The Significance of Glycemic Level of 140mg/dl (7.8mmol/L) in Diabetes

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The classification of different types of diabetes and revision of guidelines for the management of diabetes are periodically being updated. This is due to the constant research and understanding of the pathogenesis of diabetes and its management in the prevention of complications. Poorly controlled diabetes or Impaired glucose tolerance [IGT] are associated with many complications which includes both microvascular complications such as neuropathy, nephropathy, and retinopathy as well as macrovascular complications like coronary, cerebral and peripheral vascular diseases. Hence, there is a necessity to understand the various glycemic levels from which these complications manifest and progresses to optimize the therapy and to arrive at a target glycemic level for effective management and prevention of future complications.

Classification and Diagnosis

Impaired Glucose Tolerance (IGT):

IGT is diagnosed with 2hr PG ≥ 7.8mmol/L (140mg/dl) and ≤ 11.1 mmol/L (200mg/dl) with 75g oral glucose load. If 2 hr plasma glucose less than 140mg/dl is considered to represent “normal” glucose tolerance, subjects whose 2hr PG 120 – 130mg/dl are found to have lost two- third beta cell function. ³ Individual with IGT are maximally or near maximally insulin resistant and they have also lost 80% of beta cell functions.⁴ They also lost approximately half of their beta cell volume i.e. 47%. By both pathophysiological and clinical strand points IGT should be considered to have type 2 diabetes. IGT predicts both large and small-vessel vascular complications, independent of a patient’s progression to diabetes. Compared with age-matched normoglycemic control subjects, patients with IGT are at greater risk for death from all causes and have a two to fivefold increased incidence of new-onset cardiovascular ischemia, fatal and total myocardial infarction, and stroke, independent of progression to diabetes.⁷ IGT is also independently associated with traditional microvascular complications of diabetes, including retinopathy, renal disease, and polyneuropathy. In IGT population, inhibition of nitric oxide-mediated vasodilation, endothelial injury due to increased release of free fatty acids and adipocytokines from adipocytes, and direct metabolic injury of endothelial and end-organ cells contribute to vascular complications.

Gestational Diabetes Mellitus

Gestational Diabetes Mellitus (GDM) is defined as ‘carbohydrate intolerance with recognition or onset during pregnancy’, irrespective of the treatment with diet or insulin.³ GDM is diagnosed if 2hr PG ≥140mg/dl, with 75g OGTT similar to that of Impaired Glucose Tolerance outside Pregnancy.³ Women with a history of GDM are at increased risk of future diabetes, predominantly type 2 diabetes, as are their children.⁸ Additionally other compelling reasons for addressing GDM include the elevated risk of adverse pregnancy outcomes, including maternal- and peri-natal mortality, obstructed labour, infections, spontaneous abortion, congenital abnormalities and macrosomia.³⁻¹² Women with GDM have an increased lifetime risk of developing diabetes, at over 3 times compared to control population at 16 years after index pregnancy.¹³ By 17 years of age one-third of children born to GDM mothers have had evidence of IGT or Type 2 DM.¹⁴ Furthermore, women with a history of GDM are also at increased risk of future cardiovascular disease.¹⁵,¹⁶

Diabetes In Pregnancy Study Group India (DIPSI) follows WHO criteria. The criteria recommended by WHO (2hr PG ≥140 mg/dl) with 75 g oral glucose load is simple and cost effective and is practiced in many centres.¹⁷,¹⁸ Diabetes in Pregnancy Study Group India (DIPSI) also recommends that in the antenatal clinic, pregnant woman is given a 75 g oral glucose load, irrespective of whether she is in the fasting or non fasting state, without regard to the time of the last meal and GDM diagnosed if 2hr PG is ≥ 140 mg/dl.¹⁹ This one-step procedure of DIPSI serves the dual purpose of both screening and diagnosis.²⁰ Perucchini et al also suggest one-step diagnostic procedure (2hr PG ≥140mg/dl) to diagnose GDM.²¹

i. Impact of PG ≥140mg/dl on Short Term Pregnancy Outcome

A study performed by Crowther et al found that treatment of GDM diagnosed by WHO criterion reduces serious perinatal morbidity and may also improve the women's health-related quality of life.²² Diagnosis of GDM with OGTT 2hr PG ≥140 mg/dl and treatment in a combined diabetes antenatal clinic is worthwhile with a decreased macrosomia rate and fewer emergency cesarean sections. The treatment of GDM women as defined by WHO criterion was associated with a reduced risk of adverse pregnancy outcome.²³ Similarly diagnosis of GDM by DIPSI criteria of 2-h PG ≥ 7.8 mmol/L and intervention was not associated with macrosomia.²⁴ Wahi et al observed in their prospective study, the advantage of adhering to a cut-off level of 2hr PG ≥140mg/dl in diagnosis and management of GDM for a significantly positive effect on pregnancy outcomes both in relation to mother as well as the child.²⁵

ii. Impact of pg ≥140 mg/dl on Long Term Pregnancy Outcome

A long term outcome study conducted by Franks et al documented that when maternal 2hr PG was ≥140 mg/dl, the cumulative risk of offspring developing type 2 DM was 30% at the age 24 years.²⁶ Thus, both short-term and long-term morbidities in the offspring occur as maternal plasma glucose increases and this trend is perceptible from 2 h PG ≥ 140 mg/dl.

iii. International Association of the Diabetes and Pregnancy Study Group (IADPSG) Recommendations to Diagnose GDM based on Hyperglycemia and Adverse Pregnancy Outcome [HAPO] Study : The HAPO study observed a continuous relationship between maternal glycaemia and neonatal outcomes, both for the primary (birth weight,
neonatal adiposity, and cord C peptide level ≥ 90th percentile) and secondary outcomes (premature delivery, birth injury, intensive neonatal care, hyperbilirubinemia, and preeclampsia). Of these, the primary outcomes are important, as they are more likely to have permanent impact on the future development of obesity and type 2 diabetes in the offspring, whereas the secondary outcomes, which are treatable, have transitory influence on the newborn. In the HAPO study, the composite outcomes (which includes both primary and secondary outcomes) occur at 2hr PG ≥ 8.8 – 9.8mmol/L, and the primary outcome appears to manifest at 2hr PG 7.0 mmol/L – 7.7 mmol/L and is discernible from 2hr PG 7.8 mmol/L (140 mg/dL) though there is no exact inflection point.27 In the Diabetes in pregnancy awareness and Prevention Project [DIPAP] study also, the observation was that the prevalence of macrosomia was continuum as maternal glucose increased. Macrosomia was 8% at 2hr PG ≥ 6.8mmol/L (120 mg/dl) which increased to 15% at 2hr PG ≥ 7.8mmol/L (140 mg/dL).28

Glycemic Level and Complications

DECODE and DECODA studies have analyzed baseline and two hour post challenge in both European and Asian origin people and found IGT defined by 2hr glucose criteria alone, increased the risk of death from cardiovascular causes and all causes, independent of other known risk factors and the level of fasting glucose.29,30

In another longitudinal study, all – cause mortality risk increased significantly at two-hour post meal plasma glucose (PG) levels above 7.8mmol/l (140mg/dl).30 Post meal hyperglycemia and excursions have also been shown to increase carotid intima-media thickness (IMT)31 and also associated with increased oxidative stress and elevated levels of adhesion molecules (ICAM-1, VCAM-1 and E-selectin), which play an important role in the initiation of atherosclerosis.32,33 At the glycemic level of 7.8 mmol/L, vascular protecting factors are rapidly suppressed particularly endothelium dependent vasodilation and endothelial nitric oxide release.34

Even mild to moderate postmeal hyperglycemia in individuals without diabetes was demonstrated to be an independent risk factors for development of carotid intima – media thickness (CIMT), a marker of atherosclerosis.35 Treatment reduces the risk of myocardial infarction and other cardiovascular events in individuals with IGT.36

Target Glycemic Level

The International Diabetes Federation [IDF] and other organizations define normal glucose tolerance as <140mg/dl two hours following ingestion of a 75g glucose load, thus a two-hour PG level of <140mg/dl is consistent with this definition. Furthermore, because Postprandial plasma glucose usually returns to basal level two or three hours following food ingestion and also as 2hr PG ≥140mg/dl is associated with vascular complications,37 a plasma glucose goal of <140 mg/dl would seem to be a reasonable and conservative glycemic target.

Conclusion

The decisive and disturbing factor of diabetes is its complications. Both macrovascular and microvascular complications occur from 2 hr PG ≥140mg/dl. Adverse maternal and fetal outcomes also occur from this glycemic level. All the health-related morbidities are hoped to be mitigated by giving a serious thought and considering, that 2 hr PG ≥140mg/dl as abnormal both in non-pregnant and pregnant states for instituting intervention. This single value of 2 hr PG ≥140mg/dl is easy to remember by all basic health care workers.

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References


