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# A REVIEW ON GLUCOSE TOLERANCE TEST AS A LABORATORY TOOL IN CLINICAL AND LABORATORY MEDICINE

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**ABSTRACT**
Diabetes mellitus (DM) and its related complications, such as cardiovascular diseases, acquired blindness, chronic kidney disease, and non-traumatic limb loss, are major causes of morbidity and mortality in India. It has already been proven by multiple studies that strict blood glucose control is essential to prevent chronic complications of diabetes. Tight glycemic control through active intervention soon after diagnosis has been shown to prevent microvascular complications as well as macrovascular complications, denoting that early and active treatment is important. In addition, identifying patients with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG). The currently used methods to identify diabetes include the fasting plasma glucose (FPG) level test, oral glucose tolerance test (OGTT), and glycosylated hemoglobin (HbA1c) level test. we conclude that the 2-hour glucose concentration criterion on an oral glucose tolerance test for the diagnosis of diabetes should be raised from 11.1 mmol/L (200 mg/dL) to $ 13.3 mmol/L (240 mg/dL) to remain faithful to the concept that diagnostic concentrations of glucose should predict the subsequent development of specific diabetic complications.

**Key words** Diabetes mellitus, Fasting glucose, Glycosylated hemoglobin, Oral Glucose Tolerance Test.

## INTRODUCTION

In the world the prevalence of type 2 diabetes is increasing at a disturbing rate. The number of people with type 2 diabetes globally is projected to increase from 171 million in 2000 to 366 million by the year of 2030 [1]. This increase, closely linked to the upsurge of obesity, represents a global health care problem for the related micro- and macro-vascular complications [2].

Diabetes is a large, growing, and costly public health problem in the United States and disproportionately affects racial and ethnic minorities. Diabetes is the leading cause of kidney failure, nontraumatic lower extremity amputation, and blindness in working-age adults. Alarmingly, type 2 diabetes (formerly considered an adult disease) is now being diagnosed in children and adolescents and there has been a large increase in diagnosed diabetes among adults. A glucose tolerance test checks how well the body processes glucose (sugar). It involves comparing the levels of glucose in the blood before and after drinking a sugary drink. The results of this test can help doctors to detect type 2 diabetes or impaired glucose tolerance. After you eat, various foods are broken down in your gut into sugars. The main sugar is called glucose which passes through your gut wall into your bloodstream. However, to remain healthy, your blood glucose level should not go too high or too low. So, when your blood glucose level begins to rise (after you eat), the level of a hormone called insulin should also rise..

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Insulin works on the cells of your body and makes them take in glucose from the bloodstream. This decreases the amount of glucose left in the blood. Some of the glucose is used by the cells for energy, and some is converted into glycogen or fat (which are stores of energy). When the blood glucose level begins to fall (between meals), the level of insulin falls. Some glycogen or fat is then converted back into glucose which is released from the cells into the bloodstream. Insulin is a hormone that is made by cells called beta cells. These are part of little 'islands' of cells (islets) within the pancreas. Hormones are chemicals that are released into the bloodstream and work on various parts of the body. Moreover, OGTT is also used to mimic the postprandial hyperglycemia, which may provide the data regarding the hypoglycemic effect as a consequence of changes in glucose utilization.

Functionally, blood glucose levels often elevate markedly after a meal and it is returned to the normal level through compensations. But, someone(s) fail to perform in a good way and they belong to hyperglycemia at a category which is abnormal but is still not reach the criteria of diabetes mellitus (DM) [1]. Then, they are classified as the impaired glucose tolerance [2]. In clinics, oral glucose tolerance test (OGTT) is widely applied for diagnosis of the impaired glucose tolerance (IGT) and/or type-2 DM (T2DM) while IGT is identified using the plasma glucose level between 140-200mg/dL during a 2-hour OGTT [2]. The glucose tolerance signifies the ability of the body to dispose of an additional load of glucose given. This test is useful in distinguishing a person with a normal glucose tolerance from people who have increased tolerance in disease conditions [3]. Each normal individual displays a characteristic time related blood glucose response following ingestion of a known amount of glucose. It essentially involves body's ability to absorb glucose and metabolize it by secreting adequate insulin. This response is altered many a time and indicates several abnormalities of carbohydrate metabolism [4].

**General Indications:**

1. In diagnosis of diabetes mellitus and impaired glucose tolerance in doubtful subjects.
2. Evaluation of non – diabetic glycosuria.
3. Confirmation of gestational diabetes [5].

**Pre – Requisites:**

1. The patient should be on a normal unrestricted diet containing at least 150g of carbohydrate for 3 days.
2. Test should preferably be performed after an overnight fast in the morning on an empty stomach. In case of emergency, it can be done after 4 -5 hrs of last meat. A weak tea without sugar and milk can be allowed.
3. The patient should be relaxed, seated and not involved in physical activity. There should be no smoking before and during the test.
4. All medicines affecting carbohydrate metabolism should be stopped e.g., insulin and other anti-diabetic drugs, steroids, oral contraceptives etc. [6].

To identify diabetics only, a fasting glucose and a glycosylated hemoglobin test could be used. However, to describe the range of glycemia in the population and to identify those who may be insulin resistant, it is necessary to carry out an oral glucose tolerance test. Between 50 and 80% of elderly persons with abnormal glucose tolerance are asymptomatic. In population surveys, approximately 50% of diabetics and almost all participants with impaired glucose tolerance will not have been previously diagnosed. Although the fasting glucose measurement will identify some diabetics, this measurement alone will miss approximately 50% of participants with abnormal glucose tolerance. This review shall focus on the traditional diagnostic tool for diabetes, hurriedly considered obsolete and unsuitable, which deserves revisiting with proper improvements and more modern interpretations.

**DISCUSSION:**

India is being recognized as "The Diabetes Capital of the World". Diabetes is a major health problem in India with prevalence rates between 4.6% and 14% in urban areas, and 1.7% and 13.2% in rural areas respectively. India has an estimated 62 million people with Type 2 Diabetes mellitus; this number is expected to go up to 79.4 million by 2025(1). For universal screening, we suggest a single fasting OGTT with a 75 gram of oral glucose load and diagnosing women or Men with 2-hour PPG ≥140 mg/dl as DM.

**Oral glucose tolerance test in non-pregnant adult: An overview:**

**Test Preparation:**

1. Starting 3 days prior to test, the patient receives a diet containing 150 g of carbohydrate per day.
2. The patient must not be stressed by illness prior or during the test.
3. All on essential medication should be discontinued at least 3 days prior to testing many medication can impair glucose tolerance.
4. A 10-16 hr fast is recommended.
5. Exercise before or during the test is to be avoided.
6. No coffee or smoking is allowed once the fast has started or during the test.

**Dose of glucose for test:**

- 75 g orally (1.75 grams of glucose per kilogram of
- 75 Grams orally (1.75 grams of glucose per kilogram of ideal body weight up to 75 grams)
- Oral glucose solution come in 10 US fluid ounces

**Initial evaluation**:

- If the fasting glucose is < 115 mg/dL, then diabetes is excluded
- If the fasting glucose is 115-140 mg/dL, then an oral glucose tolerance test should be done
- If the fasting glucose is >140 mg/dL, then the
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- 75 g orally (1.75 grams of glucose per kilogram of
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- he fasting glucose is 115-140 mg/dL, then an

The abnormalities in glucose tolerance test must be present on at least 2 occasions before the diagnosis of diabetes mellitus is made. An oral tolerance test need not be done

If a fasting glucose is > = 140 mg/dL at least twice. a random glucose level is > 200 mg/dL and classic

A random glucose level is > 200 mg/dL and classic symptoms (polyuria, polydipsia, ketonuria, weight loss) are found

**Oral glucose tolerance test in pregnant adult female:**
**Dose of glucose for test:**

- Screening test: 50 grams orally
- Diagnostic test: 100 grams orally

**Screening test:**

If 1 hour after the 50 gram the serum glucose is >= 150mg/dL, then the full dose test should be performed.

**Gestational diabetes :**

At least 2 glucose values must exceed the following after the 100 gram loading dose

**Oral Glucose Tolerance Test In Pediatric Population**
**Test Preparation:**

(1) Starting 3 days prior to test, the patient receives a diet containing 150 g of carbohydrate per day.
(2) The patient must not be stressed by illness prior or during the test.
(3) All on essential medication should be discontinued at least 3 days prior to testing many medication can impair glucose tolerance.
(4) A 10-16 hr. fast is recommended.
(5) Undue exercise before or during the test is to be avoided.

**Dose of glucose for test:**

1.75 gram per kilogram of ideal body weight, up to a maximum of 75 grams.

**Interpretation:**

- Both an elevated fasting glucose and a sustained elevated glucose during the oral tolerance test need to be present on at least 2 occasions to make the diagnosis of diabetes mellitus.
- The oral tolerance test is not needed if classic The oral tolerance test is not needed if classic The oral tolerance test is not needed if classic symptoms are present (polyuria, polydipsia, ketonuria, weight loss) and if a random glucose exceeds 200mg/dL

**Glucose Tolerance Test, Intravenous:**
**Test Preparation :**

(1) Starting 3 days prior to test, the patient receives a diet containing 150 g of carbohydrate per day.
(2) The patient must not be stressed by illness prior or during the test.
(3) All on essential medication should be discontinued at least 3 days prior to testing many medication can impair glucose tolerance.
(4) A 10-16 hr fast is recommended.
(5) Undue exercise before or during the test is to be avoided

**Dose of glucose for test:**

0.5 gram per kilogram, body weight up to a maximum of 35 grams, given lV as 5 g glucose per 100 mL solution within 1-2 minutes

GTT can be performed in two ways depending upon the route of glucose load administration i.e., oral GTT and intravenous GTT.

After an overnight fast (8-12hrs after the last meal) the subject is ready for the test. In the early morning fasting blood and urine samples are collected. The subject is administered an oral dose of glucose, normally 75gm glucose dissolved in about 200ml water and flavored, is given. The time is noted. At intervals of 60- and 120-minutes blood samples are withdrawn and urine specimens are collected. Blood glucose levels are determined quantitatively in samples. Sugar in urine specimens is tested quantitatively. The blood glucose values are plotted on a graph sheet as a function of time[7].

**Normal response:**

The fasting blood glucose levels will be in the range of 60-100mg% .30 -60 minutes after glucose administration the blood sugar levels rises peak value of 100 – 130 mg%. The peak value does not exceed the renal threshold level of 180 mg% and there will be no glucose in the urine samples. The initial rise is observed because the quantity of glucose absorbed from the intestine exceeds the capacity of liver and other tissues to use it. Increased glucose levels in blood stimulates insulin secretion which facilities the enhanced utilization of glucose by the peripheral tissue. As a results the blood glucose levels

starts declining and may dip to a value slightly lower than the fasting levels at the end of 2 hrs [8-10].

**Decreased tolerance:**

Decreased tolerance is found in diabetes mellitus. Fasting blood sugar values above 126 mg % and 2 hrs value above 200mg% are characteristic of diabetic mellitus. diminished glucose tolerance is also observed in hyperthyroidism, in hyper activity of adrenals and in severe liver disease [11-12].

**Increased tolerance:**

The graph will appear flatter than a normal response curve. Even in some normal such a profile is found. Increased tolerance is observed in hyperthyroidism, hypoadrenalism and hypopituitarism [13]. Increased tolerance can also be observed in patients with intestinal disorders like idiopathic steatorrhea, sprue and coeliac disease, the abnormal response in these latter cases reflects an impaired absorption of glucose. In such conditions the intravenous glucose tolerance test is performed to assess the ability of the body to dispose of an additional glucose load [14 -15].

In most people a simple blood test is enough to detect diabetes. However, some people have 'borderline' results on routine blood tests and then a glucose tolerance test may help. Also, a glucose tolerance test can show when the body can't manage blood glucose levels well but not yet to the stage of diabetes. This is known as 'impaired glucose tolerance' (sometimes called pre-diabetes) and is a condition that can lead to diabetes. Page 1 of 3 In healthy people, glucose (sugar) levels in the blood always rise after a meal, but they soon return to normal as the glucose is used up or stored. A glucose tolerance test helps to distinguish between this normal pattern and the patterns seen in diabetes and impaired glucose tolerance. Prior to a glucose tolerance test you are asked not to eat for a certain length of time before the test. Then you drink a sugary drink. Normally, the body should quickly move glucose from the blood into the body's cells. This would reduce the amount of glucose found in the blood samples taken. If there is a problem moving glucose into the cells, glucose remains in the bloodstream. This shows as a higher level of glucose in the blood samples. When the results of the blood samples come back, doctors compare the level of glucose found in your blood samples taken after the test with specific values. These values can determine if you have diabetes or impaired glucose tolerance.

There are minimal risks associated with this procedure. The package label for Trutol lists the following rare but known adverse reactions: nausea, vomiting, abdominal bloating, and headache. In addition, there is a rare incidence of hypoglycemia. The risks associated with venipuncture include excessive bleeding, fainting/feeling lightheaded, hematoma, infection, and multiple punctures to identify veins. Participants eligible for OGTT will have to endure the discomfort of a second venipuncture; however, they will benefit by the report of findings that will inform them if they have impaired glucose tolerance. If the 2-hour blood glucose values are equal to or greater than 140 mg/dL, (i.e., glucose levels consistent with impaired glucose tolerance or diabetes mellitus), an early report will be sent.

The ADA emphasizes the fasting plasma glucose (FPG) level in favor of the more expensive and more difficult oral glucose tolerance test (OGTT). Furthermore, the FPG threshold for diabetes is 126 mg/dL (7.0 mmol/L; lower than the previous threshold of 140 mg/dL [7.8 mmol/L]). Diabetes' chronic manifestations include macrovascular disease (atherosclerosis leading to heart attack, stroke, and peripheral vascular disease) and microvascular disease (nephropathy, neuropathy, and retinopathy). Many patients fail to develop acute metabolic manifestations, other than hyperglycemia, and thus fail to develop acute clinical symptoms. Unfortunately, these patients still suffer the considerable morbidity and mortality of diabetes' chronic manifestations. Appropriate treatment favorably alters the course of the disease. This requires early diagnosis and monitoring, which largely depend on clinical laboratory testing. According to the 1997 guidelines, diagnosis by the OGTT is based exclusively on the 2-hour sample: the physician may eliminate 0.5-, 1.0-, and 1.5-hour samples required by the earlier 1979 guidelines. The OGTT must the patient must be on an unrestricted diet (including at least 150 g of carbohydrate daily) for the 3 days before the test, must have unrestricted activity for the 3 days before the test, and must fast for 10 to 16 hours (but may drink water) before the test. The oral glucose dose must be 75 g for nonpregnant adults, 1.75 g per kg ideal body weight for children (up to a maximum dose of 75 g), or 100 g for pregnant women (see "Gestational Diabetes Mellitus"). The oral dose must be given in liquid having a maximum glucose concentration of 25 g/dL, and the patient must drink this liquid within 5 minutes (note that 0-hour is when the patient starts to drink this dose). The patient must remain seated until the test is complete. Blood must be drawn in containers with 30 mg sodium fluoride per 5 mL of whole blood. Serum or plasma must be frozen or analyzed within 4 hours after the blood sample is drawn. Still be performed according to World Health Organization specifications (9-12). The ADA still recognizes a group of patients who have glucose levels higher than normal, but lower than diabetic. Nondiabetic patients with FPGs in the range of 110 to 125 mg/dL (6.1-6.9 mmol/L) have "impaired fasting glucose" (IFG); those with 2-hour post load glucose levels in the range of 140 to 199 mg/dL (7.8-11.0) have "impaired glucose tolerance" (IGT).

Gestational diabetes mellitus (GDM), as the name implies, develops during pregnancy. This category explicitly excludes patients with diabetes before the pregnancy. GDM is a common disease, occurring in 2% to

5% of all pregnancies.5 Patients with GDM are at risk for the same perinatal complications—fetal demise, large-for-gestational-age infants with increased rate of cesarean delivery, and chronic hypertension—as other diabetic patients, but appropriate therapy reduces the complication rate. The 100g, 3-hour OGTT continues to be the "gold standard" for diagnosing GDM. Blood samples are drawn just before, and 1, 2, and 3 hours after the patient drinks a 100-g glucose dose. If the plasma glucose concentration is at or above its cutoff value. The value of urine glucose testing is extremely limited. Glucose appears in urine only when plasma concentrations exceed the renal threshold for glucose reabsorption. This threshold varies widely, but is approximately 180 mg/dL in most persons. Fluid intake also affects urine glucose concentrations (13-15).

OGTT used to be the gold standard for diagnosing diabetes and prediabetes; however, it is now being used less because of its low reproducibility and time-consuming disadvantages [10]. However, the diagnostic value of OGTT now requires a re-evaluation considering the fact that diabetic patients with increasing postprandial glucose can be omitted due to the low concordance rate of the standards for diagnosing diabetes between FPG, 2-hour plasma glucose (2h PG) after 75 g OGTT, and HbA1c levels, while OGTT can reveal insulin resistance and β-cell dysfunction that are the fundamental pathophysiology of the state of diabetes (12-14).

Therefore, what would be gained by labeling people with a 2-hour glucose concentration on an oral glucose tolerance test of 11.1–13.3 mmol/L (200–239 mg/dL) as having diabetes? Although it is possible that being termed “diabetic” may motivate patients to achieve tighter control, approximately two thirds of these individuals will already have normal Hb A1C levels. Furthermore, given that the average Hb A1C level of people who know that they have diabetes in this country exceeds 9%,21 there is little reason to believe that simply being made aware of the diagnosis will motivate people to achieve near euglycemia. On the other hand, there are potentially negative insurance, employability, psychological, and social costs of carrying the diagnosis of diabetes (12-15).

**OGTT Advantages:**

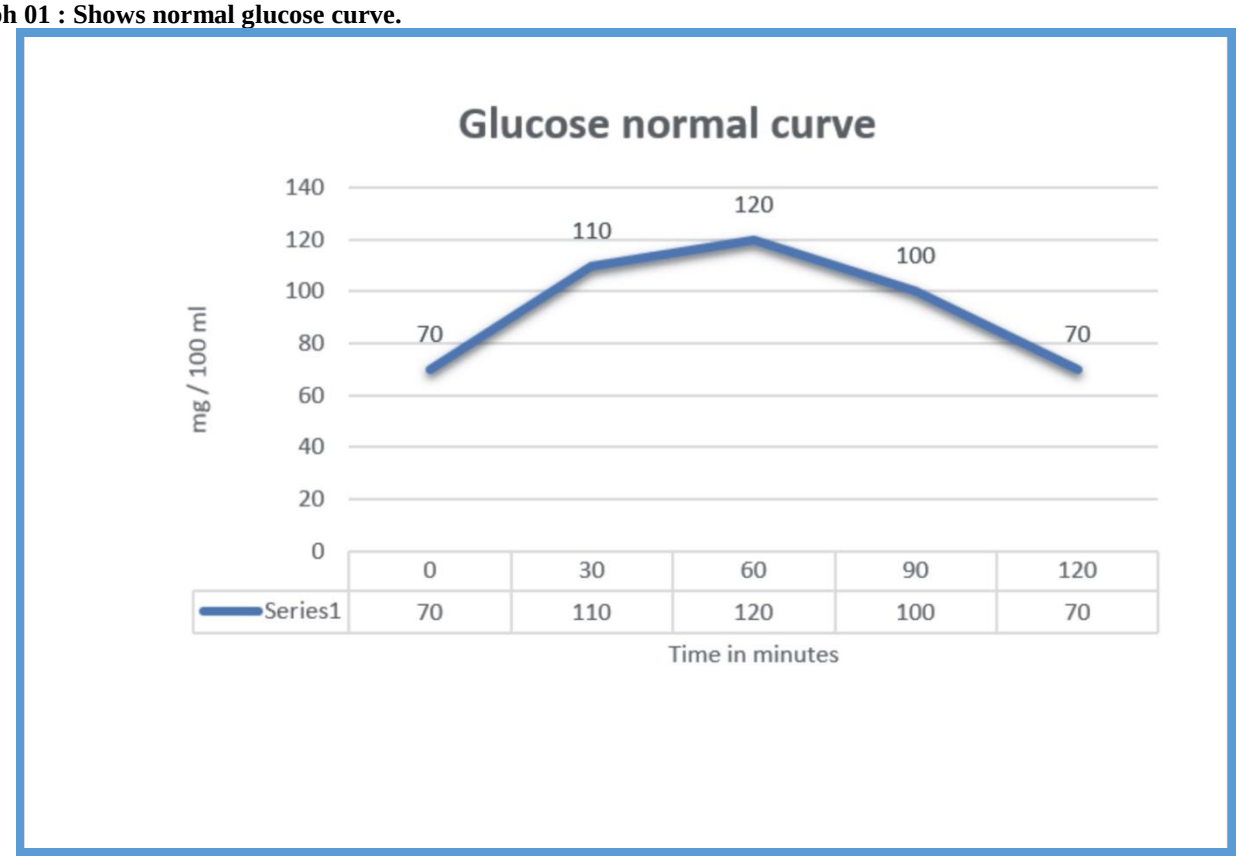
Sensitive indicator of risk of developing diabetes, Early marker of impaired glucose homeostasis, Extensive patient preparation, Time consuming and inconvenient for patient, Glucose assay easily automated – Widely available inexpensive and has reasonable sensitivity, acceptable reliable, reproducible alternative DM screening method to the OGTT for the last three decades.

**Disadvantages:**

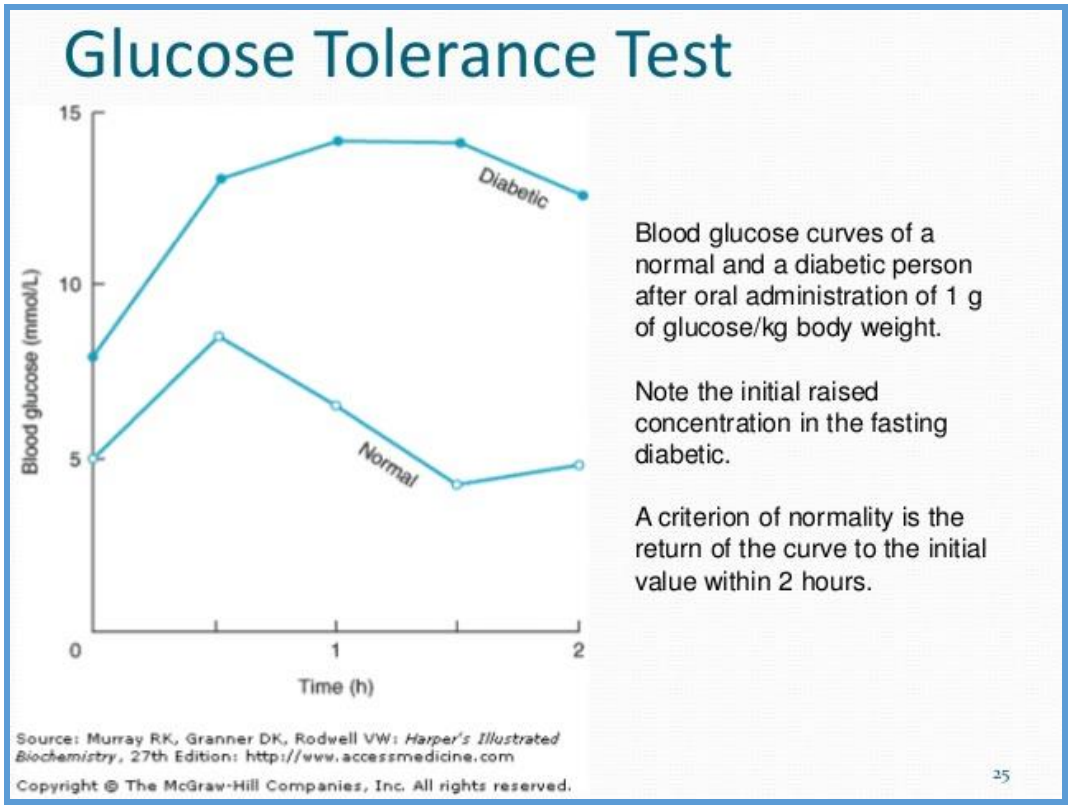
Patient must fast for >8 to 12 hrs, Large biological variability, Diurnal variation, sample not stable, some labs use serum instead of plasma

**Figure 01: Shows types of oral glucose tolerance test.**

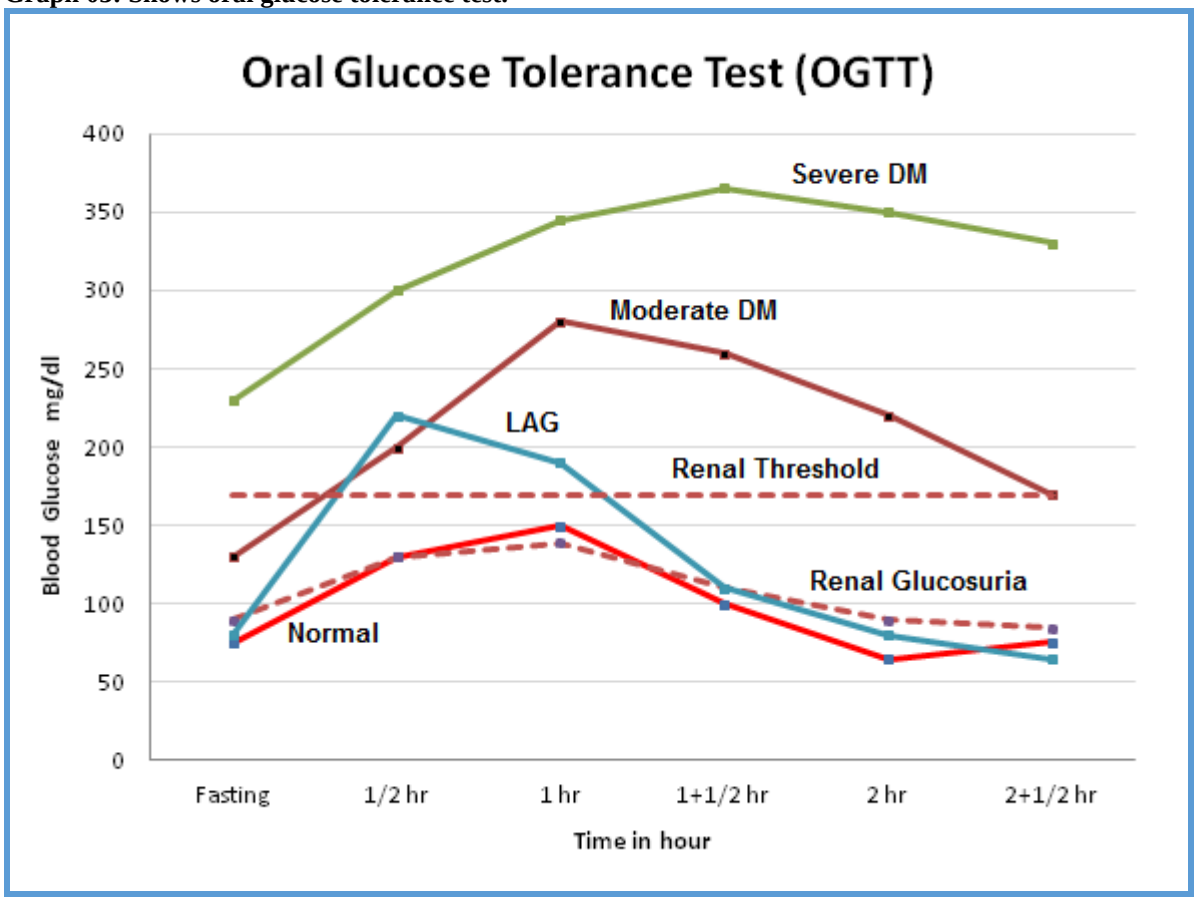
**Graph 01 : Shows normal glucose curve.**




Graph 02: Shows Glucose tolerance test in diabetes.



**Graph 03: Shows oral glucose tolerance test.**




**Conclusion:**

An OGTT is used clinically to diagnose impaired glucose tolerance and as a standardized test of carbohydrate metabolism and insulin secretion. The test is based on oral administration of glucose and subsequently following plasma glucose and insulin levels over time. A prolonged elevation (>120min) in both plasma glucose and insulin constitutes impaired glucose tolerance and insulin resistance and can be used in conjunction with fasting hyperglycemia in diagnosing Type 2 diabetes. The relationship between HbA1c and blood glucose have been described, though the reasons remain unclear. The OGTT has the disadvantage of being time consuming, inconvenient, susceptible to short term life style changes and to intra-individual biological variation. Oral glucose tolerance test (OGTT) is useful in the diagnosis of impaired glucose tolerance (IGT) in clinics. In basic research, OGTT is also useful in the development of new agent(s) for diabetic medication(s). However, it must concern the changes in basal glucose level showing at the 0 min during OGTT. The basal glucose level cannot be ignored and/or deleted in the preparation of AUC from OGTT.

OGTT detects diabetes more efficiently than FPG as it recognizes altered post-prandial metabolism. OGTT establishes whether an IFG subject has normal 2hPG. This is essential, as the majority of IFG subjects display a preserved glucose homeostasis with respect to those IFG subjects with abnormal 2hPG. FPG does not supply any metabolically relevant information, to the point that it is misleading to try to assess glucose homeostasis without information on post-prandial glucose metabolism. IGT subjects, who are always included in trials concerning type 2 diabetes prevention, cannot be recognized without OGTT. Using A1C in diabetes screening does not substitute for the information derived from OGTT, because they are not equivalent tests. OGTT lends itself to simple calculations, like the % change of 2 h with respect baseline glycemia, capable of detecting additional subjects at risk for type 2 diabetes. Oral glucose tolerance test is used not only to diagnose diabetes, but also help to provide additional information about the body's ability to metabolize blood glucose. Higher OGTT values are likely to reflect diet, lifestyle problems and problems of insulin functioning. The oral glucose tolerance test (OGTT) is the gold standard for making the diagnosis of type 2 diabetes.

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**Conflicts Of Interest**

The authors declare no conflict of interest.

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