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SHORT ARTICLE

DIPSI 2024 — Delhi Declaration — A futuristic approach towards primordial prevention of diabetes

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Abstract
Gestational diabetes mellitus (GDM) has conventionally been defined as any degree of glucose intolerance with onset or first recognition during pregnancy (Hinkle et al. in Sci Rep 8:12249, 2018). GDM has both short-term as well as long-term adverse materno-fetal consequences and increases the risk of future non-communicable diseases (NCDs), including type-2 diabetes. Probable epigenetic changes in children exposed to hyperglycemia in-utero predispose them to an increased risk for developing insulin resistance, obesity, type-2 diabetes, and associated NCDs in later life. Therefore, early detection and optimum management of GDM can go a long way in combating this rising epidemic of NCDs. It is pertinent to screen all pregnant women for glucose intolerance in pregnancy with the simple, economical and reliable single step test recommended by DIPSI and approved by the Ministry of Health & Family Welfare Government of India. An optimized strategy to achieve euglycemia can prevent the epidemic of NCD. Gestational programming is a distinctive process. The adverse stimuli (like hyperglycemia) or stresses that occur at critical or sensitive periods of fetal development ultimately lead to permanent changes in the structure, physiology, and metabolism of the growing fetus. This, in turn, predisposes these babies to increased NCD risk in their adult life — the famous J Endocrinol 2004;181:11–23 (Piper et al., 2004).

Keywords Diabetes prevention · Primordial · Gestational diabetes mellitus

Conceptualization

Maternal 2-h PPBG does not cross > 110 mg/dl at the 10th week as fetal beta cells start secreting insulin around the 11th week of pregnancy. During pregnancy 2-h post prandial blood glucose (PPBG) at the 10th week > 110 mg/dl — Early Gestational Glucose Intolerance (EGGI) predicts GDM, hence blood glucose must be brought to < 110 mg/dl as fetal beta cells start secreting insulin around 10–11 weeks. With fetal insulin secretion, changes in maternal metabolism start.

The concept

Emerging evidence from NIH analysis suggests early screening and detection of dysglycemia in pregnancy could allow a window of opportunity by giving us time for implementing lifestyle changes before the condition develops at the 10th week of gestation [3] in high-risk women identified with HBA1C value > 5.3% and the 2-h PPBS > 110 mg/dl. NIH, therefore, recommends screening at the 10th week, as the fetal beta cells are known to begin insulin secretion at the 11th week of gestation [4, 5].

Fetal handling of maternal glucose (fetal hyperinsulinemia and maternal glucose dynamics)

Fetal islet cells start secreting insulin from the 11th week in response to maternal glucose. When the maternal glucose is high, i.e., PPBS > 110 mg/dl, fetal insulin secretion

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is stimulated. Maternal glucose does not go up due to this fetal insulin handling of the maternal glucose which is therefore deceptive. The fetal hyperinsulinemia allows a persistently high glucose flux even at times when maternal glucose seems normal. "Maternal hyperglycemia pushes glucose and fetal hyperinsulinism pulls glucose" [6] which also disburses fast in the fetal tissues, while the glucose gradient is being maintained.

Based on the pattern of glycemia in normal pregnancy [7], PPBS at the 10th week > 110 mg/dl can therefore predict GDM; hence, blood glucose has to be brought down to < 110 mg/dl before the 10th week before the fetal beta cells start secreting insulin around 10–11 weeks, causing changes in maternal metabolism.

The obvious implication is that glycemic control needs to be optimized very early in pregnancy to prevent the establishment of fetal hyperinsulinemia [8], thereby necessitating PPBS should be < 110 mg/dl.

Whenever maternal PPBS > 110 mg/dl is recorded, immediate action has to be taken to reduce PPBS < 110 mg/dl, lest she will develop GDM and its consequences. This opens up the window of opportunity to implement changes that can alter the entire trajectory of NCD development, in line with the concept of "primordial prevention" of diabetes! [9].

The idea is to test for glucose tolerance in the 8th week of gestation (2 months); the reason is prediction of GDM if 2-h PPBS > 110 mg/dl in the 10th week.

Hence, in the 8th week itself, PPBS has to be checked. If PPBS is > 110 mg/dl in the 8th week, *a grace period* of 2 weeks is available to attain PPBS < 110 mg/dl in the 10th week.

When PPBS > 110 mg/dl, MNT, and metformin at 250 mg twice daily may be initiated and continued [10]. The target glycemia to be obtained is PPBS 99 ± 10 mg/dl. Metformin is safe at this time as the embryonic stage is over by the 8th week, when the likely benefit from improved blood glucose control outweighs the potential for harm.

The concept has become a reality — outcome of preliminary study

In this study, Group A, $N = 82$, antenatal women (ANW) with 2-h PPBS < 110 mg/dl at 8 weeks, with no intervention and in them, one developed GDM (1.5%) in the third trimester. In Group B, $N = 70$ ANW with PPBS at 8 weeks > 110 mg/dl were treated with MNT and metformin at 250 mg twice daily throughout pregnancy. In them, one showed GDM (1.85%) in the third trimester since she discontinued the intervention.

The successful outcome of this study establishes that primordial prevention of diabetes is possible.

Resolution

Keeping this concept in mind at the 18th Annual Conference of Diabetes in Pregnancy Study Group India — DIPSI 2024, at New Delhi – we, as clinicians, researchers, diabetologists, obstetricians and public health specialists, involved in diabetes care, resolve that:

- Pre-pregnancy planning is ideal for a better maternofetal outcome.
- It is necessary to optimize metabolic control early in pregnancy.
- The priming of the fetal beta cells is around the 11th week.
- Blood sugars 2-h PPBS > 110 mg/dl may account for the persistence of fetal hyperinsulinemia throughout pregnancy.
- Prediction of GDM — PPBS > 110 mg/dl occurs at the 10th week.
- Preventive action must therefore be taken at the 8th week so that maternal PPBS remains < 110 mg/dl throughout pregnancy.
- MNT to be followed throughout pregnancy.
- Metformin to be continued till confinement.

Pledge

- We pledge to spread awareness about primordial prevention by highlighting the importance of screening for EGGI (Early Gestational Glucose Intolerance) at 8 weeks of gestation.
- In pregnant women with early hyperglycemia, we shall help sensitize all concerned health care professionals (HCPs) to actively involve the lady and her family and strengthen the family in its capacity building in achieving euglycemia.
- We suggest all concerned health policymakers to proactively create programs for education, screening, and management of pregnant women.
- We strongly recommend that this "made in India" concept for primordial prevention of diabetes is evidence-based, feasible, and doable.
- We solicit support from allied professions, including family medicine, community medicine/public health and mental health professionals, in improving early screening of all pregnant women at 8 weeks of gestation.
- We shall initiate social media campaigns to emphasize early screening for all pregnant women, improve better follow-up adherence, and end social stigma or ostracization against expectant mothers with diabetes.

- We emphasize that awareness and sensitization on a large scale needs to be undertaken, both for all concerned HCPs and the general public through a multi-pronged approach.
- We will work towards achieving an eventual diabetes-free generation, with a successful primordial prevention strategy.

Data Availability Its a pledge by DIPSI organisation.

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