Review Article

Screening for Gestational Diabetes Mellitus:An Update

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Abstract

Detecting the evidence of diabetes mellitus in pregnancy is a major challenge as the condition is associated with diverse range of adverse maternal and neonatal outcomes. Various screening guidelines have been introduced depending upon the suitability of test to the population characteristics, cost and screening accuracy. Still there are lots of controversies as to which test to be used, when should the screening be done and on whom it should be applied. Multiplicity of the guidelines given is the reflection of lack of available evidence demonstrating a benefit of specified health outcome with any of national and international standard screening criteria. Till the search for ideal screening strategy is ongoing, factors like clinical judgement and available resources play important role in choosing best possible mode for evaluation of glucose intolerance in pregnant women.

Key Words: Gestational diabetes mellitus, glucose challenge test, glucose tolerance test.

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy [1-3]. It is seen in 1 – 14% of pregnancies but the prevalence depends on characteristics of the population screened [4].

Detecting the evidence of diabetes mellitus in pregnancy is a major challenge as the condition is associated with diverse range of adverse maternal and neonatal outcomes. Women diagnosed to have GDM are at increased risk of future diabetes predominantly type 2 DM as are their children. Thus GDM offers an important opportunity for the development, testing and implementation of clinical strategies for diabetes prevention [5]. As the practice of medicine moves towards an evidence-based paradigm, the debate about gestational diabetes focuses on the absence of prospective randomized controlled trials (RCTs) that assess the value of screening for and treating this disorder. Proponents of screening, argue that although available data is inadequate, there are biologically plausible explanations to account for adverse perinatal outcomes associated with gestational diabetes that supports the relevance for its screening. Recently, the United States preventive services task force (USPSTF), recognized that treatment of GDM improves maternal and neonatal outcomes but also states that there is lack of evidence to support screening of GDM [6].

Various screening guidelines have been introduced depending upon the suitability of test to the population characteristics, cost and screening accuracy. Still there are lots of controversies as to which test to be used, when should the screening be done and on whom it should be applied.

The different screening tests used are [5]-

1) Random blood glucose estimation
2) Fasting blood glucose estimation
3) 50 g glucose challenge test (GCT)
4) 75/100 g oral glucose tolerance test (OGTT)
5) Serum fructosamine estimation
6) Glycosylated haemoglobin (HbA1c) estimation
7) Urine test- Glycosuria

1) **Fasting blood glucose**- is an easier screening procedure with cut-off of 95 mg/dL but it is insufficient as sole marker of GDM as most cases have fasting blood glucose below putative threshold [7]. False positive rates are as high as 30 – 57% [8]. Fasting blood glucose level of > 125 mg/dL is diagnostic of overt diabetes during pregnancy [9].
2) **Random blood glucose (RBS)**- RBS value greater than 200 mg/dL is diagnostic of

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diabetes during pregnancy and precludes the need for any glucose challenge test. The diagnosis must be confirmed on a subsequent day in the absence of unequivocal hyperglycemia [10].

3) **Glucose challenge test (GCT)-** This test is performed as routine out-patient procedure without regard to last meal time. Capillary blood glucose estimation is done 1 hour after giving 50 grams of glucose to the pregnant women between 24 – 28 weeks of gestation. Cut off value of 130 mg/dL [11] has 90% detection rate for GDM whereas cut off value of 140 mg/dL [12] has 80% detection rate. GCT has test sensitivity of 79% and specificity of 87%. American College of Obstetricians and Gynaecologists (ACOG) and American Diabetes Association (ADA) state the usage of either threshold. This test needs confirmation by a diagnostic and confirmatory oral glucose tolerance test and forms a part of two step technique for GDM screening.

4) **Oral glucose tolerance test with 75/100 g glucose (one step technique)-** This test is both screening and diagnostic test and forms an effective part of one step procedure to screen for GDM. This approach may be cost-effective in high risk populations. It should be done in the morning after an overnight fast of more than 8 hours and after at least 3 days of unrestricted diet, consuming more than or equal to 150 g of carbohydrate per day. Patients should not smoke before the test and should remain seated during the test. A fasting blood glucose sample is drawn. The pregnant woman is given 75/100 gram of glucose in juice and the samples drawn at 1, 2 and 3 hours respectively. The recommended criteria for interpretation of oral glucose tolerance test are depicted in Table 1 [13].

Diagnosis of GDM is made if two or more values are abnormal on 75/100 g oral glucose tolerance test during pregnancy. All values mentioned in Table 1 depict plasma blood sugar levels except O'Sullivan and Mahan which mentions venous whole blood. Measurement of blood glucose level in capillary blood by glucometer has made screening test easy and simple as it can be done in office setting and does not require elaborate laboratory facilities. It is important to know that capillary blood glucose levels are comparable to venous blood glucose levels during fasting state but are higher after meals [2]. In the 4th International workshop conference on GDM in 1997 a consensus was reached on replacing NDDG criteria by C&C criteria which has lower threshold values for the diagnosis of GDM so as to diagnose more cases of GDM [14]. This one stage procedure is preferred over one step approach as there

Table 1: Interpretation of OGTT:

	O'Sullivan and Mahan (1964)	NDDG (1979)	Carpenter & Couston (1982)	ADA & ACOG (1997)	ADA & ACOG (1997)	WHO
Glucose intake	100 g (3hr)	100 g (3hr)	100 g (3hr)	75 g (2hr)	100 g (3hr)	75 g (2hr)
Fasting	95 mg/dL	105mg/dL	95 mg/dL	95 mg/dL	95 mg/dl	126 mg/dL
1hour	165 mg/dL	195 mg/dL	180 mg/dL	180 mg/dL	180 mg/dL	
2hour	145 mg/dL	165 mg/dL	155 mg/dL	155 mg/dL	155 mg/dL	140 mg/dL
3hour	125 mg/dL	145 mg/dl	140 mg/dL		140 mg/dL	

The blood sugar values in mg/dL can be converted to mmol/L by dividing the value by 18 i.e 180mg/dL=10mmol/L.

are less follow-up losses, earlier detection and treatment [15].

5) **Glycosylated haemoglobin (A1c) and serum fructosamine**- These tests are time consuming, and are expensive with low sensitivity. International expert committee and ADA now recommends the estimation of HbA1C (>6.5%) in the diagnosis of diabetes mellitus in general population [10,16] but for the screening of GDM, studies are underway. Serum fructosamine levels indicate glycemic control over a shorter period, but are not indicated for diagnosis of GDM.

6) **Glycosuria** – This test is affected by numerous physiological factors and has only 30% sensitivity [17].

Various screening tests mentioned above are implemented as universal tests that cover entire population or "at-risk" based selective screening.

Recommendations of various national groups are-

Diabetes UK [18] routine antenatal screening by

- Urine testing at every antenatal visit.
- RBG (random blood glucose) at booking, at 28 weeks and if glycosuria.
- A 75 g OGTT if FBG > 110 mg/dL or PPBG > 126 mg/dL (2 hrs of food).

ADA [13] recommends selective screening in pregnant woman having
- Age >25yrs
- Overweight before pregnancy
- Ethnic group with high prevalence of GDM
- Diabetes in first degree relative
- History of abnormal glucose tolerance
- History of poor obstetrical outcome

In all above pregnant women, screening with 50 g GCT and confirmation by 100 g OGTT is done. Drawbacks of ADA procedure were the number of samples drawn for screening and the number of antenatal visits for screening and confirmation [19,20].

Scottish intercollegiate guidance network (SIGN) [13]– recommends
- Routine screening
- Urine and RBG at every antenatal visit

Society of Obstetrician and Gynaecologist of Canada [21] recommends

- Routine screening at 24- 28 weeks with GCT
- High risk diagnostic test as early as possible with repeat test at 24-28 weeks.

National Institute for Clinical Excellence (NICE) – recommends no routine screening.

WHO- recommends universal screening of all pregnant women done with 75 g of OGTT [22].

Canadian Diabetes Association (CDA) - 2008 guideline recommends-

- Screening of all pregnant women between 24-28 weeks using GCT.
- Women with multiple risk factors should undergo first trimester screening using GCT, and reassessment in the subsequent trimesters if initial results are negative.
- In populations at high risk of GDM, a single 75 g OGTT can be used as a definitive screen [23].

ACOG - recommends selective screening with 50 g GCT followed by 100 g OGTT for confirmation of GDM in pregnant women [2]. Presently according to fifth international workshop conference on GDM 2005 [24], GDM risk stratification is done at first antenatal visit. The pregnant females are divided into low, middle and high risk and managed accordingly.

Low risk- No blood glucose testing is done if-
- Age < 25years
- Caucasian /member of other ethnic group
- BMI< 27
- No history of GDM or glucose intolerance
- No family history of diabetes in first degree relative
- No history of GDM associated adverse pregnancy outcome

Average risk– Blood glucose testing is done at 24–28 weeks with one step or two step technique in pregnant females of Indian, Hispanic, Afro-American, Asian ethnic groups.

High risk- Blood glucose testing is done at the earliest, and if found normal, then repeated at 24-28 weeks or at any time when there are features of hyperglycemia in pregnant females having-

- Obesity
- Family history of type 2 DM
- Previous history of GDM, impaired glucose tolerance, glycosuria

Gestational Weeks at which screening is recommended

Majority of guidelines suggest screening between 24-28 weeks as mentioned above but few studies suggest the screening to diagnose GDM in the first trimester itself [25] as early detection and care, results in a better fetal outcome [26]. If the 2–hour plasma glucose is > 200 mg/dL in the early weeks of pregnancy, she may be a pre-GDM (i.e. diabetes before pregnancy) and A1c of > 6% is confirmatory [24].

Multiplicity of the guidelines given above is the reflection of lack of available evidence demonstrating a benefit of specified health outcome with any of national and international standard screening criteria.

Universal Versus Selective Screening

Risk based screening reduces the number of women screened and decreases the burden on health care system while increasing the number of missed diagnosis. Screening with risk factor alone has sensitivity of 63% and specificity of 56%. Association of adverse maternal and fetal outcome in an untreated woman with GDM and medico-legal consequence of a missed diagnosis prompts most clinicians to follow universal screening, despite differential guidelines [27].

In **Indian** scenario, screening is essential in all pregnant women as Indians have 11-fold increased risk of developing glucose intolerance during pregnancy as compared with Caucasian women [28]. Recent data suggests 16.55% prevalence of GDM in our country [18], hence universal screening during pregnancy has become important in our country. To fulfill above requirement, simple, economical and feasible screening procedure is required. ADA recommends two-step procedure whereas WHO suggests one-step 75g OGTT. The pickup rate of WHO is three times more than ADA criteria which is suitable for the Indian setting [24]. This one-step procedure is also feasible in terms of saving time, limiting cost on repeated visits to health centre and reducing repeated invasive sampling.

Recently a large multinational epidemiologic study-Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study, demonstrated that risk of adverse maternal, fetal, and neonatal outcomes continuously increased as a function of maternal glycemia at 24–28 weeks, even within ranges previously considered normal for pregnancy. These results have led to careful reconsideration of the diagnostic criteria for GDM. International association of diabetes and pregnancy study groups (IADPSG) developed diagnostic cut points for the fasting, 1-hr, and 2-hr plasma glucose measurements after 75 g OGTT at 24–28 weeks of gestation that conveyed an odds ratio for adverse outcomes of at least 1.75 compared with women with the mean glucose levels in the HAPO study [29].

Considering the disastrous and avoidable consequences of GDM, current screening strategies seem worthwhile to implement. It can result in reduction in perinatal morbidity, identify women at risk for future type 2 diabetes mellitus, and give opportunity for life style change. Finally, till the search for ideal screening strategy is ongoing, factors like clinical judgement and available resources play important role in choosing best possible mode for evaluation of glucose intolerance in pregnant women.

Key Points

- GDM is seen in 1 – 14% of pregnancies but the prevalence depends on characteristics of the population screened. In India prevalence is 16.55%.
- Most commonly used screening tests are GCT and OGTT alone or in combination forming the one-step or two-step approach of screening.
- Majority of guidelines suggest screening between 24-28 weeks but few studies suggest the screening to diagnose GDM in the first trimester itself as early detection and care, results in a better fetal outcome.
- In Indian setting, one-step procedure recommended by WHO (75 g OGTT) is feasible in terms of better detection rate, saves time, limits cost due to repeated visits to health centre and reduces repeated invasive sampling

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