

# Clarity and Finality of Guidelines to Diagnose Hyperglycemia in Pregnancy- An Appraisal

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## INTRODUCTION

Hyperglycemia in pregnancy includes both pregestational diabetes mellitus and gestational diabetes mellitus (GDM) and this article deals with the latter. GDM is defined as carbohydrate intolerance with onset or recognition during pregnancy. Women diagnosed to have GDM are at increased risk of future diabetes predominantly type 2 diabetes mellitus (DM) as are their children. Thus, GDM offers an important opportunity for the development, testing, and implementation of clinical strategies for diabetes prevention. Timely action taken now in screen in gall pregnant women for glucose intolerance, achieving euglycemia in them, and ensuring adequate nutrition may prevent in all probability, the vicious cycle of transmitting glucose intolerance from one generation to another.<sup>1</sup>

## EPIDEMIOLOGY

The prevalence of GDM in India varied from 3.8% to 21% in different parts of the country, depending on the geographical locations and diagnostic methods used. GDM has been found to be more prevalent in urban areas than in rural areas.<sup>1,2</sup> For a given population and ethnicity, the prevalence of GDM corresponds to the prevalence of impaired glucose

tolerance (IGT) (in nonpregnant adult) within that given population.<sup>3</sup>

## SCREENING AND DIAGNOSIS

Compared to selective screening, universal screening for GDM detects more cases and improves maternal and neonatal prognosis.<sup>4</sup> Hence, universal screening for GDM is essential, as it is generally accepted that women of Asian origin and especially ethnic Indians are at a higher risk of developing GDM and subsequent type 2 diabetes.<sup>5</sup>

### *The International Association of the Diabetes and Pregnancy Study Groups (IADPSG)<sup>6</sup>*

Based on the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) suggested the guidelines. In this HAPO study, population from India, China, South Asian countries (except cities of Bangkok, Hong Kong), Middle East, and sub Saharan countries were not included. Thus, essentially HAPO study was performed in Caucasian population.

- IADPSG recommends that diagnosis of GDM is made when any of the following plasma glucose (PG) values meet or exceed: Fasting:  $\geq 5.1$  mmol/L (92 mg/dL), 1-hour:  $\geq 10.0$  mmol/L (180 mg/dL), 2-hour:  $\geq 8.5$  mmol/L (153 mg/dL)<sup>7</sup> with 75 g OGTT.

### Disadvantages and Inadequacy of the IADPSG Suggestions

- For a pregnant woman, the request to attend fasting for a blood test may not be realistic because of the long travel distance to the clinic in many parts of the world, and increased tendency to nausea in the fasting state. The dropout rate is very high when a pregnant woman is asked to come again for the glucose tolerance test.<sup>7</sup> Attending the first prenatal visit in the fasting state is impractical in many settings.<sup>6</sup>
- In all GDM, fasting plasma glucose (FPG) values do not reflect the 2-hour post glucose with 75 g oral glucose (2-hour PG), which is the hallmark of GDM.<sup>8</sup> Ethnically, Asian Indians have high insulin resistance and as a consequence, their 2-hour PG is higher compared to Caucasians.<sup>9</sup> The insulin resistance during pregnancy escalates further<sup>10</sup> 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 cut-off value, 76% of pregnant women would have missed the diagnosis of GDM made by 2-hour PG >140 mg.<sup>11</sup>
- Asian and South Asian ethnicities are both independently associated with increased insulin resistance in late pregnancy. A diagnostic FPG of 92 mg/dL was present in only 24% of those with GDM in Bangkok and 26% in Hong Kong.<sup>12</sup>
- Center to center differences occur in GDM frequency and relative diagnostic importance of fasting, 1-hour and 2-hour glucose levels. This may impact strategies used for the diagnosis of GDM.<sup>13</sup> The variations may influence the future development of optimal, cost-effective strategies for detection, and treatment of GDM.
- It is not possible to perform A1C in the less resource countries, not only because it is expensive but also due to lack of technically qualified staff. The cost and standardization of A1C testing are issues for consideration.<sup>6</sup>
- There is no high-quality evidence that women and their fetuses benefit from treatment if only the fasting value is abnormal. Randomized clinical

trial shows benefit of treating GDM women identified primarily by post load values.<sup>14</sup>

### *A Single Test Procedure to Diagnose GDM in the Community (Diabetes in Pregnancy Study Group India)<sup>15</sup>*

A single step procedure was developed due to the practical difficulty in performing glucose tolerance test in the fasting state, as seldom pregnant women visiting the antenatal clinic for the first time come in the fasting state. If they are asked to come on another day in the fasting state many of them do not return. Hence, it is important to have a test that detects the glucose intolerance without the woman necessarily undergoing a test in the fasting state and it is preferable to perform the diagnostic test at the first visit itself.

#### Procedure

In the antenatal clinic, a pregnant woman after undergoing preliminary clinical examination, has to be given a 75 g oral glucose load, irrespective of whether she is in the fasting or non-fasting state and without regard to the time of the last meal. A venous blood sample is collected at 2 hours for estimating PG by the glucose oxidase-peroxidase (GOD-POD) method. GDM is diagnosed if 2-hour PG is  $\geq 140$  mg/dL (7.8 mmol/L).

Performing this test procedure in the non-fasting state also is rational, as glucose concentrations are affected little by the time since the last meal in a normal glucose tolerant woman, whereas it will in a woman with gestational diabetes.<sup>16</sup> After a meal, a normal glucose tolerant woman would be able to maintain euglycemia despite glucose challenge due to brisk and adequate insulin response, whereas a woman with GDM who has impaired insulin secretion, her glycemic level increases with a meal and with glucose challenge, the glycemic excursion exaggerates further.<sup>16</sup> This cascading effect is advantageous as this would not result in false-positive diagnosis of GDM.

The following are the advantages of the DIPSI procedure:

- Pregnant women need not fast<sup>17</sup>

- It causes least disturbance in a pregnant woman's routine activities

## RECOMMENDATION OF INTERNATIONAL ORGANIZATION AND NATIONAL GUIDELINES TO DIAGNOSE GDM



### WHO Recommendation

WHO accepted the IADPSG criteria as the new WHO criteria (2013);<sup>14</sup> while endorsing the IADPSG criterion, WHO also accepts “a single step procedure” of DIPSI to diagnose GDM.<sup>14</sup> WHO has made a few important and pertinent observations with regard to GDM testing. OGTT is resource intensive and many health services, especially in low-resource settings, are not able to routinely perform OGTTs in pregnant women. In these circumstances, many health services do not test for hyperglycemia in pregnancy. For a pregnant woman, the request to attend fasting for a blood test may not be realistic because of the long travel distance to the clinic in many parts of the world, and increased tendency to nausea in the fasting state. Consequently, non-fasting testing may be the only practical option.<sup>14</sup> Laboratory glucose measurement is often not available, and testing with a portable blood glucose meter may be an option (DIPSI also recommends PG calibrated glucometers).



### Recommendation by International Federation of Gynecology and Obstetrics (FIGO) 201618

Indian subcontinent: Medium-to-lower source settings serving rural/semiurban/urban ethnic populations at high risk.

In all pregnant women at booking/first trimester 24–28 weeks, estimate 2-hour PG after administering 75g oral glucose in the fasting or non-fasting state and GDM is diagnosed if the value is between 7.8 and 11.0 mmol/L or 140 and 199mg/dL. If negative, repeat the test again in the third trimester.



### Recommendation by International Diabetes Federation (IDF) Congress 2017 at Abu Dhabi<sup>19</sup>

All pregnant women attending health facilities

will be tested for hyperglycemia using a single step procedure, as advocated by FIGO, IDF, and WHO.



### Recommendation by Ministry of Health Government of India<sup>20</sup>

Methodology: Test for diagnosis

Single step testing using 75g oral glucose and measuring PG 2 hours after ingestion.

Seventy-five grams of glucose is to be given orally after dissolving in approximately 300 mL water whether the pregnant woman comes in fasting or non-fasting state, irrespective of the last meal. The intake of the solution has to be completed within 5 min.

A plasma standardized glucometer should be used to evaluate blood glucose 2 hours after the oral glucose load.

If vomiting occurs within 30 min of oral glucose intake, the test has to be repeated the next day, if vomiting occurs after 30 min, the test is continued.

The threshold PG level of  $\geq 140$  mg/dL (more than or equal to 140) is taken as cut-off for diagnosis.

### Gestational Weeks at which Screening is Recommended

By following the usual recommendation for screening between 24 weeks and 28 weeks of gestation, the chance of detecting unrecognized type 2 diabetes before pregnancy (pre-GDM) is likely to be missed.<sup>21</sup> If the 2-hour PG is  $>200$  mg/dL in the early weeks of pregnancy, she may be a pre-GDM and A1C of  $\geq 6.5$  is confirmatory.<sup>22</sup> A pregnant woman found to have normal glucose tolerance (NGT), in the first trimester, should be tested for GDM again around 24th–28th week and finally around 32nd–34th week.<sup>23</sup>

## CONCLUSION

At present, most of the countries follow their own criteria. To overcome this varied approach, IADPSG introduced the guidelines to diagnose GDM which has been accepted by many parts of the world. At the same time IADPSG suggests simpler and more cost-effective strategies that do not require performing an OGTT on most pregnant women for future consideration.<sup>6</sup> The most populous countries with limited resources are not able to follow IDPSG criteria and as a consequence many do not follow

any diagnostic test. In this scenario, an alternative economical, evidence-based and doable test, “a single step procedure” of DIPSI recommended by WHO, IDF, FIGO, and Ministry of Health Government of India is the viable option.

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