of glucose intolerance in pregnancy has been proposed (Table 1)[3]. The DIPSI Diabetes in Pregnancy Study Group in India, a pioneer in developing the DIPSI Test, has suggested conducting universal screening earlier in pregnancy, around the 8th to 10th weeks, to predict the risk of gestational diabetes (GD). This early prediction allows for the introduction of metformin and specialized medical nutritional treatment for women with glycemic abnormalities in the latter part of the first trimester[3].

Category	Cut-off values	Associated risks
GDM	2-hour BG ≥140 mg/dL	Adverse pregnancy outcome and future T2DM
Gestational Glucose Intolerance (GGI)	2-hour BG >120 mg/dL and <140/dL	Adverse Pregnancy Outcome and Future T2DM
Early Gestational Glucose Intolerance (EGGI) (8^{th} - 12^{th} weeks)	2-hour BG >110mg/dL	Prone to develop GDM

TABLE 1: Sub-categorization of glucose intolerance in pregnancy.

GDM- gestational diabetes mellitus; GGI- gestational glucose intolerance; EGGI- early gestational glucose intolerance; BG- blood glucose; T2DM- type-2 diabetes mellitus

Credit: V Seshiah

Why are Indians more prone to Type 2 Diabetes mellitus (T2DM)?

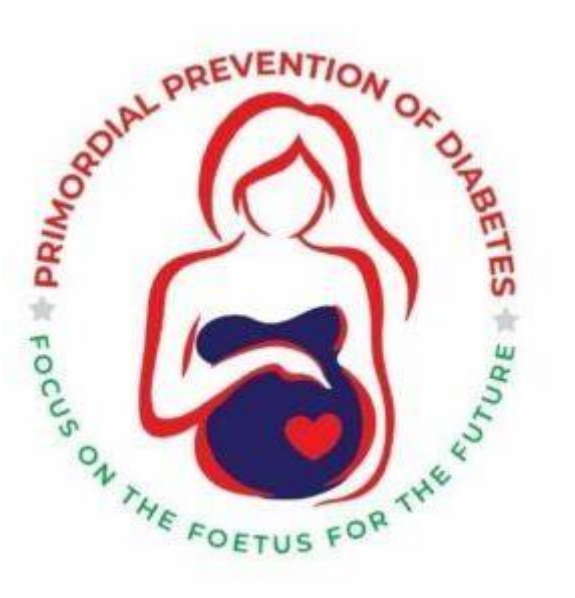
The typical South Asian Phenotype has the following features, which makes them more prone to Type 2 Diabetes mellitus.

1. Low birth weight – "Thin, fast Indian." (FTO)[4]
2. Lower age of onset.
3. Lower threshold for BMI.
4. Increased serum insulin levels and insulin resistance.
5. Rapid decline in beta cell function.
6. Characteristic dyslipidemia – low HDL cholesterol, elevated Triglycerides, and small dense LDL.
7. Low levels of adiponectin.
8. Increased level of inflammatory markers – High sensitivity – C-reactive protein (Hs-CRP), IL-6
9. Low muscle mass.
10. Increased abdominal obesity and visceral fat
11. Increase Steatotic liver disease (SLD) (old terminology – non-alcoholic fatty liver disease- NAFLD).

Guidelines currently recommend standard screening for gestational diabetes mellitus (GDM) at 24–28 weeks of pregnancy, with early screening offered to those deemed high-risk. The International Federation of Gynaecology and Obstetrics (FIGO) strongly recommends that all pregnant women undergo early screening for hyperglycemia during pregnancy using a Single Test procedure[5]. The Diabetes in Pregnancy Study Group of India (DIPSI) recommends universal screening for all pregnant women during the first trimester using a simple, cost-effective, and feasible Single Test procedure involving a 75-gm glucose challenge to diagnose GDM[6]. DIPSI's guideline captures pregnant women with high insulin resistance as reflected in the Postprandial Blood Glucose ≥140 mg/dl. The IADPSG Guidelines recommend that GDM be diagnosed if any one value is abnormal in OGTT, but the diagnosis can only be made if OR=1.5 is implemented rather than 1.75 [7].

A study from Italy that used both DIPSI and IADPSG criteria in the same pregnant women found that both guidelines had almost the same prevalence but missed cases of GDM due to different criteria [8]. In a multi-centric study including India with a high incidence of hyperglycemia during pregnancy, the Towards a

Better Outcomes in Gestational Diabetes Mellitus (TOBOGM) study emphasizes the critical importance of early screening at the beginning of pregnancy, followed by tailored interventions for identified GDM cases. The study found a 24.9% adverse neonatal outcome rate in the immediate treatment group and a 30.5% rate in the control group, although after adjustment, the risk difference was non-significant [9]. In Nigeria, Africa, a cross-sectional comparison of universal and selective risk factor-based screening for GDM found that selective risk factor-based screening missed 31.11% of patients with GDM compared to universal screening using a 75g oral glucose tolerance test OGTT [10]. There's an interest in investigating if a similar scenario exists for GDM when screening is limited to high-risk patients [11].



Picture 1: Primordial Prevention of Diabetes

There is a pressing need to differentiate Early Gestational Glucose Intolerance (EGGI) from eGDM diagnosis (<24 weeks or average gestational age of 15.6 ± 2.5 weeks in the TOBOGM study). In contrast, the usual practice is to diagnose after 24 weeks. This differentiation is crucial and should be a priority in maternal and fetal health care.

In summary, the evidence and experiences we have presented strongly advocate for the implementation of universal Early Gestational Glucose Intolerance (EGGI) By 10thWeek of gestation with ≥110 mg/dl value, timely identification and intervention with MNT & Metformin can significantly improve pregnancy outcomes.

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