Journal of Education and Science (ISSN 1812-125X), Vol: 30, No: 3, 2021 (95-103)
Special Issue for Proceeding of 3rd National (1st international conference of biology) (ICBSUM 2021) 5, 6 July
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The Evaluation of Hba1c Test as A Diagnostic Test for Diabetes Mellitus Type 2

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(Received June 04, 2021; Accepted June 30, 2021; Available online August 28, 2021)

DOI: 10.33899/edusj.2000.168658, © 2021, College of Education for Pure Science, University of Mosul.

ABSTRACT

The HbA1c test and the blood glucose test were compared in order to diagnose type 2 diabetes and determine the best cut-off point for the HbA1c test for optimal sensitivity in the population of Mosul city (inside it and some rural areas around it). The test was performed on a group of people between the ages of 40 and 85 who came to our laboratory after being diagnosed with or without type 2 diabetes by specialists in internal medicine and endocrinology. The HbA1c and FBS analysis were carried out between January 2020 and January 2021. And, by using ROC curve, the results for 80 individuals with an average age of 56 years produced a HbA1c test with a value of 6.8 percent, a sensitivity of 94 percent, compared to the result of 126 mg/ml for FBS as a diagnostic criterion , and the optimal cutoff point for HbA1c was reached for 6.86% in diagnosing disease diabetes type 2 was given the highest Yuden index by ROC curve analysis. **Conclusion:** We recommend that the optimal value of Hb^2 with a percentage of 6.86 percent be used as the best test in diagnosing type 2 diabetes and obtaining the best medical and health care for the Mosul population.

Keyword: HbA1c, Diabetes, Type 2

تقييم فحص السكر التراكمي HbA1C كاختبار تشخيصي لمرضى السكري من النوع الثاني

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الخلاصة:

تم إجراء دراسة مقارنة بين فحص السكر التراكمي HbA1c وفحص الجلوكوز في الدم لغرض تشخيص مرض السكري من النوع الثاني وإيجاد نقطة القطع المثلى لاختبار الـ HbA1c من أجل الوصول الى الحساسية المثلى للفحص لدى سكان مدينة الموصل (من داخل المدينة وبعض المناطق الريفية المحيطة بها). تم إجراء الفحص على مجموعة من الأشخاص تتراوح أعمارهم بين 40 و 85 عامًا ممن حضروا إلى مختبرنا وتم تشخيص إصابتهم بالسكري من النوع الثاني أو عدمه من قبل المتخصصين في الطب الباطني

والغدد الصماء تم إجراء اختبارات HbA1c و FBS في الفترة الزمنية بين كانون الثاني 2020 وكانون الثاني 2021. وأظهرت النتائج لـ 80 فردًا بمتوسط عمر 56 عامًا نتيجة إختبار HbA1c بقيمة 6.8٪ ، حساسية 94٪ ، مقارنة بـ نتيجة 126 ملجم / مل لـ FBS كمعيار تشخيصي من خلال منحنى الـ ROC ، وتم الوصول إلى نقطة القطع المثلى لـ HbA1c لـ 6.86٪ في تشخيص مرض السكري من النوع الثاني و التي أعطت أعلى مؤشر يودن بواسطة تحليل منحنى الـ ROC . **الإستنتاجات** : نوصي باستخدام القيمة المثلى لـ HbA1c بنسبة 6.86٪ كأفضل اختبار في تشخيص مرض السكري من النوع الثاني والحصول على أفضل رعاية طبية وصحية لسكان مدينة الموصل.

الكلمات المفتاحية : السكر التراكمي ، السكري ، النوع الثاني

1. Introduction

Diabetes is a chronic metabolic disease characterized by high blood sugar levels, and it causes significant damage to the nerves, blood vessels, kidneys, and eyes over time (IDF2013).[1] Diabetes type 2 has become the most common and prevalent in the last four decades. The incidence of this disease has increased in all countries and at all levels. More than 422 million people in the world suffer from diabetes type 2. Also, 1.6 million deaths every year are attributed to this disease (Brooks *et al*).[2] And there is a global agreement to prevent this disease and eliminate obesity by 2025.[1] Diabetes type 2 is characterized by a long clinical phase, so early and accurate diagnosis is critical (Singer *et al*).[3] The World Health Organization recommends using a 6.5 percent glycated hemoglobin HbA1c test as the diagnostic cut-off limit for this disease. HbA1c is primarily defined as an atypical hemoglobin for diabetics over the age of forty years.[4,5] Glycoproteins are formed after conversion through a slow, non-enzymatic interaction between blood sugar (glucose) and amino groups on proteins, which is an important and clinically useful indicator. For average blood sugar during the previous 120 days (which is the average age of red blood cells).[6] and the introduction of the HbA1c test as a diagnostic tool for diabetes and the cut-off point is the focus of controversy and study for many years, and many studies have been conducted in this field and for residents from different countries to reach the limit.[7] Diagnostic interval. Carefully controlled studies have documented a close relationship between HbA1c concentration and glycemic control. And in this regard, the people of Mosul should be provided with a high level of care in order to avoid spreading the disease. As a result, this study was carried out to determine the cut-off value and diagnostic tool for HbA1c levels in the Mosul population.

2. Materials And Methods

The study was conducted in a specialized pathology analysis laboratory licensed by the Iraqi Ministry of Health on 80 residents of Mosul from January 2020 to January 2021, all of whom were over 40 years old. As 17 of them were diagnosed as having diabetes type 2 by certified specialists who were newly diagnosed with monitoring their blood pressure measurement. Diabetes is diagnosed by measuring blood glucose levels after fasting for 8 to 12 hours and finding that the level is greater than 126 mg/dl. Their infection was known from taking the treatment. Those with a history of blood transfusions within three months, those taking aspirin, and those with chronic liver and kidney disease were excluded. The family history of diabetes was studied for each individual along with age, height,

weight, blood pressure, waist circumference and hip circumference. Boditech's I CHROMA TM II +® kit was used to measure HbA1c levels. HbA1c and total hemoglobin are measured using integrated advanced immunoassay and dry chemistry technology, respectively.The capillary blood sample was used with appropriate precautions. Calibrated according to the blood sample set and other standard materials supplied to us by the manufacturer.

3. Statistics

The analysis was carried out using the statistical software program Minitab version 17 with the assistance of statistical experts. The SPSS program version 23 was used to create the sensitivity curve and the rock curve, and all of these programs are available on my personal computer.

4. Ethics

The consent of all study subjects was obtained. Note that it is an analytical and statistical study and it did not harm any individual material, health or moral.

5. Thanks and Appreciation

I extend my thanks and gratitude to Al-Kawthar Laboratory for Pathological Analysis (a private laboratory licensed by the Iraqi Ministry of Health) for helping me complete the practical aspect of the research.

6. Results

The diabetes type 2 group consisted of 9 females and 8 males, while the non-diabetic group consisted of 36 females and 27 males among the 63 people. Table No. 1 shows the characteristics of the study participants. With the determination of HbA1c values, the blood glucose test (FBS) was adopted as a diagnostic criterion for type 2 diabetes with the estimation of HbA1c levels (Table No. 2) To determine the relationship between FBS and HbA1c (Fig. 1), a linear regression analysis was performed, and the stability of the highest and most credible analysis degree was demonstrated (Table No. 3, 4 and 5) and the equation produced the relationship between the two tests was produced by the equation:

HbA1c (%) = 2.021 + 0.03932 x FBS (mg/dl)

And for the value of 126 mg/dl for the FBS test, it is 6.97%, and for the value for 6.5% for the Hb1Ac test, the value is 113.911 mg/dl.

Table 1 : A comparison of patient groups

Variables	Diabetic	Non Diabetic
Age	57.25 ± 8.25	56.04 ± 6.52
BMI	22.13 ± 1.98	21.83 ± 2.07
Waist circumference	90.21 ± 5.65	89.23 ± 5.17
Hip circumference	92.81 ± 5.03	88.16 ± 4.18

Table 2: HbA1c diagnostic performance comparison

FBS (mg/dl)	HbA1c (%)		TOTAL
	≥ 6.5	< 6.5	
< 126	18	45	**63**
≥ 126	17	0	**17**

Table 3: Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Regression	1	41.4591	41.4591	1454.11	0.000
FBS (mg/dl)	1	41.4591	41.4591	1454.11	0.000
Error	78	2.2239	0.0285		
Lack-of-Fit	47	1.6434	0.0350	1.87	0.034
Pure Error	31	0.5805	0.0187		
Total	79	43.6830			

Table 4: Model Summary

S	R-sq	R-sq(adj)	R-sq(pred)
0.168854	94.91%	94.84%	94.47%

Table 5: Coefficients

Term	Coef	SE Coef	T-Value	P-Value	VIF
Constant	2.021	0.117	17.34	0.000	
FBS (mg/dl)	0.03932	0.00103	38.13	0.000	1.00

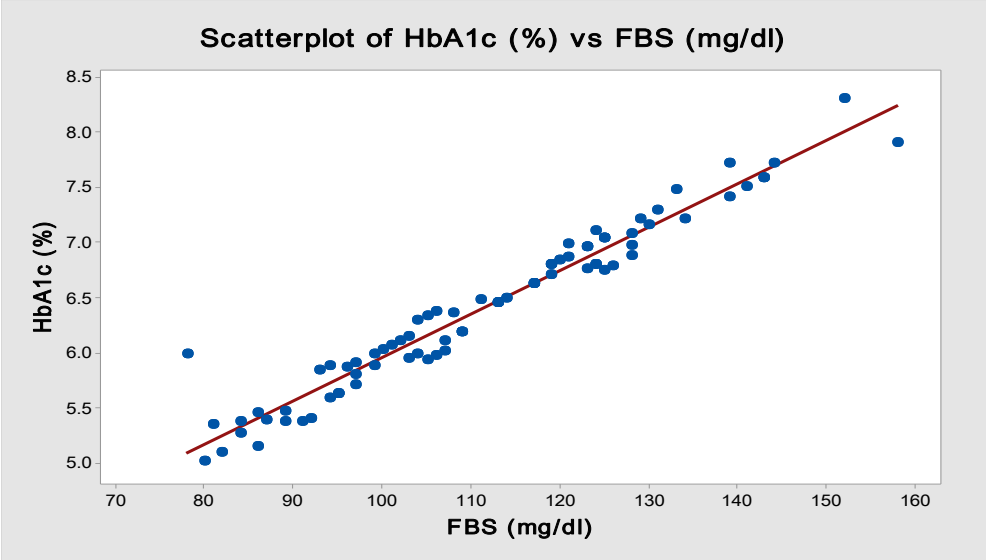

Figure 1: Regression Analysis: HbA1c (%) versus FBS (mg/dl)

A rocker curve was created to determine the optimal cut for the resulting values (Fig. 2) (Table No. 6). The value 6.5 % for HbA1c assay showed a sensitivity of 100% and the optimum cutoff value for HbA1c assay was 6.86%, which recorded a sensitivity of 94%, which gave the maximum Youden Index. With a value of 84% (Table No. 7 & histogram).

Table 6: Area Under the Curve. Test Result Variable(s): HbA1c

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.979	.014	.000	.951	1.000

a. Under the nonparametric assumption b. Null hypothesis: true area = 0.5

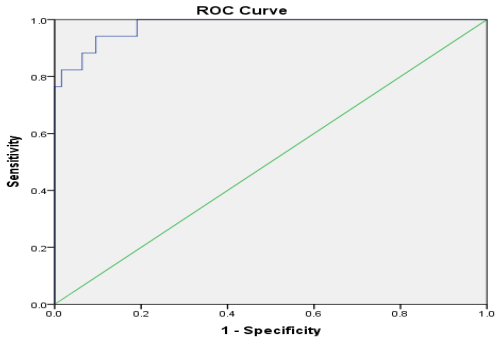

Figure 2: ROC curve

Table 7: Coordinates of the Curve. Test Result Variable(s): HbA1c

Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity	Youden Index
6.555	1	0.286	0.714
6.66	1	0.238	0.762
6.72	1	0.222	0.778
6.75	1	0.206	0.794
6.77	1	0.19	0.81
6.79	0.941	0.19	0.751
6.82	0.941	0.127	0.814
6.85	0.941	0.111	0.83
6.865	0.941	0.095	0.846
6.915	0.882	0.095	0.787
6.965	0.882	0.063	0.819
6.975	0.824	0.063	0.761
7.01	0.824	0.048	0.776
7.055	0.824	0.016	0.808
7.085	0.765	0.016	0.749
7.125	0.765	0	0.765
		Optimal cut-off =	0.846

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

7. Discussion

It is known that the HbA1c test has a lower sensitivity in Europeans compared to Asians, as was indicated by Mustafa *et al*[8]. In this study, we demonstrated the high sensitivity of the HbA1c test for Mosul residents, and the value of 6.5 % is a sensitivity of 100 %, which is an extremely high value. Also, the linear relationship between FBS test and HbA1c test is HbA1c = 1.51 + 0.0414 x FPG as explained by Liang *et al* [9], which gives the value 6.72% for the test of HbA1c compared with the value of 126 mg/dl for the test. It gives a value of 120.5 mg/dl for 6.5% of the HbA1c test. And our linear analysis showed that the most accurate and the most sensitive relationship is HbA1c (%) = 2.021 + 0.03932 × FBS (mg/dl), so the ratio of FBS = 126 mg/dl is equal to 6.97% of HbA1c and for the value of 6.5% of HbA1c is equivalent to 113.911 mg In his study, Ogawa *et al* [10] suggested that the FBS value of 111.4 mg/dl is equivalent to 6.5% of HbA1c and is lower than what was suggested by the World Health Organization, and the FBS value = 126 mg/dl is equivalent to 7.5% of HbA1c in the region. his study. The question of the cut-off value of HbA1c testing in diagnosing diabetes type 2 is a subject of controversy and debate all over the world. Scientists have suggested Gomyo *et al* [11], Farhan *et al* [12], Adamska *et al* [13], Martin *et al* [14], Bae *et al* [15], Tankova *et al* [16], Ghazanfari *et al* [17], Li *et al* [18], Kim *et al* [19] The following values are 5.5,5.8, 5.9,5.9, 5.95, 6.1, 6.15, 6.3 and 6.45, which are all below the limit set by the World Health Organization, respectively. There are also studies that have put values higher than those set by the World Health Organization as in Jung *et al* [20] (6.75%) and Higgins *et al* [21] (7%). A 6-year study conducted by (NHANES) Buell *et al* [22] (National Health and Nutrition Examination Survey) suggested 7% as the cut-off value for diagnosis. The Association of British Diabetes Doctors [23,24] (ABCD) provided a higher level of 7.2% to reduce the incidence of diabetes type 2. The US Department of Defense's Veterans Affairs also introduced a 7% cut-off point for the HbA1c test.[25,26] In this study, we excluded many factors that impair access to the ideal focal point, such as kidney failure, anemia, blood transfusion, and taking medications that affect the study. Conducting such studies on the population of the city of Mosul is considered to be of great benefit in diagnosing or controlling diseases, especially chronic diseases.

8. Conclusions

A cut-off value of 6.86% is considered the diagnostic criterion for diabetes type 2 as it gave the optimum sensitivity to the HbA1c test. The relationship between HbA1c and FBS is: HbA1c (%) = 2.021 + 0.03932 x FBS (mg/dl)

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