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Review Article

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Management of Blood Sugar Degrees in Hyperglycemia in Pregnancy (Hip) Reduces Perinatal, Infant Morbidity & Mortality as a Result of a Large Prospective Cohort Learn From Up, India

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Abstract

Background: *Gestational diabetes mellitus (GDM) is a glucose intolerance that occurs or is identified for the first time all through pregnancy. Perinatal & Neonatal morbidity mortality is significant in pregnant women in GDM with extra hazard of growing diabetes later in life. Uttar Pradesh is a largest state of India with one of the highest rate of the infant as well as maternal mortality which might be, at least partially due to GDM. Thus, Careful evaluation, administration & Training of HCPs for GDM can improve the outcomes in National health Mission supported Govt funded Program, supported by World Diabetes foundation, Denmark.*

Aims & Objectives: *Primary objective of this study to be determine the Maternal-Fetal outcomes of GDM and management of Hyperglycemia in Pregnancy HIP reduces Neonatal & Perinatal Mortality as per the NHM, GOI Guidelines for GDM, As this will go long way help us in reduction of Perinatal & infant mortality. Thus, this study was once undertaken to recognize the extent of the burden on the healthcare and formulating further policy for Implementation of Gestational Diabetes Program in the largest state of Uttar Pradesh.*

Materials and Methods: *A prospective cohort study was done for 2 year from October 1, 2016, to September 31, 2018, at 828 GDM screening units as a part of the Gestational Diabetes Prevention and Control Project, Uttar Pradesh approved by the Indian Government in the state of Uttar Pradesh, India, largest state with second Highest MMR & IMR, A total of 515,532 pregnant women were screened during their 16–32th weeks of pregnancy by impaired oral glucose test (OGTT) as per NHM Guidelines for GDM, 12784 GDM & 7287 Non GDM maternal and perinatal outcomes were followed up in both GDM and non-GDM categories in the 2 year (2016-2018) after blood sugar management (September 2016-October 2018) was executed at 828 (DHs, CHCs & PHCs healthcare) facilities, 515532 Pregnant Women have been screened at 16-20 Weeks & 24th-28 weeks of pregnancy as per Guidelines of National health Mission, GOI Guideline.*

Results: *Perinatal mortality increased significantly from 2.6% to 9.1% when blood sugar levels increased from 120 mg/dl to 199 mg/dl and above. Perinatal mortality in GDM cases were significantly to the control of blood sugar levels ($P < 0.0001$). Relative Risk of Stillbirth, Perinatal & neonatal mortality have been respectively 2.5, 2.3 & 2.5 times greater in GDM compare Non GDM (Table 1). Most of the GDM used to be identified in primigravida (52%). It was also found in our study those GDM who were strictly controlled with Hyperglycemia in pregnancy (HIP) to <120 mg/dl, Post Prandial blood sugar, have lowest risk for perinatal and neonatal mortality compare to those GDM pregnant women Blood sugars were not controlled, Risk for Perinatal mortality increases steadily and reaches 9.1% beyond blood sugar> 200 mg/dl.*

Conclusion: *All the Pregnant women need screening in Public health facilities & Implementation of National health Mission, GOI Guidelines for GDM has to be followed to improve outcome for Mother and Newborn, As the lack of information about GDM amongst pregnant women is high, to decrease the risk, increase awareness & full Implementation of NHM GDM Guidelines is key to Perinatal and neonatal mortality reduction in Public health care facilities where large number of ANC visit for Maternal and fetal health care.*

Keywords: HIP (Hyperglycemia in Pregnancy); Gestational Diabetes; Perinatal Complication; Maternal Complication; Neonatal Mortality, NHM, FOGSI, 16 Weeks, 24-28 Weeks, CHC (Community health Centre), PHC (Primary health Centre), DH (District Hospital), DIP (Diabetes in Pregnancy).

Introduction

Any degree of glucose intolerance with the onset or first recognition during pregnancy is defined as Gestational Diabetes Mellitus GDM [1].

Diabetes Detected in Non-pregnant women as per the WHO Criteria is when goes into Pregnancy which is called diabetes in pregnancy and with Gestational Diabetes its constitute Hyperglycaemia in pregnancy HIP [2].

Prevalence estimates for hyperglycaemia in pregnancy

As per IDF 2017 estimate, around 21.3 million live births (16.2%) were affected by some form of hyperglycaemia in pregnancy. Approximately 18.4 million of these cases were due to gestational diabetes mellitus (GDM), accounting for 86.4% of all hyperglycaemia in pregnancy. Other cases were due to diabetes detected prior to the pregnancy (6.2%) and other types of diabetes, which were detected in pregnancy (7.4%). The South East Asia region (SEAR) had the highest prevalence of hyperglycaemia in pregnancy with 26.6% (Figure 1). Similar to the prevalence of diabetes and IGT, the majority of cases were in (LMIC) low-and middle-income countries. The prevalence of HIP increases with age, the prevalence was 9.8% for women in the age range of 20-24 years; the prevalence was 45.1% in women who are 45-49 years [3].

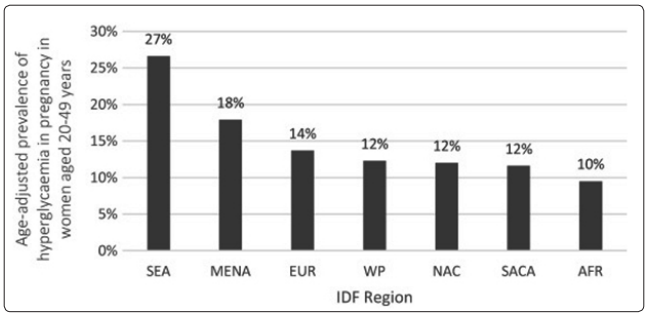

Figure 1

Age-adjusted prevalence (%) of hyperglycaemia in pregnancy in women aged 20–49 years by IDF region, 2017.

Women with a history of GDM are at an increased risk of adverse maternal and perinatal outcome and also at increased risk of future diabetes predominantly Type II including their children and therefore there are two generations at risk [4]. Any degree of glucose intolerance during pregnancy is associated with adverse maternal and fetal outcome. The adverse maternal complications include hypertension, preeclampsia, urinary tract infection, hydramnios, increased operative intervention and future DM. In the fetus and neonates it is associated with macrosomia, congenital anomalies, metabolic abnormalities, RDS, etc. and subsequent childhood and adolescent obesity [5]. There is no international consensus regarding the timing of screening method and the optimal cut-off points for diagnosis and intervention of GDM. DIPSI recommends non-fasting Oral Glucose Tolerance Test (OGTT) with 75g of glucose with a cut-off of ≥140 mg/dl after 2-hours, whereas WHO recommends a fasting OGTT after 75g glucose with a cut-off plasma glucose of ≥ 140 mg/dl after 2-hour. The recommendations by ADA/IADPSG for screening women at risk of diabetes is as follows, for first and subsequent trimester at 24-28 weeks a criterion of diagnosis of GDM is made by 75 g OGTT and fasting 5.1mmol/l, 1 hour 10.0mmol/l, 2 hour 8.5mmol/l by universal glucose tolerance testing.

NICE Guidelines 2015 for Screening and Diagnosis of GDM

Assess risk of GDM using risk factors in a healthy population. If women had GDM in previous pregnancy do 75g OGTT as soon as possible, if negative repeat again at 24-28 weeks. Other women with any other risk factors screen at 24-28 weeks by 2-hour OGTT with 75 g glucose load.

Do not use fasting plasma glucose, random blood glucose, HbA1C, glucose challenge test or urine analysis for glucose to assess the risk of developing GDM.

Glycosuria of 2+ or more on one occasion or of 1+ or above on 2 or more occasions by the reagent strip on ANC needs further testing to exclude GDM.

Diagnosis of GDM made if the women have either fasting plasma glucose level of 5.6mmol/l or above or a 2-hour plasma glucose level of 7.8mmol/l or above.

Who should be screened for GDM: Previous reviews were not definite whether to do universal screening or risk-based screening. American Diabetes Association (ADA) states that low risk women, those with age less than 25 years, not a member of ethnic group, BMI 25kg/m^2 or less, no previous history of abnormal glucose tolerance or adverse obstetric outcomes and no known history of diabetes in first degree relatives, in these women there is no need to screen and less likely to benefit from any screening [6].

Placental hormones mediate insulin resistance which increases GDM as the pregnancy advances so testing too early may not be helpful in some patients. Similarly, performing tests too late in the third trimester limits the time in which metabolic interventions can take place. Because of these reasons, it is advised to perform the tests at 24-28 weeks of gestation. The recommendations given by International Association of Diabetes and Pregnancy Study Group (IADPSG) which was endorsed by ADA based on Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study is to do on the first prenatal visit, fasting plasma glucose, HbA1C or random plasma glucose in all women. If results are not diagnostic of overt DM and fasting plasma glucose ≥ 92 mg/dl diagnosis of GDM is made. If fasting glucose is < 92mg/dl at the first antenatal visit a 2-hour 75g OGTT should be repeated at 24-28 weeks.

International Association of Diabetes and Pregnancy Study Groups consensus panel (IADPSG) International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycaemia in pregnancy [7].

Disadvantages of the IADPSG suggestions are:

- Most of the time pregnant women do not come in the fasting state because of commutation and belief not too fast for long hours. The dropout rate is very high when a pregnant woman is asked to come again for the glucose tolerance test [8]. Attending the first prenatal visit in the fasting state is impractical in many

settings.

- The insulin resistance during pregnancy escalates further and hence FPG is not an appropriate option to diagnose GDM in Asian Indian women. In this population by following FPG > 5.1 mmol/L as the cut-off value, 76% of pregnant women would have missed the diagnosis of GDM made by WHO criterion [11, 12].

National Indian Guidelines for GDM, Govt of India:

Government of India released a "National Guidelines on Diagnosis and Management of Gestational Diabetes Mellitus in 2014 to address the need of high prevalence of GDM in India. The initiatives led to integration of GDM diagnosis and management within ANC care package in public health system. This resulted in many field level learnings in Indian context. Recently, globally many more evidences were generated on safety and effectiveness on oral hypoglycemic drugs recommending use of "Metformin" for GDM management. For this reason, GOI constituted an expert group to deliberate on GDM in detail & revise the national guidelines for India incorporating the recent global evidences on use of Metformin and in country experiences.

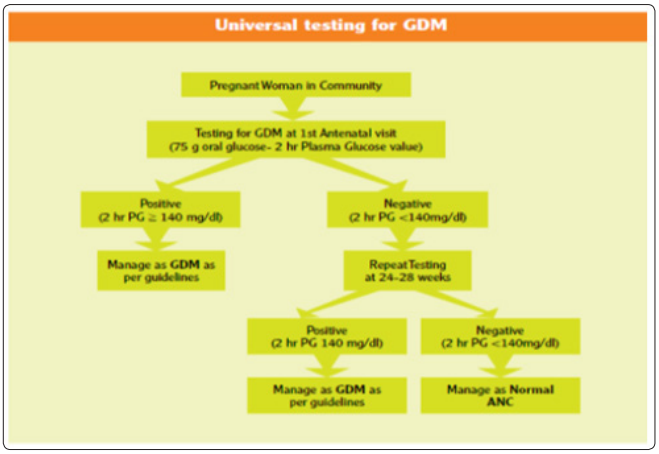

Figure 2

The present guideline has been prepared based on the recommendations of the experts & available national/International evidences. Gestational Diabetes Mellitus (GDM) is defined as Impaired Glucose Tolerance (IGT) with onset or first recognition during pregnancy.

National guideline for diagnosis and management of Gestational Diabetes endorses the single step test recommended by WHO for diagnosis of GDM using a 75gm glucose, through Oral Glucose Tolerance Test (OGTT) irrespective of the last meal with a threshold value of 2-hour BS >140 mg/dL. Guidelines advocate for universal screening of all pregnant women at first antenatal contact. If the first test is negative, second test should be done at 24-28 weeks of gestation.

GDM Pregnant women should be managed by Medical Nutrition Therapy (MNT), and insulin therapy/metformin as required. In the postpartum period, OGTT should be repeated at 6 weeks after delivery, if blood sugar <140 mg/dL, then women should be referred to NCD clinic for Post Prandial Blood Sugar (PPBS) testing annually [13].

Table 1: Fetal outcomes in Gestational diabetes mellitus versus Non GDM

Outcomes in neonate	GDM present (n=12784) N (%)	GDM present (n=12784) N (%)	RR	*p-value*
Stillbirth	406 (3.17)	92(1.26)	2.51	<0.0001
Neonatal death	191 (1.49)	47 (0.6)	2.32	<0.0001
Perinatal death	597 (4.67)	139 (1.91)	2.45	<0.0001

As the blood sugar level rose above 120 mg/dl, perinatal mortality rises significantly from (2.6% to 9.1%) when blood sugar level rises from 120 mg/dl to >200 mg/dl respectively (Figure 3).

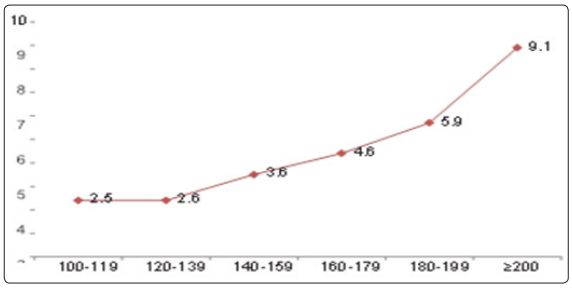

Figure 3: N (GDM > 140 mg%, at Risk GDM 120-139 mg% and Non GDM< 120 mg) after OGTT Govt of India National GDM Guidelines, Perinatal mortality (%) in gestational diabetes mellitus cases in relation to the maternal blood sugar levels (in g/dl)

Management of Gestational Diabetes Mellitus: Treatment Target Maintaining a mean plasma glucose (MPG) level ~105–110 mg/dL is desirable for a good fetal outcome [14]. This is possible if FPG and 2-hour postprandial peaks are ~90 mg/dL and ~120 mg/dL, respectively.

Medical Nutrition Therapy All women with GDM should receive nutritional counselling. The meal pattern should provide adequate calories and nutrients to meet the needs of pregnancy. The expected weight gain during pregnancy is 300–400 g per week and total weight gain is 10–12 kg by the term. Initiating Insulin Therapy Once diagnosis is made, medical nutritional therapy (MNT) is advised initially for 2 weeks. If MNT fails to achieve control, i.e. FPG ~90 mg/dL and/or post-meal glucose ~120 mg/dL, insulin may be initiated.

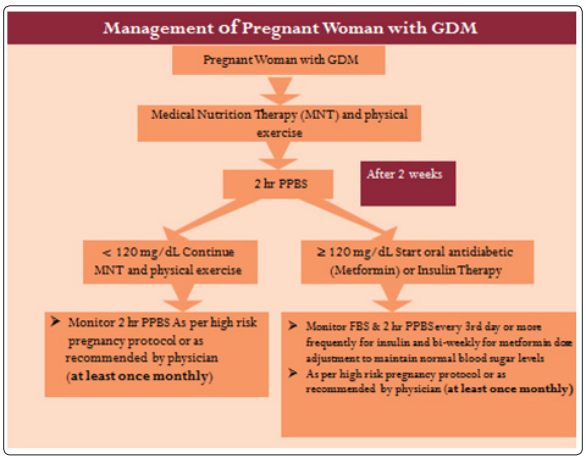

Figure 4

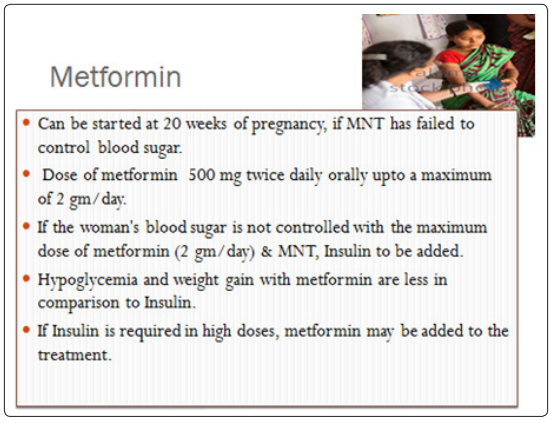

Figure 5

Preferable to start with Premix insulin 30/70 of any brand* Starting dose: 4 units before breakfast ↓ Every 4th day increase 2 units till 10 units ↓ If FPG remains > 90 mg/dL advise → 6 units before breakfast and 4 units before dinner ↓ Review with blood sugar test → Adjust dose further Total insulin dose per day can be divided as two-thirds in the morning and one-third in the evening. *Initially if post-breakfast plasma glucose is high → Start Premix 50/50 2. If GDM is diagnosed in the third trimester; MNT is advised for 2 weeks. Insulin is initiated if MNT fails.

If 2-hour PG >200 mg/dL: At diagnosis, a starting dose of 8 units of premixed insulin could be administered straightaway before breakfast and the dose has to be titrated on follow-up. Along with insulin therapy, MNT is also advised. Insulin Analogs If postprandial glucose is still not under control-considers using rapid-acting insulin analogs.

Monitoring Glycaemic Control: The success of the treatment for a woman with GDM depends on the glycaemic control maintained with the meal plan or pharmacological intervention. Studies suggest 1, 1.5 and 2-hour post-meal for monitoring glycemic control, 2-hour post-meal monitoring is preferred as the diagnosis of GDM is also based on 2-hour PG. It is easier to remember this timing, as the time for diagnosis and also for monitoring is the same, i.e. 2 hours? However, whichever time is targeted for monitoring glycemic control and adjusting insulin dose, blood tests must be performed at the same time at each visit [15]. They should be advised to perform self-monitoring of blood glucose (SMBG) on a daily basis, failing which, at least weekly monitoring should be encouraged. If self-monitoring is not possible, laboratory venous plasma glucose has to be estimated for adjusting the dose of insulin. Oral Antidiabetic Drugs Insulin secretagogue (glibenclamide) is being used in a few centers in India and abroad, but not yet approved by drug controller of India. Metformin (alone or with supplemental insulin) was not associated with increased perinatal complications as compared with insulin.30 Metformin has been found to be useful in women with polycystic ovarian disease (PCOD) who failed to conceive [16].

Measuring Other Parameters: Maternal blood pressure has to be monitored during every visit. If blood pressure is found to be more than 130/80, advise alpha-methyldopa 125 mg and dose to be adjusted on follow-up. Examination of the fundus and estimation of micro albuminuria, every trimester is recommended particularly in women with pregestational diabetes. Fetal surveillance: Ultrasound fetal measurement: Ultrasound monitoring is recommended at least every trimester. The timing of delivery: Delivery before full term is not indicated unless there is evidence of macrosomia, polyhydramnios, poor metabolic control or other obstetric indications (e.g. pre-eclampsia or intrauterine growth retardation). A few obstetricians prefer to terminate pregnancy around 38 gestational weeks to avoid stillbirth.

Delivery: During labor, it is essential to maintain good glycemic control, while avoiding hypoglycaemia. Lower insulin requirements are common during labor (often no insulin is necessary). Maternal blood glucose level should be monitored after delivery, 24 hours postpartum and if found to be high, checked again on follow-up. A neonatologist's presence at the time of delivery is ideal, more so if significant neonatal morbidity is suspected.

Follow-Up of Gestational Diabetes Mellitus: Gestational diabetic women requires follow-up. An OGTT with 75 g oral glucose, using WHO criteria for the nonpregnant population should be performed at 6–8 weeks postpartum. If found normal, glucose tolerance test is repeated after 6 months and every year to determine whether the glucose tolerance has returned to normal or progressed. A considerable proportion of gestational diabetic women may continue to have glucose intolerance. It is important that women with GDM be counselled with regard to their increased risk of developing permanent diabetes.

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