

Impact of Glycated Haemoglobin on salivary glucose among type 1 diabetic mellitus patients aged 18-22 years

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ABSTRACT

Background: Diabetes mellitus consists of a group of diseases characterized by abnormally high blood glucose levels. Glycated haemoglobin (HbA_{1c}) is a form of haemoglobin used to identify the average concentration of plasma glucose over prolonged periods of time. It is formed in a non-enzymatic pathway by normal exposure of hemoglobin to high levels of plasma glucose. The main alterations observed in the saliva of Type 1 diabetic patients are hyposalivation and alteration in its composition, particularly those related to the levels of glucose. The aim of the present study was to assess the effect of Glycated haemoglobin level on the level of salivary glucose which may have an effect on oral health condition.

Materials and methods: The total sample composed of 50 adults aged 18-22 years. Divided into two groups: 25 uncontrolled diabetes mellitus (HbA_{1c} > 7), 25 controlled diabetes mellitus (HbA_{1c} ≤ 7). Stimulated salivary samples were collected under standardized condition according to the criteria of Tenovuo and Lagerlöf (1994). Salivary glucose was estimated by using spectrophotometric analysis. The data were analyzed by using SPSS version 18 (Statistical Package for Social Sciences) to specify the statistical differences between the two groups.

Results: the data of the present study assessed the correlation coefficients of HbA_{1c} and salivary glucose and found that among uncontrolled diabetic group the relation between HbA_{1c} and salivary glucose was significantly in positive direction ($r = 0.483$ $p < 0.05$). While among controlled diabetic group, there was no relation between HbA_{1c} and salivary glucose as the correlation coefficient was found to be equal to zero.

Conclusion: the measurement of glycosylated hemoglobin, that is one of the well-established means of monitoring glycemic control in patients with diabetes mellitus, had a positive effect on the level of salivary glucose as its level increase with increasing the severity of diabetic disease. (*J Bagh Coll Dentistry 2018; 30(3): 54-58*)

INTRODUCTION

Elevated blood sugar levels and numerous systemic manifestations are the most characteristic features of diabetes mellitus (DM)⁽¹⁾. In the physiological state, pancreatic β -cells respond to hyperglycemia by producing insulin which will acts via receptors at various end organs to reduce the elevated glucose levels by converting glucose to glycogen, fats and other storage forms. In patients with DM, this normal response to elevated glucose level will be interrupted. This may be secondary due to an inability of the pancreas to produce the adequate amount of insulin. It is also possible that the produced insulin is not functioning properly as a consequence of receptor malfunction or intrinsic protein alteration. Additionally, it may result from autoimmune process or antibodies being directed against the pancreatic β -cells receptors or both^(2,3). Four main types of diabetes mellitus have been defined: type 1 or insulin-dependent diabetes mellitus (IDDM), type 2 or non-insulin dependent diabetes mellitus (NIDDM), gestational diabetes and diabetes related to other conditions. The forms of diabetes mellitus other than type 1 or type 2 are comparatively rare⁽⁴⁾. Type 1 diabetes is β -cell destruction, usually leading to absolute insulin deficiency. The cause of this type is either due to Immune mediated or Idiopathic⁽⁵⁾. The term 'glycosylated' (nomenclature) was used initially, but it had been pointed out that

this term strictly refers to glycosides. Therefore, the Joint Commission on Biochemical Nomenclature had proposed that the term 'glycation' was appropriate for any reaction that links a sugar to a protein, or in the particular case of a reaction with haemoglobin, the term "glycated hemoglobin" can be used⁽⁶⁾. In the American Diabetes Association, HbA_{1c} had been referred to as A_{1c}⁽⁵⁾. It is a good indicator of average glycemic concentrations during the previous 90 to 120 days^(7,8). American Diabetes Association recommend that A_{1c} should be performed at least twice a year in patients who are meeting their treatment goals (and who have stable glycaemic control), and quarterly in patients whose therapy has changed or who are not meeting their glycaemic goals⁽⁵⁾.

Erythrocytes are freely permeable to glucose. In cells, glucose attaches to the free amino ends of haemoglobin molecules, and this process, called non-enzymatic glycosylation that causes glycosylated haemoglobin to be formed directly in proportional to the blood glucose concentration. As the average erythrocyte life span is about 120 days, glycated haemoglobin levels give information on the mean average of blood glucose levels over the past 2 to 3 months⁽⁹⁾. The normal HbA_{1c} level among individuals without diabetes falls between 4 and 6 percent, so for adults with diabetes, the target is to maintain HbA_{1c} levels of 7 percent or lower. HbA_{1c} levels above 9 percent reflect poorly controlled diabetes, which will need more aggressive management⁽¹⁰⁾. HbA_{1c} values between 6% and 7%

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were considered as assign of good control of the diabetes, HbA_{1c} values between 7.1% and 8% indicated moderated control, and HbA_{1c} value >8% were designated as poor control of diabetes⁽¹¹⁾. The use of glycated hemoglobin levels (HbA_{1c}) as a screening and diagnostic criteria for diabetes mellitus has been recommended because it is convenient, reflect long-term hyperglycemia, and reliable when standardized⁽¹²⁾.

However HbA_{1c} results will be misleading in certain situations (change in RBC life span) for example in haematological conditions where there is abnormal red cell turnover, or abnormal haemoglobin, or in renal or liver disease and in hemolytic anemias or in nutritional anemias such as iron deficiency anemia. In pregnancy, HbA_{1c} may be slightly lower. In the presence of abnormal haemoglobin or in conditions with altered red cell survival rates, HbA_{1c} results may not be reliable⁽⁹⁾.

Glucose is the main product of dietary carbohydrate. It is found in traces (0.5-1 mg/100 ml) as free form in fasting saliva⁽¹³⁾, while the level of glucose in whole - mixed saliva is 1.5-1.9 mg/100 ml⁽¹⁴⁾. Individuals with type 1 diabetes mellitus and poor glycemic control (FBS 180mg/dl; HbA_{1c} >8) have elevated salivary glucose concentration as a result of hyperglycemia, reduction of the salivary glucose clearance, disturbance of the neuroregulatory mechanism of the salivary glands and increased permeability of the basal membrane of the parotid glands^(15,16).

The oral cavity is considered a mirror of the nutritional status of the body. Karjalainen et al.⁽¹⁷⁾ and Belazi et al.⁽¹⁸⁾ found that in type I diabetic mellitus patients (children and adolescents), there was an increase in salivary glucose levels which was significantly correlated with that of blood, Suggesting that high blood glucose could increase the salivary glucose levels. Amer, et al.⁽¹⁹⁾ conducted a study on diabetic patients and found a significant association between the glucose levels in blood and saliva. The findings thereby indicated that salivary glucose evaluation might be a potential tool to monitor diabetics. Al- Rawi(2009)⁽²⁰⁾ showed that the highest glucose value was represented in the saliva of the long duration diabetic group, followed by the newly diagnosed group then the control, but there was no statistical significant association between the glucose levels in serum and saliva⁽²⁰⁾. The present study was conducted among patients with type1 diabetic mellitus (controlled and uncontrolled) aged 18-22 years to assess the effect of the level of glycated haemoglobin on salivary glucose level that may have an effect on the oral health condition. The aim of the present study was to assess the effect of Glycated haemoglobin level on the level of salivary glucose which may have an effect on oral health condition

MATERIALS AND METHODS

In the present investigation, the study group included 50 diabetic adults, their age ranged from 18-22 years of. They were examined at the Diabetic and Endocrinology Center, AL-Kindy Teaching Hospital in Baghdad City during the period from the 1st of November 2011 till the end of April 2012. They were all with confirmed diagnosis of type IDDM with minimum duration of diabetes of at least 5 years (5-10years). The samples were divided into two groups based on the HbA_{1c}⁽⁵⁾: 25 uncontrolled type 1 diabetes mellitus patients (HbA_{1c} > 7), and the other 25 patients were controlled type 1 diabetes mellitus (HbA_{1c} ≤ 7). Saliva was collected for the diabetic patients at the same day of the blood sample aspiration for HbA_{1c} assessment by measuring the absorbance of the glycohemoglobin and the total hemoglobin fraction at 415 nm in comparison with a standard glycohemoglobin preparation carried through the test procedure (Human-Biochemical, 2011, Germany). The collection of stimulated salivary samples was performed under standard condition according to Tenovuo and Lagerlöf⁽²¹⁾. Then Biochemical analyses of salivary samples were done using spectrophotometric analysis. Salivary glucose level was measured by enzymatic method glucose-oxidase method, according to Srinivasan *et al* 2003⁽²²⁾. Glucose level concentrations of saliva were expressed in mg/dl.

$$\text{Glucose conc. (mg/dl)} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times 100 (\text{Standard conc.})$$

Statistical Analysis and processing of the data were carried out using SPSS version 18. Student's t-test and Pearson correlation coefficients were used. The level of significance was accepted at P< 0.05, and considered highly significance when P< 0.01.

RESULTS

In the present study, table (1) illustrates that 25 uncontrolled patients with mean value for HbA_{1c} % (8.61±1.20) and minimum (7.30) and maximum (11.00), and from controlled diabetes mellitus included 25 patients with mean value (6.09±0.57) with minimum (4.50) and maximum (7.00). The correlation coefficient of HbA_{1c} and salivary glucose can be seen in table (2). This table shows that among uncontrolled diabetic group the relation between HbA_{1c} and salivary glucose was significant in a positive direction (r = 0.483 p<0.05). While among the controlled diabetic group, there was no correlation between HbA_{1c} and salivary glucose.

Table (1): HbA_{1c} (%) (mean and standard deviation) among uncontrolled and controlled diabetic groups.

Biochemical Tests	Uncontrolled diabetic				Controlled diabetic			
	Mean	±SD	Mini	maxi	Mean	±SD	mini	maxi
HbA _{1c}	8.61	1.20	7.30	11.0	6.09	0.57	4.50	7.0

Table (2): Correlations coefficients between HbA_{1c} and salivary glucose among uncontrolled and controlled diabetic groups

Salivary constituents	Uncontrolled diabetic		Controlled Diabetic	
	HbA _{1c}		HbA _{1c}	
	R	P	R	P
glucose	0.483*	0.015	0.000	1.000

*P<0.05

DISCUSSION

Diabetes and oral diseases often look as the two sides of a coin, a lot of attention was paid to the level of metabolic control, as poor metabolic control had been shown to be related to diabetes-associated alterations in tissues and it was a key factor in the development of diabetic organ complications⁽²³⁻²⁵⁾. Therefore, it was assumed that poor glucose control would affect the occurrence of oral complications as well. Changes in the salivary physiochemical properties had been reported among the diabetic group and it was considered as a risk factor affecting severity and occurrence of dental caries and periodontal diseases⁽²⁶⁾.

HbA_{1c} reflects average plasma glucose over the previous 2–3 months in a single measure, which can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made it the gold standard for assessing glycaemic control in people with diabetes and have resulted in its consideration as an option for assessing glucose tolerance in people without diagnosed diabetes. On the other hand, the HbA_{1c} result was influenced by several factors including anemia, abnormalities of hemoglobin, pregnancy and uremia⁽²⁷⁾. In addition, HbA_{1c} is insensitive in the low range and a normal HbA_{1c} cannot exclude the presence of diabetes⁽²⁸⁾.

The present work was carried out to elucidate the relationship between the characteristics of type 1 diabetes among some people in Baghdad city in Iraq. Its aim was to obtain more precise information by selecting the subjects carefully and controlling the data analysis. The goal was to use homogenic study populations to be able to control for various confounding factors. Type 1 and type 2 diabetes have differences in their genetic

background, etiology, treatment strategies and the presence of complications. Therefore, only subjects with type 1 diabetes were included in this work. Two different study populations (previously diagnosed type 1 diabetes) were used, divided them into two groups according the level of HbA_{1c}: Uncontrolled type 1 diabetes mellitus (HbA_{1c} > 7) and controlled type 1 diabetes mellitus (HbA_{1c} ≤ 7)⁽⁹⁾. Tervonen and Oliver⁽²⁹⁾ were the first to use multiple HbA_{1c} values to determine long-term metabolic control of diabetes. Dividing patients into poorly controlled and controlled type 1 diabetes groups was used in Safkan- Seppälä⁽³⁰⁾, where grouping was based on patients' medical status in addition to glycated haemoglobin values.

The study groups selected aged 18-22 years, as at these ages the type 1 diabetes mellitus are predominate. Typically, type 1 diabetes mellitus occurs in young subjects with acute-onset with typical symptoms of diabetes together with weight loss and propensity to ketosis⁽²⁸⁾. The role of metabolic control in relation to oral health was considered a feasible target of investigation in young subjects, in whom metabolic control is the best, and often the only, indicator of the diabetic status, because complications are rare in these age groups, as the long-term effects of the disease are not yet obvious⁽³¹⁾. Accordingly, variation in the duration of diabetes is also more limited than in olds populations, in the present study only 5-10 years durations of diabetes were involved.

In spite of that the high value of HbA_{1c} can indicate that the patient had hyperglycaemic periods during the past 2–3 months; these values do not give information about the actual situation at the time when the salivary test was performed. Data of the present study gave information about the significant positive correlation between salivary glucose and

HbA_{1c} among uncontrolled diabetes group, but not among controlled diabetes group, one can suggest that such significant relation appear only when high HbA_{1c} values (>7%) is present, these results were in agreement with Costa et al.⁽³²⁾ study. While the present results were in disagreement with the study of Darwazeh et al.⁽³³⁾, who reported that glucose levels in unstimulated mixed saliva was correlated with actual blood glucose levels but not with the HbA_{1c} values. This could be attributed to the differences in saliva collection techniques, glucose metabolic control methods, degrees of patient dehydration, and the wide age span.

However, some researchers showed in their report that the measurement of salivary glucose concentration may also represent a simple, quick, and inexpensive method for screening of diabetic autonomic neuropathy⁽³⁴⁾. On the other hand, Tenovuo et al.⁽³⁵⁾ found that high blood glucose did not result in any notable elevation of salivary glucose of some subjects.

In conclusion, dental professionals need to have comprehensive knowledge of their diabetic patients, knowledge that the patient has diabetes is not sufficient to assess the effects of diabetes with respect to oral diseases and dental treatment. Finally, co-operation and consultation between all the members of the team responsible for the treatment of patients with diabetes is highly recommended.

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الخلاصة

مرض السكري من الأمراض التي تتصف بالارتفاع الغير طبيعي لمستوى السكر بالدم. أن اختبار الكلايكتيد هيموغلوبين هو شكل من اشكال الهيموغلوبين الذي يستخدم لتحديد معدل تركيز كلوكوز بلازما خلال فترات زمنية. وهو يتكون بطرق غير انزيمية خلال التعرض الطبيعي للهيموغلوبين لتراكيز عالية من الكلوكوز. ان التغيرات الرئيسية التي تحدث للعباب مرض السكري النوع الاول هي انخفاض معدل تدفق اللعاب وتغيرات في محتوى اللعاب, وبالاخص تلك المتعلقة في مستويات الكلوكوزباللعاب. ان هدف الدراسة الحالية هو تقديرمدى تأثير مستوى الكلايكتيد هيموغلوبين على مستوى الكلوكوز بالللعاب و الذي يعكس حالة صحة الفم.

شملت الدراسة على 50 بالغ بعمر 18-22 سنة قسموا الى مجموعتين 25 مريض مصاب بداء السكري غير المنضبط ($HbA_{1C} < 7$) و 25 مريض مصاب بداء السكري المنضبط ($HbA_{1C} \geq 7$). جمعت عينات اللعاب المحفز ضمن ظروف قياسية اعتمادا على طريقة (1994 Tenovuo and Lagerlöf). حدد مستوى الكلوكوز بالللعاب باستخدام المطياف الضوئي وحلت النتائج احصائيا باستخدام spss.

أن نتائج الدراسة الحالية بينت ان معامل الارتباط HbA_{1C} مع مستوى الكلوكوز بالللعاب كان معنويا واجابيا عند المرضى المصابين بداء السكري غير المنضبط ($r = 0.483$ $p < 0.05$) اما في مرضى داء السكري المنضبط لم تتضح هكذا علاقة بين HbA_{1C} ومستوى الكلوكوز بالللعاب وان معامل الارتباط كان مساويا للصفر.

أن قياس الكلايكتيد هيموغلوبين وهو احد الطرق المهمة لمتابعة مدى السيطرة على مرض داء السكري لدى مرضى السكري وله تأثير موجب على مستوى الكلوكوز بالللعاب الذي يزداد مستواه بزيادة شدة مرض داء السكري.