Role of antiGAD65 Ab., C-peptide level and clinical characteristics in classification of newly diagnosed diabetes in patients aged 20-40 years

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Abstract:

Classification of newly diagnosed diabetes in patients aged 20-40years and the further decision to treatment may be difficult depending on clinical manifestation alone. The purpose of the study to identify the role of specific tests (antiGAD65 Ab, and level of C-peptide) and their relation to clinical characteristics in the classification of diabetes. One hundred newly diagnosed diabetes patients aged 20-40years enrolled in this study between Jan.2013-Dec.2017.The parameters of age, gender, history of osmotic symptoms, ketoacidosis, SBP & DBP measurement height, weight, BMI, were taken. C-peptide level and (anti-GAD65Ab) were conducted to all patients. While FBS and 2 hours post-GTT and HbA1c conducted at first visit and after 3 months. In patients with positive results of anti-GAD65Ab, there was significant low level of C-peptide (P <0.0001), history of DKA (P <0.0001), absence of family history of diabetes (P<0.0001), thinner (P <0.0001), low BMI (P <0.0001), less SBP & DBP (P<0.0001for both). In patients with positive anti-GAD65Ab; FBS and RBS at first presentation were higher (P =0.001 and P <0.0001 respectively) and FBS and RBS after 3months were again higher in patients with positive anti-GAD65Ab (P =0.01 and P=0.004 respectively). In conclusion, newly diagnosed diabetes aged 20-40 years with positive anti-GAD65Ab; had a significant relationship with low C-peptide level, lean BMI, history of ketoacidosis, lower systolic & diastolic blood pressure, the clinical presentation with osmotic symptoms and/or absence of a family history of diabetes, and significant response to insulin therapy. While those with negative anti-GAD65Ab had an association with other metabolic features.

Key words: Diabetes mellitus, DKA, AntiGAD Ab, C-peptide, classification of diabetes, type1 DM, type 2 DM.

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Introduction

Diabetes Mellitus (DM) can be classified into type 1, type 2, gestational, and other specific syndromes. However, there is increasing evidence suggests other subtypes of disease (e.g., LADA, MODY) [1]. Differentiation of adult-onset type 1 from type 2 diabetes through clinical presentation may be difficult but may become obvious with time [2]. The patients in both types are at risk of the same complications once the hyperglycemia developed, despite the differences in the rate of progression [1]. In type 1 DM patients have a variable percentage of antibodies against the antigen of pancreatic Langerhans islets cells like glutamic acid decarboxylase (GAD65) or IA2 antibodies [3]. While type 2DM characterized by insulin resistance that further accompanied by defective insulin release with time. Actually, there is an estimation that 5-15% of type 2 diabetes may have type 1 DM or latent autoimmune diabetes of adults (LADA) [4]. The purpose of this study was designed to assess the role of anti-GAD Ab and C-peptide levels as well as clinical characteristics in the classification of diabetes in patients aged 20-40years.

Patients and Method

This is an analytical prospective study in which 100 newly diagnosed diabetes mellitus (DM) patients aged between 20-40 years presented to the outpatient clinic of 2 tertiary centers of diabetes between January 2013 and December 2017 have been enrolled and followed for 3months. Exclusion criteria were known history of malignancy, autoimmune diseases, acute illness or infections during the last two weeks before starting the study. From all the patients the following clinical and laboratory data obtained; like age, gender, history of presence or absence of osmotic symptoms(polyuria, polydipsia, nocturia with or without weight loss), history of ketoacidosis, measurement of height in centimeters and weight in kilogram and body mass index (BMI), systolic and diastolic blood pressure measurement (mean of 3 different results). At first visit and after 3 months of follow up and treatment; the following blood tests were taken, comprising fasting blood glucose and 2 hours post glucose tolerance test (GTT), glycosylated hemoglobin (HbA1c by High-Performance Liquid Chromatography). The fasting C-peptide level (in ng/ml) and autoantibodies to glutamic acid decarboxylase (anti-GAD65Ab) (by Chemiluminescence immunoassay) were measured for all patients.

However, the factors that determined the treatment were; positive anti-GAD65Ab and/or low C-peptide, low BMI, presence of DKA, presence of osmotic symptoms; treated with insulin. Otherwise, the patient treated with oral antihyperglycemic medications. The study was conducted according to the Helsinki Declaration and informed consent wasgained from all patients.

The data were analyzed through IBM SPSS (version 16.0). The Student t-test, Pearson chi-square test, and ANOVA were used to analyses the differences between variables. The independent two-sample t-test was used to compare the levels of FBS, RBS, and HbA1c within the first presentation and 3months after treatment and follow-up. These variables were described as mean ± standard deviation (SD). The differences considered statistically significant if the P-value <0.05 for all results.

Results

One hundred newly diagnosed patients with diabetes mellitus whose ages between 20-40years (mean 31.7± 7) enrolled in this study. Fifty-two (52%) male and 48(48%) females. Fifty-two (52%) patients presented with osmotic symptoms and 38(38%) had a history of diabetic ketoacidosis either at presentation or during the follow-up period for 3months. Thirty-two (32%) were hypertensive and 58(58%) patients had a family history of diabetes. Twenty six (26%) had positive anti-GAD65Ab. Thirty (30%) had a low level of c-peptide level, 50 (50%) had a normal level while 20(20%) had a high level.Forty two(42%) considered as type 1 diabetes mellitus and treated with different insulin types and the other 58(58%) considered as type 2 diabetes mellitus and treated with oral antihyperglycemic drugs.

Table 1: The clinical characteristics of anti-GAD-positive patients in comparison with anti-GAD-negative patients:

Variables	Characteristics	Anti-GAD65Ab		Total	P value*
		Positive No. (%)	NegativeNo. (%)		
Gender	Male	14(26.9)	38(73.1)	52(100)	0.5
	Female	12(25.0)	36(75)	48(100)	
Family history of diabetes	Present	2(3.4)	56(96.6)	58(100)	<0.0001
	Absent	24(57.1%)	18(42.9%)	42(100)	
Osmotic symptoms	Present	22(42.3)	30(57.7)	52(100)	<0.0001
	Absent	4(8.3)	44(91.7)	48(100)	
C-peptide(ng/ml)	Low	22(73.3)	8(26.7)	30(100)	<0.0001
	Normal	4(8)	46(92)	50(100)	

	High	0(0)	20(100)	20(100)	
History of DKA†	Present	22(57.9)	16(42.1)	38(100)	<0.0001
	Absent	4(6.5)	58(93.5)	62(100)	
Type of Diabetes	Type 1	26(61.9)	16(38.1)	42(100)	<0.0001
	Type 2	0(0)	58(100)	58(100)	
Total No. (%)		26 (26)	74(74)	100(100)	

* Pearson chi square test
†DKA: diabetic ketoacidosis

There was significant reduction of FBS, RBS, and HbA1c between first presentation results and the results after 3 months (231.30 ± 76.421 vs 130.86 ± 31.949 P<0.0001, 307.09 ± 83.230 vs 180.02 ± 45.888 *P<0.0001* and 10.5582 ± 2.19051 vs 7.6374 ± 1.42149 respectively *P <0.0001*) Figure (1). The enrolled patients subdivided according to the presence or absence of anti-GAD65Ab into two main groups to assess the relationship of its presence with a different variable. In patients with positive results of anti-GAD65Ab, there was a significantly low level of C-peptide (*P<0.0001*), history of DKA (*P<0.0001*), absence of a family history of diabetes (*P<0.0001*), and the patients diagnosed as type 1 DM (*P<0.0001*). There was a significant absence of osmotic symptoms in patients with negative anti-GAD65Ab. (*P<0.0001*)(table1).

The patient with positive anti-GAD65Ab were thinner (*P*<0.0001), had low BMI (*P*<0.0001), with less SBP &DBP(*P*<0.0001for both). In patient with positive anti-GAD65Ab; the FBS and RBS at first presentation was higher (274.46+/-63.6 vs 216.14+/-75 *P*=0.001 and 375.81+/-80.9 vs 282.95 +/-69.84 *P*<0.0001 respectively) .As well as the FBS and RBS after 3months were also higher in patients with positive anti-GAD65Ab (144.62+/-44.54 vs126.03 +/-24.77 *P*=0.01 and 201.85+/-51.097 vs 172.35 +/-41.62; *P*=0.004respectively).

Table 2: The clinical characteristics among the groups of patients divided according to their age:

Variable	Characteristics	Age at presentation /years				Total	P value*
		20-25	26-30	31-35	36-40		
Gender	Male	14(26.9)	8(15.4)	11(21.2)	19(36.5)	52(100)	0.859
	Female	11(22.9)	9(18.8)	8(16.7)	20(41.7)	48(100)	
Family history of diabetes	Present	6(10.3)	12(20.7)	10(17.2)	30(51.7)	58(100)	<0.0001
	Absent	19(45.2)	5(11.9)	9(21.4)	9(21.4)	42(100)	
Osmotic Symptoms	Present	19(36.5)	7(13.5)	9(17.3)	17(32.7)	52(100)	0.05
	Absent	6(12.5)	10(20.8)	10(20.8)	22(45.8)	48(100)	
History of DKA†	Present	17(44.7)	3(7.9)	5(13.2)	13(34.2)	38(100)	0.003
	Absent	8(12.9)	14(22.6)	14(22.6)	26(41.9)	62(100)	
Anti-GAD65Ab	Present	11(42.3)	3(11.5)	5(19.2)	7(26.9)	26(100)	0.1
	Absent	14(18.9)	14(18.9)	14(18.9)	32(43.2)	74(100)	
C peptide level	Low	15(50)	3(10)	5(16.7)	7(23.3)	30(100)	<0.0001
	Normal	6(12)	10(20)	6(12)	28(56)	50(100)	
	High	4(20)	4(20)	8(40)	4(20)	20(100)	
Type of diabetes	Type 1	15(35.7)	3(7.1)	9(21.4)	15(35.7)	42(100)	<0.05
	Type 2	10(17.2)	14(24.1)	10(17.2)	24(41.4)	58(100)	
	Not hypertensive	23(33.8)	11(16.2)	9(13.2)	25(36.8)	68(100)	

* ANOVA †DKA : diabetic ketoacidosis.

Then the enrolled patients further subdivided into 4 main groups according to their age/years into (A=20-25, B=26-30, C=31-35 and D=36-40) to identify the significance of different variable in relation to age. There were significant differences among the 4 groups regarding family history of diabetes which present more in group D and absent in group A(*P<0.0001*). There were significant differences among the 4 groups regarding the presence of osmotic symptoms and history of DKA in group A (P <0.05 & 0.003 respectively).C-peptide level was statistically low in group A, high in group C and normal in group D (*P <0.0001*). Diagnosis of type 1 diabetes was significantly more in group A while type 2 diabetes was more in group D (*P<0.05*). Hypertension was significantly more in group D (*P <0.05*) (table 2).

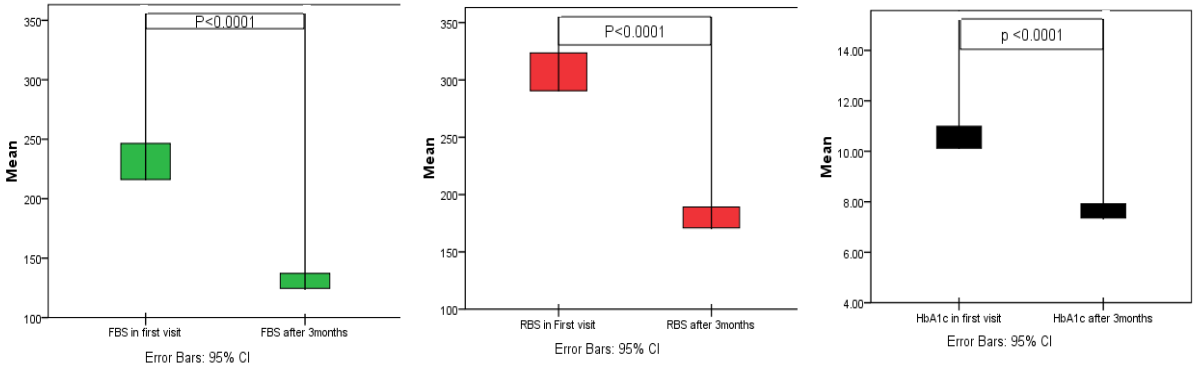

Figure1: the significance of reduction in FBS (left), RBS (middle) and HbA1c (right) between first visit and after 3months of treatments and follow up.

There were significant differences among the 4 groups regarding weight and BMI; these groups, B&C were excessively overweight or obese (P <0.0001). SBP was statistically higher in group C (*P <0.01*). RBS at first presentation was higher in both group A&D (*P <0.0001*).FBS &RBS after 3months of treatment were higher in group D (*P <0.0001*). While the positivity of anti-GAD65Ab has no differences among the 4 groups.

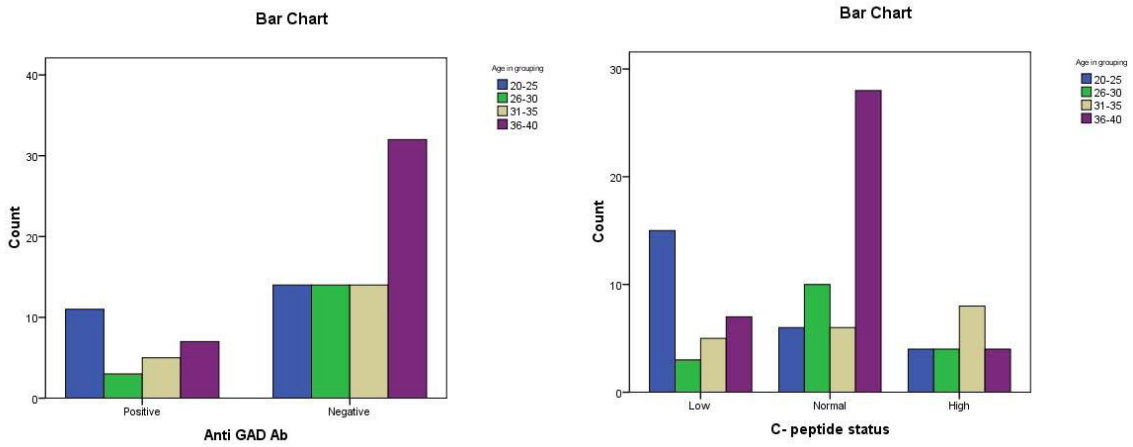

Figure 2: The distribution of anti-GAD Ab positivity (left) and C-peptide levels among groups of patients divided according to age.

Discussion

Forty-two percent considered as type 1 diabetes mellitus treated with different insulin types and the other 58% considered as type 2 diabetes mellitus treated with oral antihyperglycemic drugs. Out of all the enrolled patients, there were 26% had positive anti-GAD65Ab. These results can be accepted in comparison with other studies that report a variable prevalence of anti-GAD65Ab in adult patients with diabetes that found (11.6%) [5], 35.5% [6] and (50.8%) [7]. In this study, there is a significant relationship between patients with positive anti-GAD65Ab and history of DKA and the absence of a family history of diabetes like another study [8].Besides that; patients with positive anti-GAD65Ab had a significant relationship with low c-peptide which is similar to another study [8,9]. As well as patients with positive anti-GAD65Ab had low BMI like other studies [5, 10]. Furthermore, these patients had lower systolic and diastolic blood pressure similar to findings by Chan, *et. al,*[11]. The division of patients according to age; type 1 diabetes diagnosed more in patients aged 20-25years while type 2 was more in patients aged 36-40years. Type 1 DM per se diagnosed in 42% out of all patients in this study. These results can be accepted in comparison with Christina L Vandewalle*et. al,*[12] which found 60% of patients between 15-39 years had type 1 DM; these differences could be related to different environmental variations, genetic predilection, and other risk factors. In conclusion, newly diagnosed diabetes aged 20-40 years with positive anti-GAD65Ab, had a significant relationship with low c-peptide level, lean BMI, history of ketoacidosis, lower systolic & diastolic blood pressure, the clinical presentation with osmotic symptoms and/or absence of family history of diabetes, as well as significant response to insulin therapy. While those with negative anti-GAD65Ab had an association with other metabolic features. All of these variables should be considered for the classification of diabetes in newly diagnosed patients aged 20-40 years.

Ethical clearance

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

Conflict of interest

The authors declare that they have no conflict of interest.
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