



## The Diagnostic Value of the Glucose Curve in Individuals with and without Diabetes

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### Authors' contributions

This work was carried out in collaboration between both authors. Author MNEN carried out the bench work performed the statistical analysis and wrote and monitored the manuscript. Author MSEG managed and supervised the experiment protocol and literature searches. Both authors read and approved the final manuscript.

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### ABSTRACT

**Aim:** Of this study is to demonstrate the importance of glucose curve test in monitoring pre and post-meal variation in diabetic and normal individuals.

**Methodology:** The individuals subjected to this study mainly grouped in two categories the (DM2 group) and the (Control group), they instructed to come fasting at which blood sample will be collected in EDTA and blank tube then after 30 min. the first post-prandial blood sample collected and then after every 1,2,3,4,5,6,7,8 hours blood sample collected subsequently, then serum separated from each sample (except the EDTA tube) analysed biochemically for glucose and glycated haemoglobin HbA1c (from EDTA tube).

**Result:** We found that, the calculated glucose based on mean glycated haemoglobin HbA1c% results underestimate the real concentrations all over the glucose in control group but in DM2 group it underestimate the mean and some actually measured concentration in some points of the curve which adds more burden on the diabetic patient and the responsibility of adjusting the dose and time of administration.

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**Conclusion:** from our prospect we recommend the use of blood glucose curve as a monitoring and diagnostic tool generally for glucose metabolism in normal, pre-diabetic, diabetic and uncontrolled diabetic patients before and during therapeutic conditions.

*Keywords: Glycated haemoglobin HbA1c%; blood glucose curve; diabetic patients.*

## 1. INTRODUCTION

Diabetes mellitus (DM) is described as a group of metabolic disorders caused by many different mechanisms and characterized by chronic hyperglycaemia or high levels of glucose with disturbances of carbohydrate, fat, and protein metabolism on target tissues, caused by deficient insulin secretion and/or resistance to its action (hepatic and peripheral glucose uptake) [1].

Type 2 diabetes results from a combination of genetic predisposition, unhealthy diet, and physical inactivity, the mechanisms for the genetic explanation have not been completely described, but different studies give support to this hypothesis. Among the supported findings are the strong family associations (higher type 2 diabetes in relatives and similar in twins), the high variability in prevalence in different populations and the fact that certain subgroups (Pima Indians, Nauruans, etc) have a disproportionate prevalence [2].

Hyperglycaemia in type 2 diabetes is considered as an abnormal elevation in blood glucose level, which is caused by impaired insulin-stimulated glucose uptake and uncontrolled hepatic glucose production [3].

Glycated haemoglobin (HbA1c) is a form of haemoglobin which is measured primarily to identify the average plasma glucose concentration over prolonged periods. It is being observed that it is formed in a non-enzymatic glycation pathway by haemoglobin's exposure to plasma glucose [4].

## 2. MATERIALS AND METHODS

### 2.1 Candidate Grouping

The individual's subjected to this study mainly grouped in two categories the (DM 2 group) and the (Control group), members of (DM2 group) must be previously diagnosed with diabetes mellitus type2 from more than 6 month, both groups are asked to complete a form contains fields for name , age, sex.

### 2.2 Sample Collection

The candidate's instructed to come in the next morning fasting from 7 pm to 7 am at which the fasting blood sample will collected (1.5 ml) in EDTA tube and (3.5 ml) in blank tube then they must complete the standard meal in less than 10 minutes and after 30 minutes the first post-prandial blood sample (3.5 ml) collected then after 1, 2, 3, 4, 5, 6, 7, 8 hours blood sample collected subsequently with restrictions on food intake, then the tubes centrifuged (except the EDTA tube) for 10minutes at 3250 rpm after that the serum collected and transferred in labelled Eppendorf tube to the lab freezer at -21°C.

### 2.3 Blood Estimated Parameter

The serum collected from each sample was analysed biochemically for glucose by the enzymatic colourimetric quantitative method according to [5].

EDTA blood tubes collected from each individual were quantitatively analysed to determine glycated haemoglobin HbA1c % according to the method in [6].

The average blood glucose concentration will be calculated from measured glycated haemoglobin HbA1c % according to the method in [7].

### 2.4 Statistical Analysis

The data were presented and graphed as mean and mean  $\pm$ SD (Standard deviation) for the most estimated parameter.

## 3. RESULTS

The individuals subjected to this study are totally from hospitals and privet clinics in Port Said, samples collection completed with 104 cases 85 of them are males and 19 females, these individuals manly grouped in two categories the (DM2 group) 58 case and the (control group) 46 case, members of (DM2 group) must be previously diagnosed with diabetes mellitus type 2 from more than 6 months, the DM2 group

represented with 50 male, 8 female and the control group represented with 35 male, 11 female (Fig. 1).

The range of age for all individuals in this study is between 21 and 67 years old, the range of age for (DM2 group) is between 24 and 67 years old and the range of age for (control group) is between 21 and 58 years old, the statistical mean for age of (DM2 group) is 51 years and 45 for the (control group), the statistical standard deviation for age of (DM2 group) individuals is 10.9 years and 9.7 for the (control group) (Fig. 2).

(Fig. 3 and Table 1) represent and summarize the full pattern of change in mean glucose concentration curves in DM2 and control groups.

The mean of measured glucose concentrations is (170 mg/dl and 107 mg/dl) with standard deviation (24% and 13%), the mean measured HbA1c is (7.0% and 4.7%) with a standard deviation (1.5% and 0.4%) and the calculated average blood glucose concentration based on measured glycated haemoglobin HbA1c% is (155 mg/dl and 89 mg/dl) respectively for DM2 and control groups (Table 2).

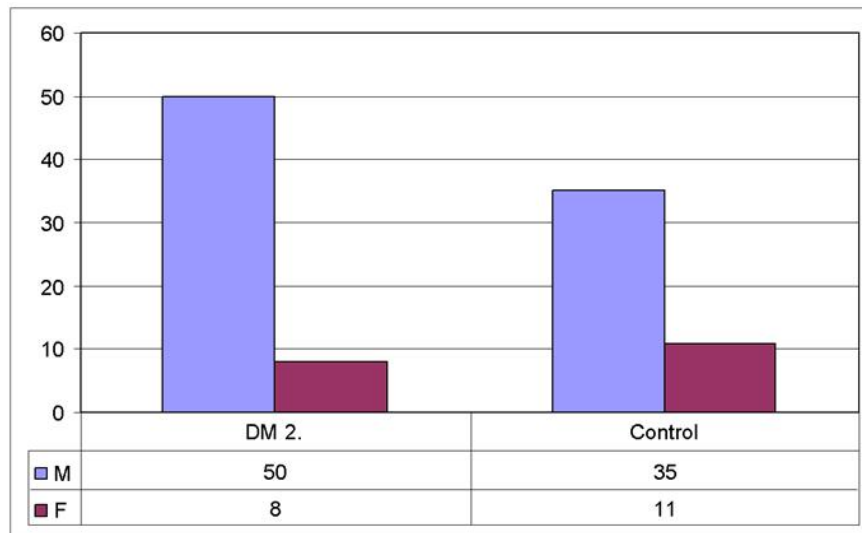


Fig. 1. Male and female distribution in groups DM2 and control

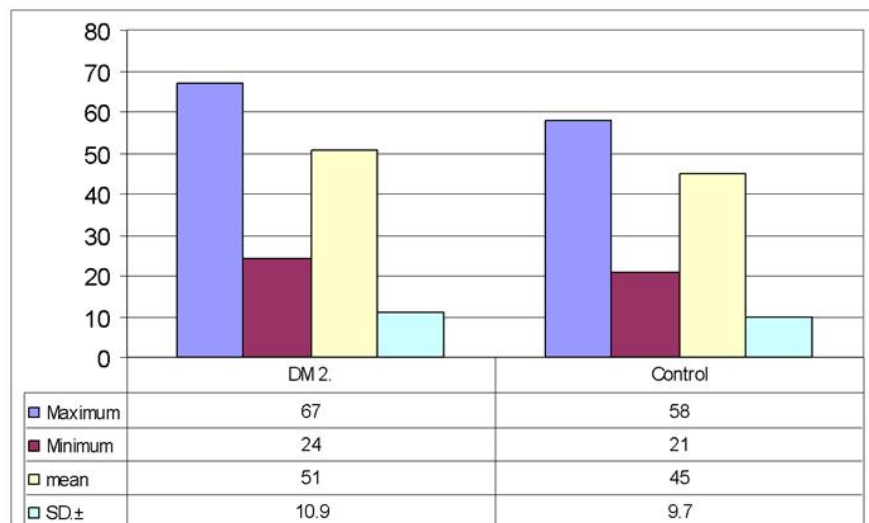
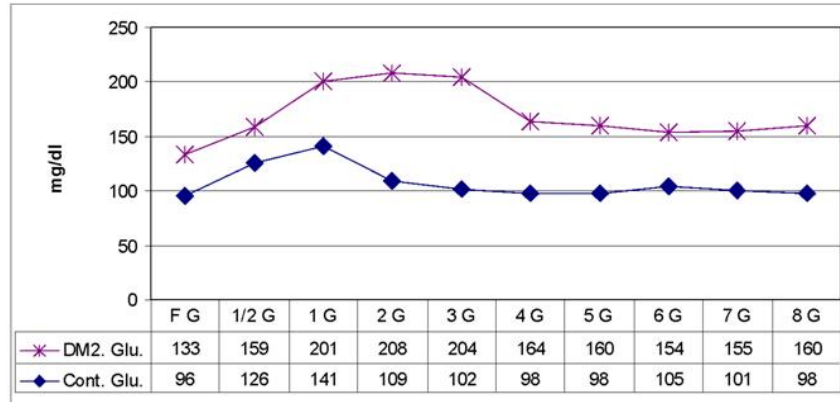


Fig. 2. Age parameter and variability between DM2 and control showing the maximum, minimum, mean, standard deviation values in each group

**Table 1. The mean glucose concentration (mg/dl) and the standard deviation between DM2 and control groups**

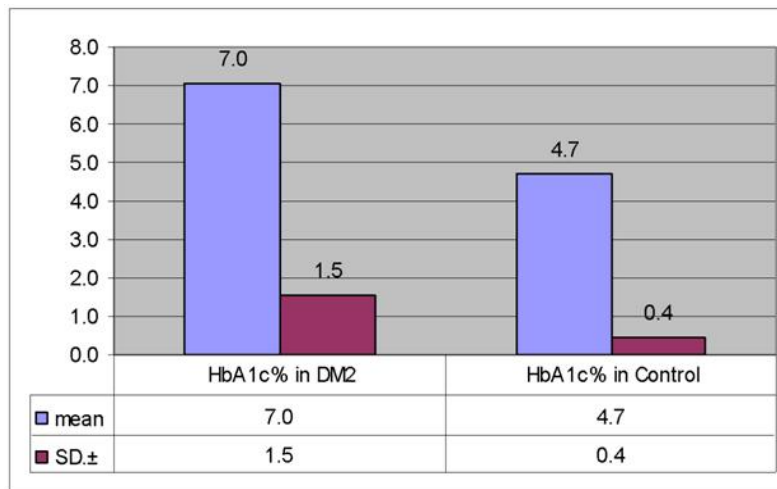
Group		Glucose concentration ( mg/dl ) after									
		Fasting	1/2 h	1 h	2 h	3 h	4 h	5 h	6 h	7 h	8 h
DM 2	mean	133	159	201	208	204	164	160	154	155	160
	SD.±	41	48	63	55	55	34	37	40	41	30
Control	mean	96	126	141	109	102	98	98	105	101	98
	SD.±	12	26	26	12	15	39	9	39	9	8



**Fig. 3. The variation in mean glucose concentration (mg/dl) between DM2 and control groups**

**Table 2. The mean and standard deviation for measured glucose concentration, glycated haemoglobin HbA1c and calculated glucose concentration based on HbA1c% in DM2 and control groups**

Group		Measured Glucose (mg/dl)	Hba1c %	Calculated glucose (mg/dl)
DM2	mean	170	7.0	155
	SD.±	24	1.5	
Control	mean	107	4.7	89
	SD.±	13	0.4	



**Fig. 4. The mean and standard deviation of glycated haemoglobin HbA1c % in DM2 and control groups**

#### 4. DISCUSSION

Two major types of diabetes are commonly described. Type 1 diabetes is characterized by having virtually complete lack of endogenous pancreatic insulin production due mainly to autoimmune-mediated destruction of pancreatic cell islet, consequently, people with this disease require insulin to survive [8], type 2 diabetes is characterized by relative hypoinsulinemia or insulin resistance. Although in general, people with type 2 diabetes do not require insulin to survive, some of them will require it as an adjunctive alternative to reach a better blood glucose control [9].

The reports on the effect of carbohydrates on type 2 diabetes are measured through GI. (glycemic index) and/ or GL. (glycemic load), where GI. is the relative measure of post-prandial glucose to given carbohydrate intake and GL. is the mathematical product of the GI. of food and its carbohydrate content. Studies have indicated that people with high GI. and/or GL. diets have a greater risk of type 2 DM as was shown in other studies [10,11].

For many people with diabetes, glucose monitoring is key for the achievement of glycemic targets. Major clinical trials of insulin-treated patients have included self-monitoring of blood glucose as part of multifactorial interventions to demonstrate the benefit of intensive glycemic control on diabetes complications [12].

In our study, The mean glucose concentration curves in DM2 group showed its maximum value at the 4<sup>th</sup> sample with a noticeable flattened pattern between samples 3, 5 and the maximum value in control group, in contrast, appeared at the 3<sup>rd</sup> sample and represented as a wide peak,

The American Diabetes Association and the American Association for Clinical Chemistry have determined that the correlation ( $r = 0.92$ ) in the international A1c-Derived Average Glucose trial is strong enough to justify reporting both the HbA1c result and the estimated average glucose result when a clinician orders the HbA1c test [13].

In this study the range of participants mean glycated haemoglobin HbA1c concentration In this study appear to be 7.0% in DM2 group and 4.7% in control group with a standard deviation 1.5%, 0.4% for the (DM2 and control group) respectively which indicate that : in control group all normal individuals glycated haemoglobin

HbA1c% did not different so much from each other.

In 2017 Beck reported that the mean glucose measured with continuous glucose monitoring device versus central laboratory-measured HbA1c in 387 participants in three randomized trials demonstrated that HbA1c may underestimate or overestimate mean glucose Thus, as suggested, a patient's continuous glucose monitoring profile has considerable potential for optimizing his or her glycemic management [14].

In this study, the calculated glucose concentration based on glycated haemoglobin HbA1c% concentration appears to be 155 mg/dl in DM2 group and 89 mg/dl in control group but the mean measured glucose concentration appear to be 170 mg/dl , 107 mg/dl for (DM2 and control group).

The American Diabetes Association in 2019 reported that self-monitoring of blood glucose is thus an integral component of effective therapy of patients taking insulin. In recent years, continuous glucose monitoring has emerged as a complementary method for the assessment of glucose levels. Glucose monitoring allows patients to evaluate their response to therapy and assess whether glycemic targets are being safely achieved [13].

In our results if we compare the glucose concentration curve with the mean glucose concentration in each group we shall note that, fasting sample concentration did not differ much from the mean in control group but in DM2 group the difference appears and from the prospect of elevation more than the mean we shall see in control group it appears only for a 30min but in DM2 group the elevation appeared for 120 min.

Moghissi reported that the patient who is eating meals, glucose monitoring should be performed before meals and the patient who is not eating, glucose monitoring is advised every 4–6 h [15]. More frequent blood glucose testing ranging from every 30 min to every 2 h is required for patients receiving intravenous insulin [16].

There is a great importance of post-prandial testing for individuals who have pre-meal glucose values within target but have HbA1c values above target. Measuring post-prandial plasma glucose 1–2 h after the start of a meal and using treatments aimed at reducing postprandial plasma glucose values to <180 mg/dL may help to lower HbA1c% [13].

In another ward if we compare the calculated glucose based on glycated haemoglobin HbA1c% results and the glucose curve from actually estimated glucose concentration we note that, in control group the calculated glucose underestimate the real concentrations all over the glucose curve but in DM2 group it underestimate the mean and some actually measured concentration in some points of the curve.

In many reports, hypoglycemia is associated with increased mortality rates in patients with or without diabetes during hospital setting [17] and the American Diabetes Association in 2015 changed its pre-prandial glycemic target from 70–130 mg/dL to 80–130 mg/dL. This change reflects the results of the ADAG study, which demonstrated that higher glycemic targets corresponded to HbA1c goals, an additional goal of raising the lower range of the glycemic target was to limit over-treatment and provide a safety margin in patients titrating glucose-lowering drugs such as insulin to glycemic targets [18].

According to the American Diabetes Association, glucose concentration level less than 70 mg/dL is considered clinically important, independent of the severity of acute hypoglycemic symptoms. Level 2 hypoglycemia (defined as a blood glucose concentration <54 mg/dL) is the threshold at which neuroglycopenic symptoms begin to occur and requires immediate action to resolve the hypoglycemic event. Lastly, level 3 hypoglycemia is defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery [13].

From our point of view the main target in treating diabetes mellitus patients is to maintaining glucose concentration in between hyper and hypoglycemic condition as in normal individuals but hyperglycemic condition appears to have more safety margin than hypoglycemic condition that's why the target range in some treatment plan is to keeping pre-prandial glycemic concentration less than 140mg/dl and post-prandial glucose concentration less than 180 mg/dl, and so we found treatment plans based only on glucose concentration test or fasting glucose test with glycated haemoglobin HbA1c ratio which may underestimate the post-prandial personal and therapeutic variation on glucose concentration.

## 5. CONCLUSION

Finally from our prospect, we recommend the use of blood glucose concentration curve as a monitoring and diagnostic tool generally for glucose metabolism in pre-diabetic, diabetic and un-controlled diabetic patients. Also, we give considerable support to the approach of individualizing the treatment plan by the fine-tuning of dose and time of administration which based primarily on personal measurements of glucose curve whether if the curve generated from continuous glucose monitoring device or by laboratory quantitative test of blood glucose.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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