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Hyperglycemia in Pregnancy-Consequences and Salvation

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Abstract

Across the globe there is rise in prevalence of diabetes. Persons who are diagnosed with impaired glucose tolerance (IGT) could possibly prevent or postpone the disease progression to a stage of overt diabetes by incorporating modification in their lifestyle and using intervening drugs. These are known as post primary prevention strategies. For reversal or halting the epidemic of the disease, primary prevention is considered as a most important effort. Gestational Diabetes Mellitus (GDM) affected women groups are considered ideal for primary prevention strategies as they and their children are most likely to develop type 2 Diabetes Mellitus (DM) predominantly in future. Highest prevalence of diabetes has been reported among Pima Indians of Arizona. The reason ascribed for this is, the babies have been exposed to maternal diabetes in utero. Therefore as a program strategy to detect GDM and the impact on infants, a 75 gm Oral Glucose Tolerance Test (OGTT) had been advocated to all pregnant Pima Indian females during third trimester. Women of Asian Indian ethnicity are also having a higher prevalence of diabetes and in comparison to Caucasian women they have 11.3 times increased relative risk of suffering from GDM. In India it is necessary to recommend early universal screening tests for pregnant women to detect GDM. In India and in other countries the gestational diabetes which remained undiagnosed in the past has contributed probably to the rise in prevalence of diabetes. Prompt and appropriate preventive action include conducting glucose tolerance tests in all pregnant women, to attain euglycemia and ensure adequate nutrition in them which in turn will stop India being the diabetes capital of the world.

Keywords: Diabetes mellitus; Gestational diabetes mellitus; Pregnancy

Introduction

In the diabetes epidemic scenario, India is no exception. The concern is that India would be having the highest population of diabetes by 2025 [1]. The rise in prevalence is due to growing aging population, more urbanization, increase in physical inactivity and the obesity epidemic [2]. While most of these causes are leading to diabetic epidemic, the exposures to adverse intrauterine milieu at an early development stage of life have emerged as probable risk factors. The adult health issues and disease conditions may be critically influenced by gestational programming which is proposed in the hypothesis of "fetal origin of adult disease" [3]. During the process of gestational programming various stress and stimuli may happen at critical or sensitive period of development which results in permanent structural changes, alteration in physiology and metabolism, there by predisposing the individual to the disease in adulthood [4]. Commonly and conclusively, modifications of lifestyle and medicinal interventions have shown delay in the development of overt diabetes in individuals having impaired glucose tolerance. These are considered under post primary preventive strategies. The modalities of primary prevention of type 2 DM involves keeping persons normoglycemic who are genetically or otherwise susceptible and not just prevention of development of type 2 DM [5]. For reversal or halt of the epidemic nature of the disease the efforts of primary prevention is considered as more necessary than the post primary prevention. GDM women groups are considered ideal for primary prevention of diabetes mellitus [6]. as these persons are at higher risk of developing diabetes mostly type 2 DM as are their children. GDM is commonly defined as intolerance of carbohydrate of variable intensity or severity with onset or first detected during the current pregnancy [7]. Pregnant women with GDM have higher life time risk of having diabetes, more than three times in comparison to controls at 16 years following index pregnancy [8]. Evidence of IGT or type 2 DM had been observed in one third of children by the age of 17 years who were born to GDM mothers [9]. In our community based project sponsored by World Diabetes Foundation, 33% of the women who developed GDM had maternal history of diabetes.

Role of genetics and intrauterine environment in predisposing the development of type 2 DM

Both genetic factors and intrauterine environmental factors mediate the hereditary susceptibility to type 2 DM. The genetic factors of significant contribution can be chiefly due to the function of maternal mitochondrial Deoxyribonucleic Acid (DNA) in the hereditary transmission of diabetes. The ovum or egg is rich with maternal mitochondria but the sperm contains a few paternal mitochondria but those few cannot persist in the offspring. During fertilization, it is only the nucleus of spermatazoan that makes entry into the ovum and there by all the cytoplasm, mitochondria and mitochondrial DNA are entirely inherited from mother. The maternal

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inheritance is due to mutation in the genes of mitochondrial DNA and is usually transmitted on regular basis by an affected mother to her child [10]. However many studies have also revealed, lower genetic risk of type 2 DM, exposure to hyperglycemia in fetal life significantly increases the risk of type 2 DM during adult hood [11]. Conclusion and major finding of the clinical study was that exposure to risky diabetic environment during fetal life in the uterus was related to increased incidences of IGT and a erroneous insulin secretary response in adult offspring, independent of hereditary predisposition to type 2 DM [12]. Some studies reveal that children having exposure in utero to diabetes condition of mother are at a increased risk of both obesity and diabetes mellitus than their unexposed siblings, indicating that the high risk of the exposed offspring is not absolutely genetic [13,14]. This kind of observations provides clear indication to the need of focus areas like the intra uterine environment. Pregnant women having glucose intolerance usually carry excess of maternal fuels like glucose, amino acid and lipids (mixed nutrients) which are able to cross the placental barriers and stress the fetal beta cells of pancreas. The fetal pancreas responds by releasing large amount of insulin to these mixed nutrients. It results in increase of adipose tissue and accumulation of visceral fats that would eventually cause reduction in fetal pancreatic reserves and the infant ultimately is at risk of developing DM. Alternatively, intrauterine malnutrition leads to Intrauterine Growth Retardation (IUGR) and this kind of under nutrition is related to reduction of pancreatic reserve. Hence both small for dates babies and large for dates babies are at increased risk of developing diabetes [15]. In India, and in many developing and less resource settings both under-nutrition and over-nutrition exist during pregnancy.

Prevalence of GDM and its consequences

In world over the next two to three decades there would be 80 million women of reproductive age group with diabetes. It is projected that India alone will have 27 million of them. Accepting the average prevalence of GDM in India would be 10% the number of GDM would be around 3 million a huge burden, which will produce a potential for unusually higher rates of maternal and infant morbidities [16]. The global prevalence of hyperglycemia in pregnancy in women (20-49 years) is 16.9% or 21.4 million live birth in 2013. The highest prevalence of GDM was found in South East Asian region of 25% compared with 10.4% in North American and Caribbean region [17]. One in six live births occur to women with some form of hyperglycemia and 84% of which are due to GDM. Women affected by GDM, present with overt diabetes at a younger age, considerably increasing the life time risks of getting possible diabetes complications

Solution

High prevalence of DM globally calls for universal screening of glucose intolerance during pregnancy and ensuring adequate nutrition for the developing fetus. For universal screening the test procedure has to be simple, economical and evidence based. Presently there are two accepted guidelines to diagnose GDM.

1. International Association of Diabetes in Pregnancy Study Group (IADPSG)

The IADPSG recommends 75 gm OGTT during 24th week to 28th week of pregnancy. The diagnosis of GDM is made if any one glucose value meets or exceeds Fasting 92 mg/dl, 1 hour 180 mg/dl and 2 hours 153 mg/dl. This recommendation is based on the Hyperglycemia and Adverse Pregnancy Outcome Study (HAPO) but population from South Asian countries including India was not included in this study [18].

A single step procedure for diagnosis of GDM

In this procedure 75 gm glucose is given orally to a pregnant woman in the fasting or non-fasting state, irrespective of the last meal timing and GDM is diagnosed with 2 hr plasma glucose ≥140 mg/dl (7.8 mmol). This procedure is being followed by Diabetes in pregnancy study group India (DIPSI). Ministry of health Government of India has also approved this procedure [19,20].

WHO and International Federation of Gynecologists and Obstetricians (FIGO) recommend both IADPAG and A Single step procedure for diagnosing GDM, while favoring the later for the less resource settings as an option [21,22].

Ideal trimester to screen for GDM

The screening test for glucose intolerance in women is mostly done around 24 to 28 weeks of pregnancy. However a statistically significant number of GDM mothers have delivered big size babies despite better glycemic control during the third trimester of pregnancy [23]. This is as a result of the undetected glucose intolerance in these pregnant women in the early weeks of gestation that would have influenced the fetal growth [24]. The islets of Langerhans of fetal pancreas gets differentiated in 10th and 11th week of intrauterine development and start releasing insulin in response to various nutrients by 11th to 15th weeks of gestation [25,26]. During early gestation the fetal pancreatic beta cells gets primed which leads to hyperinsulinemia of fetus`s entire duration of pregnancy and the accelerated growth risk persists even during later part of pregnancy when there is good control of metabolism [27]. Changes in intrauterine environment particularly, the evolution of hyperinsulinemia is strongly related to the progression of obesity and IGT in childhood and adolescence [28]. Early maternal metabolic imprints can affect the growth of fetus. This observation suggests that screening has to be conducted in the first trimester of pregnancy as the fetal pancreatic beta cell detects and starts responding to glycemic level of the mother at 16th week of pregnancy [29].

Conclusion

In conclusion, rise in maternal hyperglycemia is related to increased morbidity during pregnancy and higher chances of subsequent development of diabetes mellitus in the mother. Additionally, maternal hyperglycemia can have direct effect on the fetal pancreas development and it is also associated with increased susceptibility for diabetes in the infants, an effect that is independent of hereditary factors [6]. Among different ethnic groups in countries of South Asia, pregnant women from India have the maximum frequency of Gestational diabetes mellitus requiring universal screening in India for glucose intolerance in pregnancy [30]. Possibly the undiagnosed cases of glucose intolerance which had been occurring in the past might have resulted in the high prevalence of diabetes in India. Furthermore, women who are having GDM, due to their higher diabetes risk and younger age, are ideally suitable to be targeted for lifestyle modification or drug interventions to delay or

postpone the onset of overt diabetes mellitus.

Colombo declaration 2016

It is worth mentioning here the "Colombo declaration" made during South Asian Initiative for Diabetes and Pregnancy (SAIDIP) made at Colombo 8th to 11th September 2016.

Diabetes mellitus is escalating worldwide; it already affects over 85 million people in South Asia and is projected to affect over 150 million people by 2040. There is an equally high burden of pre-diabetes - approximately 45 million are estimated to have pre- diabetes.

Hyperglycemia in Pregnancy (HIP) is one of the most common medical condition affecting women during pregnancy - an estimated 25% of live births in South Asia are impacted by hyperglycemia during pregnancy. The majority of women with HIP have Gestational Diabetes Mellitus (GDM), which develops due to hormonal changes of pregnancy and is confined to the duration of pregnancy

Hyperglycemia during pregnancy significantly increases risk of pregnancy complications- hypertension, obstructed labor, postpartum hemorrhage, infections, still births, premature delivery, newborn deaths due to respiratory problems, hypoglycemia and birth injuries

Without preventive care, almost half of women with GDM develop type 2 diabetes and a significant proportion develops premature cardiovascular disease, within 10 years of childbirth. Children born to women with GDM are at very high risk of obesity, early onset type 2 DM and cardiovascular disease, whereby, HIP perpetuates the risk of diabetes into the next generation

Focusing attention on GDM is a sustainable and cost effective way of addressing the double disease burden of high maternal and newborn morbidity and mortality and rising rates of obesity, diabetes and cardiovascular diseases; providing an opportunity for addressing two important components of the sustainable development goal 3 (maternal and newborn health and NCDs) with one comprehensive intervention. The concern is that maternal and child health is inextricably linked with non-communicable diseases and their risk factors, specifically such as prenatal malnutrition and low birth weight create a predisposition to obesity, high blood pressure, heart disease and diabetes later in life, and that pregnancy conditions, such as maternal obesity and gestational diabetes, are associated with similar risks in both the mother and her offspring.

Advocates for the inclusion of non-communicable disease prevention and control within sexual and reproductive health and maternal and child health programs, especially at the primary health-care level, as well as other programs, as appropriate, and also integrate interventions in these areas into non-communicable disease prevention programs. That hyperglycemia in pregnancy is a significant public health challenge impacting maternal, newborn and child health and the future burden of type 2 DM and cardio metabolic disorders globally, but in particular, South Asia.

That until and unless urgent action is taken to systematically address the issue it has the potential to undo the gains in maternal and newborn health and worsen the ongoing diabetes epidemic. That focusing on HIP provides a unique opportunity to integrate services, to lower traditional maternal and perinatal morbidity and mortality indicators and address inter-generational prevention of NCDs such as diabetes, hypertension, CVD and stroke.

References

1. Hilary King, Ronald E.Aubert, William H. Herman. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998; 21: 1414-1431.
2. Hunt KJ, Schuller KL. The increasing prevalence of diabetes in pregnancy. Obstet Gynecol Clin North Am. 2007; 34: 17399.
3. Barker DJ. Fetal origins of coronary heart disease. BMJ. 1995; 311: 171-174.
4. Lucas A, Bock GR, Whelan J. Programming by early nutrition in man the childhood environment and adult disease. Chichester (UK): John Wiley & Sons. 1991; 38-55.
5. JaakkoTuomilehto. A paradigm shift is needed in the primary prevention of Type 2 DM, Prevention of DM. John Willey & sons limited. 2005.
6. Dornhorst A, Michela Rossi. Risk and Prevention of Type 2 Diabetes in women with Gestational Diabetes. Diabetes Care. 1998; 21: 43-49.
7. Metzger BE. Summary and recommendations of the Third International Workshop Conference on Gestational Diabetes Mellitus. Diabetes. 1991; 40: 197-201.
8. Henry OA, Beischer NA. Longterm implications of gestational diabetes for the mother. Baillieres Clin obstet Gynaecol. 1991; 5: 461-483.
9. Silverman BL, Rizzo TA, Cho NH, Metzger BE. Long –term effects of the Intrauterine Environment. The Northwestern University Diabetes in Pregnancy Center. Diabetes Care. 1998; 21: 142-149.
10. Nausheen Khan, IshaqMohd, Khan Gazala, Prabhakar Sastry. Early Age at Onset and High Frequency of Associated Complications in Maternally Transmitted Type 2 Diabetes Mellitus. Int J Diab Dev Countries. 2004; 24: 36-39.
11. Gill-Randall R, Adams D, Ollerton RL, Lewis M, Alcolado JC. Type 2 diabetes mellitus—genes or intrauterine environment ? An embryo transfer paradigm in rats. Diabetologia. 2004; 47: 1354-1359.
12. Sobngwi E, Boudou P, Mauvais-Jarvis F, Leblanc H, Velho G, Vexiau P, et al. Effect of a diabetic environment in utero on predisposition to Type 2 diabetes. Lancet. 2003; 361: 1861-1865.
13. Pettitt DJ, Aleck KA, Baird HR, Carraher MJ, Bennett PH, Knowler WC. Congenital susceptibility to NIDDM. Role of intrauterine environment. Diabetes. 1988; 37: 622-628.
14. Hanson RL, Elston RC, Pettitt DJ, Bennett PH, Knowler WC. Segregation analysis of non insulin dependent diabetes mellitus in Pima Indians: evidence for a majorgene effect. Am J Hum Genet. 1995; 57: 160-170.
15. Jovanovic L. American Diabetes Association's Fourth International Workshop – Conference on Gestational Diabetes Mellitus: Summary and Discussion. Diabetes Care. 1998; 21: 131-137.
16. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational diabetes mellitus in India. J Assoc Physicians India. 2004; 52: 707-711.
17. Guariguata L, Linnenkamp U, Beagley J, Whiting DR, Cho NH. Global estimates of the prevalence of hyperglycaemia in pregnancy. Diabetes Res Clin Pract. 2014; 103:176-85.
18. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010; 33: 676-682.
19. Anjalakshi C, Balaji V, Balaji MS, Ashalata S, Suganthi S, Arthi T, et al. A Single test procedure to diagnose gestational diabetes mellitus. Acta Diabetol. 2009; 46: 51-54.
20. National guidelines for diagnosis and management of GDM. Government of India, Maternal health division, Ministry of Health and Family Welfare, New Delhi.

21. Colagiuri S, Falavigna M, Agarwal MM, Boulvain M, Coetzee E, Hod M, et al. Strategies for implementing the WHO diagnostic criteria and classification of hyperglycemia first detected in pregnancy. Diabetes Res Clin Pract. 2014; 103: 364-372.

22. Hod M, Kapur A, Sacks DA, Hadar E, Agarwal M, Di Renzo GC, et al. The International Federation Of Gynaecology and Obstetrics (FIGO) initiative on Gestational Diabetes Mellitus: A Pragmatic guide for diagnose, management and care. Int J Gynaecol Obstet. 2015; 131: 173-211.

23. Balaji V, Balaji MS, Seshiah V, Mukundan S, Datta M. Maternal glycemia and neonates birth weight in Asian Indian women. Diabetes Res Clin Pract. 2006; 73: 223-224.

24. Buchanan TA, Kitzmiller JL. Metabolic interactions of diabetes and pregnancy. Annu Rev Med. 1994; 45: 245-260.

25. Reiher H, Fuhrmann K, Noack S, Woltanski KP, Jutzi E, Hahn von Dorsche H, et al. Age dependent insulin secretion of the endocrine pancreas in vitro from fetuses of diabetic and non diabetic patients. Diabetes Care. 1983; 6: 446-451.

26. Milner RDG, Ashworth MA, Barson AJ. Insulin release from human fetal pancreas in response to glucose, leucine and arginine. J Endocrinol. 1972; 52: 497.

27. Schwartz R, Gruppuso PA, Petzold K, Brambilla D, Hiilesmaa V, Teramo KA. Hyperinsulinemia and macrosomia in the fetus of the diabetic mother. Diabetes Care. 1994; 17: 640-648.

28. Dornhorst A, Beard RW. Gestational diabetes a challenge for the future. Diabet Med. 1993; 10: 897-905.

29. Nahum GG, Wilson SB, Stanislaw H. Early pregnancy glucose screening for gestational diabetes mellitus. J Reprod Med. 2002; 47: 656-662.

30. Ravinder Madan. Chair of the S. East Asian region IDF – 17th IDF congress, Mexico. 2000.

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