Laboratory Report on Oral Glucose Tolerance Test and the Efficacy of Diagnosis for Diabetes Mellitus

INTRODUCTION 1.0

Diabetes mellitus is a chronic disease that is characterized by an impaired ability of the body to respond to and produce insulin, a hormone needed in order to remove excess glucose from the blood. As a result of a lack of functioning insulin, the blood becomes hyperglycaemic (*Britannica, 2022).* The consequences of constant high blood glucose levels result in advanced glycation end-products (AGEs) which cause damage to arterial walls, blood vessels and nerves, increasing the risk of kidney failure, myocardial infarction, blindness and strokes (*Holford, 2013*).

GLUCOSE IN THE BODY 1.1

Blood glucose levels in the body are regulated by a negative feedback loop in which digestion of carbohydrates and the release of hormones, insulin and glucagon, are controlled to ensure blood glucose remains in the normal range of 4.4 -6.7 mmol/L (*Waugh & Grant, 2018*). Both chemical and mechanical digestion of carbohydrates begins in the mouth where mastication and salivary amylase enzymes begin to break down the carbohydrate molecules. Mechanical digestion of carbohydrates continues through peristaltic contractions of the stomach moving chyme into the duodenum. It is here that the pancreas β-cells secrete and release insulin, sending signals to body cells to remove glucose from the blood to be transported to cells via insulin-receptors. Here, they are utilized as energy and in anabolic processes (*Medicine Libre Texts, 2020*). Insulin also signals glucose to be converted and stored away as glycogen in the liver and muscle tissues. Consumption of carbohydrates increase insulin secretion, and as blood glucose levels begin to drop below the normal range after meals, glucagon is secreted by the pancreas α-cells to forgo glycogenolysis to convert the glycogen stores into glucose to be released into the bloodstream (*Waugh & Grant, 2018),* thus maintaining the blood-glucose balance through negative feedback. Evidently, impairments made to both insulin and receptor sensitivities will largely affect the proficiency of carbohydrate metabolism and glucose levels in the blood.

DIABETES MELLITUS 1.2

Type-1 diabetes mellitus (T1DM) and type-2 diabetes mellitus (T2DM) are the most common forms of the condition. T1DM is an autoimmune disease that occurs most commonly in children and young adults where β-cells in the pancreas that secrete insulin are destroyed by the body's antibodies, therefore resulting in a severe deficiency of insulin (*Waugh & Grant, 2018*). The most common form, which accounts for 90% of diabetes cases in the UK (*Diabetes UK, 2022*) is T2DM with predisposing factors including, obesity, increasing age, sedentary lifestyle, and genetic factors. T2DM is identified as an ineffective use of insulin produced, becoming insulin-resistant where a lack of functioning insulin results in high glucose levels remaining in the blood, causing damage to cells. Whilst T1DM patients suffer with insufficient levels of insulin causing hyperglycaemia, T2DM patients experience

hyperglycaemia, usually with high levels of insulin present due to insensitivity of insulin and insulin-receptors.

DIABETES MELLITUS STATISTICS 1.3

In the UK alone, there are 4.9 million cases of diabetes, 90% of which are T2DM, 8% T1DM and 2% rarer types of diabetes (*Diabetes UK, 2022*). The prevalence of diabetes cases worldwide is identified in concerning statistics that from 1980 with 108 million diagnosed diabetics, the figures made a staggering increase to 422 million in 2014. In 2019, diabetes directly accounted for 1.5 million deaths becoming one of nine leading causes of death, half of which were under the age of 70 (*WHO, 2021*). With figures estimating approximately 850,000 people in the UK living with diabetes who are yet to be diagnosed (*Diabetes, 2022*), the methods of diabetes diagnosis remain an important topic of discussion.

COMPARING METHODS OF TESTING 2.0

Testing for diabetes requires a blood sample to identify glucose present in the blood. Though a blood-sample analysis is the primary method of identifying glucose levels, urinalysis is also a useful tool in contributing to a diagnosis. Kidney function is a great indicator of a patient's blood glucose as limits that exceed the renal threshold pass through the kidneys, tubular reabsorption of glucose does not occur and is micturated via urine.

FASTING PLASMA GLUCOSE 2.1

Fasting Plasma Glucose (FPG) testing is a widely useful, inexpensive method of identifying blood glucose levels. FPGs require the patient to fast overnight, then proceed to have their blood extracted the following morning using finger-prick devices and lancets or via venepuncture. In FPG testing a person recording 126 mg/dL would be likely diabetic. A reading of 70-99 mg/dL would be considered a normal and "healthy" range (*CDC, 2021*). The benefit of this method is the convenience of immediate results and is inexpensive and simple to carry out. Though convenient, it should be considered that failure to meet the fasting guidelines and ingestion of any food and drink will provide an inaccurate result (*Bohl, 2021*). A single FPG test is not a sufficient diagnosis for diabetes, thus a repeated test is necessary. It is also shown to be less sensitive in providing accurate results, than for example, in an oral glucose tolerance test.

ORAL GLUCOSE TOLERANCE TESTING 2.2

Oral Glucose Tolerance Testing (OGTT) is used to detect blood glucose through a method that requires the patient to ingest a glucose solution, after over-night fasting, followed by an hourly sample of blood taken from the patient over a 2–3-hour period (*Ahren, 2013*). Whilst this is a time-consuming method, results are regarded to be accurate and is proficient in detecting the efficiency at which the patient's body regulates blood glucose levels. During this method, urine samples can also be tested at each interval to detect any glucose being passed. Figure 1 below displays results taken to identify the visible difference between a non-diabetic and a diabetic patient. An OGTT is an acceptable diagnostic method for diagnosing diabetes according to World Health Organisation (*WHO, 2019*).

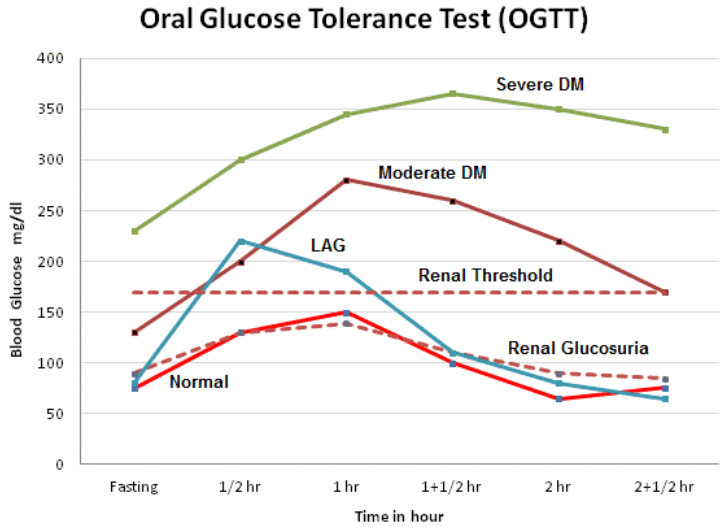

Figure. 1 *A line graph displaying the results obtained from patients identifying the measurements taken from an OGTT for normal and diabetic patients. This graph also presents the renal threshold as a marker for identifying normal blood glucose regulation (Emmanuel, 2022).*

Another method for diagnosing diabetes is an A1c test, otherwise known as a HbA1c test which measures glycosylated haemoglobin over a period of 8-12 weeks. When a patient is hyperglycaemic, the haemoglobin in red blood cells (erythrocytes) become glycosylated, essentially coated in glucose, which are indicative of sugar spikes. Erythrocytes have a 3-month life cycle, where, once they become glycosylated, they remain that way. The more glycosylated haemoglobin is detected in a blood sample, the more evident it is of frequent high blood glucose (*Holford, 2013*). In this method, the patient is not required to fast and provides reliable results with a better sensitivity than that of FPG testing. A study revealed that where FPG testing didn't provide sensitive results, HbA1c testing provided enough accuracy to detect early onset of diabetes (*Chung, 2017*). HbA1c testing is proficient in providing reliable and accurate results and is an acceptable method of diabetes diagnostics however it is a time-consuming test and is more expensive to run which may not be convenient for some.

OGTT is a reliable, efficient and accurate method of testing diabetes in patients to provide accepted results. In this study, the focus is on the analysis of a participant's result using the OGTT method, to assess whether the participant has diabetes.

METHOD 3.0

The details of the participant are presented in table 1. From the information provided it is understood that the participant has a sedentary occupation and a father with a T2DM diagnosis from an African-Caribbean background. The participant also recorded difficulty in sleeping.

The participant was requested to submit a consent form prior to the test. An Analox GM7 Microstat analyser was calibrated using glucose standard at 8 mmol/L. A pre-test blood sample was taken from the participant to measure blood glucose levels following an 8-hour overnight fast. The participant was instructed to ingest 75g glucose in 100ml water solution. A blood sample was collected using a single-use lancet and a Gilson pipette was used to measure 10µl of the sample in the Analox

GM7 Microstat analyser. Blood samples were taken every 30 minutes following the consumption of the glucose solution. The test was run over a 3-hour period.

A sample of urine was also collected from the participant at each 30-minute interval and was tested for glucose using diabetes test strips, otherwise known as dipsticks, to identify any glucose present in the urine.

Table 1. Participant Details

Age	45 years
Sex	Male
Ethnicity	African-Caribbean
Occupation	Telemarketing
BMI	34.3 (obese)
Smoker?	Yes
Difficulty sleeping?	Yes

RESULTS 4.0

The results below in figure 2 show that the participant had a fasting blood glucose concentration under the renal threshold of 10 mmol/L at 8.3 mmol/L. Between 30 and 60 minutes there was a steep spike in blood glucose and remained high at 15 mmol/L until 150 minutes when it began to fall to 13.1 mmol/L. The highest recorded blood sugar level was 15.4 mmol/L at 120 minutes, where a non-diabetic would be expected to record a reading less than 7.8 mmol/L. From the pre-test measurement to 120 minutes postprandial, there was a significant 85.5% increase in blood sugar concentration. This is indicative of insulin-resistance where the insulin shows a lack in ability to maintain a normal blood-glucose range. From 150 minutes, the blood glucose levels started to decline gradually, though it was not able to achieve the pre-test glucose measurements.

Figure 2. Participant OGTT Results – Blood Glucose Concentration

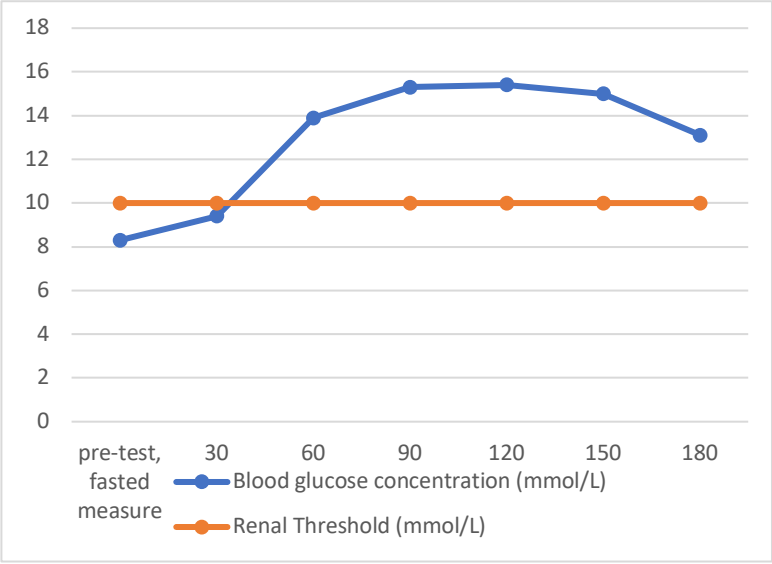

Figure 2. displays the results taken from the participant's OGTT with a reference to the renal threshold of 10 mmol/L to provide clear indication of signs of pre-diabetes (renal threshold - Heishima et al, 2020).

After 3 hours, the blood glucose concentration failed to meet the pre-test fasted measure, which would be expected in a diabetic participant where normal blood glucose ranges should return to pre-test measurements 3-hours postprandial. The participant records 4.8 mmol/L above their pre-test measurement.

The data collected in table 2 demonstrates that the participant didn't micturate any glucose during their pre-test fasted measure and did not show to micturate any glucose after 30 minutes. However, the participant presented a positive result at 60 minutes and thereafter.

Table 2. Participant Results – Urinary Glucose

Time (mins)	**Urinary Glucose**
pre-test, fasted measure	-
30	-
60	+
90	+
120	+
150	+
180	+

Table 2. displays the glucose micturated in the participant's urine at each 30-minute interval.

DISCUSSION 5.0

The risk of having diabetes increases with age, the American Diabetes Associations (ADA) stating a 57% increased risk of developing overt diabetes from pre-diabetes in men aged 45 and over where regular testing is recommended (*Ligthart et al, 2020*). Studies also show the increased risk of having T2DM of African-Caribbean ethnicity living in the UK is at least double than that of White British (*Pitts-Tucker, 2021*).

OBESITY AND DIABETES 5.1

In accordance with WHO, obesity is classified as those with a body mass index (BMI) of 30+. Obesity is defined as an excessive fat accumulation and poses a serious risk to a person's health (*WHO, 2022*) . Obesity is linked to an increased risk of developing T2DM as the condition can elicit changes to the body's metabolism that cause adipose tissues to release increased amounts of pro-inflammatory cytokines and other such factors that are involved in desensitizing insulin-receptors (*GOV, 2022).* When paired with a dysfunction in pancreatic islet β-cells, blood glucose regulation is heavily impaired. Based on the information provided by the participant, it is likely that the risk of having T2DM is highly likely as obesity, age, and

genetics all play a large role in the body's ability to sufficiently regulate blood sugar levels.

URINALYSIS 5.2
A T2DM participant would be expected to show positive results in their urine samples. The participant passed glucose in their urine after 60-minutes postprandial, thus will require further analysis to monitor blood glucose levels. This participant showed the difficulty their body had managing their blood glucose levels and showed signs of insulin-resistance. As the blood glucose levels exceed the renal threshold of the kidney, the process of glucose reabsorption in the proximal and distal tubules is decreased therefor allowing the glucose to be passed in the urine. A study made on rats with T2DM concluded that urine testing and urinalysis is a simple method of monitoring blood glucose levels in order to detect disordered urine glucose levels to improve analysis of pre-diabetic patients (*Yin et al, 2017*). In doing so, health professionals may be able to detect pre-diabetes earlier in their patients via regular testing to provide support and assistance in preventing and prolonging a diabetes diagnosis.

DIAGNOSTIC TEST RESULTS 5.3
Though this participant recorded a reading of 8.3 mmol/L for their fasted blood sugar measurement, 1.7 mmol/L within the renal threshold of 10 mmol/L, a normal pre-test fasting measurement would be expected to be 5.6 mmol/L or lower. Table 3 below exemplifies the measurements used as a diagnostic tool for diabetes by the Centres for Disease Control and Prevention (CDC). From the data displayed below, it is identified that the participant showed a diabetic result with a fasting glucose measurement of 8.3 mmol/L, higher than the given 5.5 mmol/L and lower for a normal range.

Table 3. CDC diabetes diagnosis (Adapted from Centre of Disease Control)

	A1c Test	***Fasting Blood Sugar Test***	***OGTT***
Diabetes	*6.5%*	*7 mmol/L +*	*11.1 mmol/L +*
Prediabetes	*5.7-6.4%*	*5.6 -6.9 mmol/L*	*7.8 -11.1 mmol/L*
Normal	*Below 5.7%*	*5.5 mmol/L or below*	*7.8 mmol/L or below*

Table 3 results interpreted from CDC diagnostic criteria provided to determine and measure normal, pre-diabetic and diabetic ranges (CDC, 2021).

The participant recorded a reading of 15.4 mmol/L at the peak of their OGTT results at 120 minutes. With the data presented in table 3, it further evidences this participant is likely to have T2DM on the grounds of surpassing the 11.1 mmol/L threshold by a significant 4.3 mmol/L on the OGTT.

In figure 3 below it is identified that non-diabetic and pre-diabetic participants were able to regulate their blood glucose concentration to their pre-test fasted measurements however the graph illustrates that the diabetic participant was unable to do so after 180-minutes postprandial (*Zhou, 2006).*

Figure 3. Example of Blood Glucose Regulation in OGTT

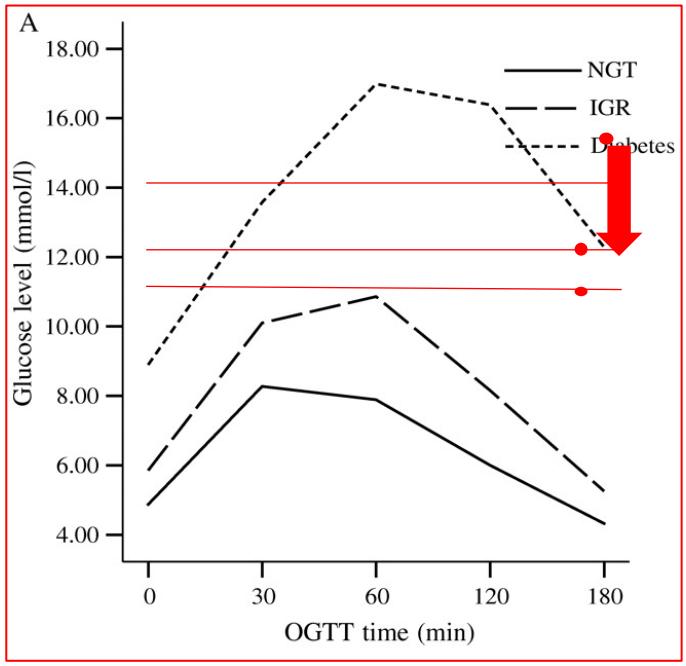

Figure 3. shows results taken in an OGTT where the red line has been interpreted to indicate the point at which pre-test blood glucose concentration are returned to at 180-minutes after ingestion of glucose solution. In a diabetic participant, the pre-test measurement was not met at 180 minutes (Zhou, 2006).

The results presented by the participant in figure 2 show that they experienced inhibited insulin productivity and the participant's blood glucose was not able to return to pre-test fasting measurements which, as identified in figure 3, would be expected in normal and pre-diabetic patients. A similar sudden incline can be identified in both the participant's results in figure 2 and the diabetic results in figure 3 (Zhou, 2006). This is seen to occur within the first 60 minutes of both OGTTs where the ingestion of the glucose solution causes a quick release of insulin, though in a participant with T2DM, there is a lack of functioning insulin and decreased insulin-receptor sensitivity, consequently resulting in an uncontrollable increase of glucose in the blood.

SMOKING AND DIABETES 5.4

The participant, being a smoker, has a greater risk of developing T2DM based on the 2014 Surgeon General's Report that suggested there were a multitude of ways in which smoking increased the risk of T2DM (*HHS, 2021*). Studies report that smokers are 30-40% more likely to develop the condition than non-smokers. The chemicals present in cigarettes interfere with normal cell function and cause inflammation, interrupting and decreasing the effectiveness of insulin. The chemicals inhaled from the cigarette reacts with oxygen and causes oxidative stress, ultimately causing cell damage (*FDA, 2022*) . The inhalation of harmful chemicals when smoking poses a serious health risk and inhibits insulin function.

SLEEPING AND DIABETES 5.5

Though sleeping may be referred to as a passive condition, it is rather a paramount process in regulating, repairing and restoring the body. Sleep disturbance and T2DM are commonly associated whereby sleep deprivation can inhibit the modulation of a variety of metabolic, endocrine and sympathetic nervous(*Khandelwal et al, 2017*). Where the participant reported difficulty sleeping, a meta-analysis review demonstrated that disturbed sleep proved to be a significant risk to developing T2DM, effectively similar to statistics of other risks such as inactivity, obesity and gene inheritance. A concept analysis reported sleeping difficulty to be a symptom of T2DM, the results presenting compromised quality of sleep in T2DM patients leads to impaired daytime functioning and next-day fatigue (*Zhu B et al, 2018*). Mismanaged sleeping patterns disrupts the orexin system in that it becomes overactive leading to overeating during periods of tiredness during the day. There is an increased release of ghrelin and a decreased release of leptin, essential in communicating satiety. A study presented results of higher insulin response to OGTT in a state of sleep deprivation than that of a participant in a normal sleep condition (*Khandelwal et al, 2017*). The study established that there was a state of insulin-resistance induced by acute sleep disturbance where blood glucose regulation was inhibited by a lack of functioning insulin.

CONCLUSION

Based on the identified risks of the information provided and the results obtained from the OGTT, it would be advised that the participant should consider partaking in a repeat OGTT to rule out any laboratory errors made before making an official diagnosis. Nonetheless they must seek nutritional guidance and regular testing to monitor their condition as their results indicate fasting hyperglycaemia and an inability to regulate their blood glucose levels during 3-hours postprandial. According to WHO diagnostics, this participant, based on their current OGTT results, would receive a diabetes diagnosis for T2DM.

As earlier discussed, there are approximately 850,000 people in the UK who are yet to be diagnosed, thus simple and time-effective methods of monitoring and testing such as OGTT is key to providing people with the support they require to prevent diabetes and diabetes-related illness from occurring such as myocardial infarction, diabetic retinopathy and ketoacidosis. Though OGTT provides a reliable and efficient diagnosis, it has been recommended by some organisations that due to the accuracy of HbA1c testing, it may be a preferred method of testing to provide the most accurate results for diagnosis.

APPENDIX

Results were taken in mg/dL; calibration of Analox GM7 Microstat analyser in mmol/L thus results were converted from mg/dL to mmol/L using the equation below:

Formula to calculate mmol/l from mg/dl: mmol/l = mg/dl / 18

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