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Original Article

Frequency of type I and II diabetes in newly diagnosed diabetic patients: Measuring C-Peptide level

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ABSTRACT

Aims: Diabetes mellitus is a metabolic disease that manifested as hyperglycemia due to the defect in secretion or function of insulin. This study aimed was to survey about frequency type I and II diabetes in newly diagnosed diabetic patients base on c-peptide and anti-glutamate acid decarboxylase (GAD) tests.
Materials & methods: This study was conducted as a prospective study on 70 diabetic patients aged 15–45 years old who referred to diabetes clinics in Ahvaz city during 2012–2014 and their diabetes was diagnosed for the first time, but their type of diabetes was not clinically definitive. Patients with anti-GAD positive and fasting C-peptide level of less than 0.65 were diagnosed as type I diabetes. Patients with anti-GAD negative fasting C-peptide level of greater than or equal to 0.65 were considered as type II diabetes.
Results: Eighty two patients (49 males and 33 females) with a mean age of 21.64 ± 4.36 years (range 15–34) and a mean BMI of 22.05 ± 4.41 kg/m^2 (range 14–18) were studied. Twenty three patients (28.5%) had type I diabetes and 59 patients (71.95%) had type II diabetes. In patients with type I diabetes, the mean BMI was 24.86 ± 2.36 kg/m^2 and the number of patients with family history (56.22%) was higher. In type II diabetic patients, the number of women (62.71%) was higher than that of men.
Conclusion: Anti-GAD test can be used as a predictive test for early diagnosis of disease and screening of people with a diagnosis of diabetes based on the type of diabetes.

1. Introduction

Diabetes mellitus is a metabolic disease that manifested as hyperglycemia due to the defect in secretion or function of insulin [1]. Type 2 diabetes is the most common type of diabetes due to the interference of environmental and genetic factors, which results in insulin dysfunction with insulin resistance [2]. The second most common type of diabetes is type I diabetes [3]. The pancreatic beta cell autoantigens include: (a) ICA (islet cell antigens), (b) insulin and proinsulin, (c) GAD (glutamate acid decarboxylase), and (d) IA-2 (protein tyrosine phosphatase). An autoantibody assay against these antigens can be effective in detecting type I diabetes [4]. The third type of diabetes involves monogenic forms of diabetes, such as genetic defect in insulin secretion or genetic defect in hormone activity. The most abnormal form of the genetic defect in beta cells is a group of disorders called MODY (Maturity onset diabetes of the young). MODY is usually diagnosed at the age of 20 or 30. The onset of MODY is usually asymptomatic and is not usually associated with diabetic ketoacidosis [5]. In MODY, c-peptide levels are not increased and there are no beta cell autoantibodies, and a definitive diagnosis is based on genetic tests. Differentiation of type I and type II diabetes in the clinic is not difficult, but sometimes patients do

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not show typical symptoms of a type of diabetes [6]. In some people with type I diabetes, diabetes occurs after 30 years of age and has no acute and specific symptoms [7,8] called LADA (Latent Autoimmune Diabetes in Adults) [8]. The immediate diagnosis of LADA patients to receive insulin is of particular clinical importance. In LADA patients, the C-peptide is decreased and anti-GAD positive. Sometimes, MODY diabetes is confused with type II diabetes and genetic tests are used to differentiate them. C-peptide is a useful and widely used method of assessing pancreatic beta cell function [9]. To diagnose type I and II diabetes, c-peptide and anti-GAD tests are also performed. Regarding the overlap between types of diabetes in young people, the present study was conducted to differentiate them para-clinically.

2. Materials & Methods

This study was approved by the Ethics Committee of Ahvaz Jundishapur University (Code: ajums.REC.1393.3) and conducted as a prospective study on 70 diabetic patients aged 15–45 years old who referred to diabetes clinics in Ahvaz city during 2012–2014 and their diabetes was diagnosed for the first time, but their type of diabetes was not clinically definitive. blood sample (one with EDTA anticoagulant) were taken from patients in fasting state (at least 8 h). Blood samples were sent to the Diabetes Center laboratory for C-peptide and anti-GAD tests. Mercodia's ELISA kit was used for the C-Peptide test and the German GRD's ELISA kit was used for the anti-GAD test. In order to observe the cold chain, samples taken by COOL BOX were sent to the Diabetes Center and were then centrifuged for 10 min at a rate of 3500-1500 rpm. Then, the serum was isolated and kept in a freezer at −70 °C for maintenance until the test was performed. Patients with anti-GAD positive and fasting C-peptide level of less than 0.65 **ng/ml** were diagnosed as type I diabetes. Patients with anti-GAD negative fasting C-peptide level of greater than or equal to 0.65 **ng/ml** were considered as type II diabetes. The study conditions were fully described for patients and consents were collected from all of them. Patients could be excluded whenever they wish. Descriptive statistics were used to measure the prevalence and Chi-square test was used to compare the prevalence rate in different age and sex groups. The significance level was less than 0.05.

3. Results

In this study, 82 patients (49 males and 33 females) with a mean age of 21.64 ± 4.36 years (range 15–34) and a mean BMI of 22.05 ± 4.41 (range 14–18) were studied. The type of diabetes was diagnosed based on blood test results (type-Anti-GAD and C-peptide values). 23 patients (28.5%) had type I diabetes and 59 patients (71.95%) had type II diabetes (Table 1).

The relationship between age, gender, BMI and family history of patients with diabetes was separately studied. In patients with type I diabetes, the number of men and women was nearly equal. Most of the patients were aged 15–19 (52.17%) and 20–24 (39.13%). The mean BMI in these patients was 24.86 ± 2.36 and most of them (91.3%) had a BMI of 18.5 ± 24.9. The number of patients with family history (56.22%) was higher.

In type II diabetic patients, the number of women (62.71%) was higher than that of men. Most of the patients were aged 15–19 (45.76%) and 20–24 (37.29%). The mean BMI in these patients was 22.28 ± 4.99 and most of them (69.49%) had a BMI of 18.5–24.9. The number of patients with family history (57.63%) was higher (Table 2).

Table 1
Distribution of patients according to the type of diabetes diagnosed.

Variable	Type I	Type II
Anti-GAD type (N, %)	23 (28.05%)	59 (71.95%)
C Peptide ng/ml (Mean ± SD)	0.51 ± 0.122 (0.25–0.65)	1.93 ± 1.3 (0.7–5.44)

Table 2
The relationship between demographic factors and types of diabetes diagnosed.

Variable		Type 1 N (%)	Type 2 N (%)
Gender	Female	11 (47.83%)	37 (62.71%)
	Male	12 (52.17%)	22 (37.29%)
Age	15–19	12 (52.17%)	27 (45.76%)
	20–24	9 (39.13%)	22 (37.29%)
	25–29	1 (4.35%)	7 (11.86%)
	30–34	1 (4.35%)	3 (5.08%)
BMI	<18.5	2 (8.7%)	8 (13.56%)
	18.5–24.9	21 (91.3%)	41 (69.49%)
	25–29.9	0 (0%)	4 (6.78%)
	≥30	0 (0%)	3 (5.08%)
Family History	Yes	10 (43.48%)	34 (57.63%)
	No	13 (56.52%)	25 (42.37%)

Table 3
DKA and Acanthosis Nigricans presence and lose weight for each type of diabetes.

Variable		Type 1 (n = 23)	Type 2 (n = 59)
DKA	Yes	6 (26.09%)	17 (28.81%)
	No	17 (73.91%)	42 (71.19%)
Acanthosis Nigricans	Yes	0 (0%)	0 (0%)
	No	0 (0%)	0 (0%)
Lose weight (kg) (Mean ± SD)		7.96 ± 5.07 (2–22)	8.49 ± 6.26 (0–36)

Patients were evaluated based on the presence of diabetic ketoacidosis (DKA), Acanthosis Nigricans, and weight loss by type of diabetes diagnosed. DKA presence was reported in 26.09% of patients with type I diabetes and in 28.81% of patients with type II diabetes. No patients were reported with Acanthosis Nigricans. On average, patients with type I and II diabetes lost weight of 7.96 kg and 8.49 kg, respectively (Table 3).

4. Discussion

The evaluation of demographic characteristics (age, gender, family history) and immunological status, including Anti-GAD autoantibodies (GADA), are known as useful tools for screening and early diagnosis of disease in people at risk for diabetes [10,11].

Mean values of C-peptide in patients with type I and II diabetes were 0.51 ± 0.122 **ng/ml** and 1.93 ± 1.2 **ng/ml** respectively. The results of a study by Webb PG et al. showed that patients with low fasting C-peptide (≤0.16 nmol/L) inhibited type I diabetes symptoms and those with high fasting C-peptide (≥0.16 nmol/L) inhibited type II diabetes symptoms, which was consistent with the results of the present study [12]. The results of the study by Gjessing HJ et al. showed that patients with fasting C-peptide values of less than 0.2 nmol/L, glucagon-stimulated C-peptide less than 0.32 nmol/L, and urine C-peptides less than 5.4 nmol/24 h, mainly had type I diabetes, and these values were higher in type II diabetic patients [13]. The study by Flint et al. (2001) also considered antigenic markers and antibody measurements made by pancreatic beta cells to be useful in differentiating type I and II diabetes [14]. In addition, the results of the study by Vahlkamp T et al. showed that fasting C-peptide cannot be a good distinguishing feature for type I and II diabetes, but the glucagon-stimulated C-peptide is a good distinguishing feature for type I and II diabetes [15].

In the present study, most patients had aged between 15 and 19 (52.17%) and 20–24 (39.13%), and the number of patients with

family history (56.22%) was higher. In the study of Alanani et al., from 99 new cases of type I diabetes, 17.7% of the patients had a family history of diabetes, which was less than that in the present study [16]. In the present study, type II diabetic patients in female was higher than male (62.71% vs. 37.29%). Most patients were aged 15–19 (45.76%) and 20–24 (37.29%), and 57.63% of patients had a positive family history. In the study of Ahmadi et al., 45% of patients with type II diabetes had a positive family history, which was lower than the reported in the present study [17]. A study in the United States found that positive family history is often associated with an increased risk of type II diabetes. Other studies in the United States and Korea reported that positive family history of type II diabetes could be considered as a risk factor for coronary artery disease and atherosclerosis [18,19]. DKA presence was reported in 26.09% of patients with type I diabetes and in 28.81% of patients with type II diabetes. In the study of Naeem et al., 47% of patients with type I diabetes had DKA, which was higher than the reported value in our study [20]. In the study of Szypowska et al., 26% of patients with type I diabetes were diagnosed with DKA, which were consistent with the present study [21]. No patients were reported with Acanthosis Nigricans. On average, patients with type I and type II diabetes lost weight of 7.96 kg and 8.49 kg, respectively. Finally, more attention by physicians to the symptoms of the disease and education through the media is recommended in order to raise the awareness of the families to reduce the delay in diagnosis.

5. Conclusion

According to the obtained results in this study, anti-glutamic acid decarboxylase autoantibodies (Anti-GAD) measurements can be used as an immunological characteristic for screening people at risk for diabetes in order to properly manage the disease and prevent the complications.

Ethics code

IR.AJUMS.REC.1393.3.

Conflicts of interest

The authors have declared that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.04.018.

References

[1] Yazdanpanah L, Shahbazian HB, Moravej Aleali A, Jahanshahi A, Ghanbari S, Latifi SM. Prevalence, awareness and risk factors of diabetes in Ahvaz (South West of Iran). Diabetes Metab Syndr 2016;10(2 Suppl 1):S114–8.
[2] Malecki MT, Klupa T. Type 2 diabetes mellitus: from genes to disease. Pharmacol Rep 2005;57:20–32.
[3] Atkinson MA, Eisenbarth GS. Type 1 diabetes: new perspectives on disease pathogenesis and treatment. Lancet 2001;358(9277):221–9.
[4] Lindberg B, Ivarsson SA, Landin-Olsson M, Sundkvist G, Svanberg L, Lernmark İ. Islet autoantibodies in cord blood from children who developed type I (insulin-dependent) diabetes mellitus before 15 years of age. Diabetologia 1999;42(2):181–7.
[5] Fajans SS, Bell GI, Polonsky KS. Molecular mechanisms and clinical pathophysiology of maturity-onset diabetes of the young. N Engl J Med 2001;345(13):971–80.
[6] Pontiroli AE. Type 2 diabetes mellitus is becoming the most common type of diabetes in school children. Acta Diabetol 2004;41(3):85–90.
[7] Turner R, Stratton I, Horton V, Manley S, Zimmet P, Mackay IR, et al. UKPDS 25: autoantibodies to islet-cell cytoplasm and glutamic acid decarboxylase for prediction of insulin requirement in type 2 diabetes. Lancet 1997;350(9087):1288–93.
[8] Pozzilli P, Di Mario U. Autoimmune diabetes not requiring insulin at diagnosis (latent autoimmune diabetes of the adult). Diabetes Care 2001;24(8):1460–7.
[9] Leighton E, Sainsbury CA, Jones GC. A practical review of C-peptide testing in diabetes. Diabetes Therapy 2017;8(3):475–87.
[10] Davies H, Mannan S, Brophy S, Williams R. Routine glutamic acid decarboxylase autoantibody (GADA) testing: patients' perspective. Fam Pract 2008;25(3):176–80.
[11] Weber P, Ambrosova P, Canov P, Weberova D, Kuklinek P, Meluzinova H, et al. GAD antibodies in T1D and LADA–relations to age, BMI, c-peptide, IA-2 and HLA-DRB1* 03 and DRB1* 04 alleles. Advances in gerontology= Uspekhi gerontologii 2011;24(2):312–8.
[12] Welborn T, Garcia-Webb P, Bonser AM. Basal C-peptide in the discrimination of type I from type II diabetes. Diabetes Care 1981;4(6):616–9.
[13] Gjessing H, Matzen L, Faber O, Frł,land A. Fasting plasma C-peptide, glucagon stimulated plasma C-peptide, and urinary C-peptide in relation to clinical type of diabetes. Diabetologia 1989;32(5):305–11.
[14] Flint A, Arslanian S. Treatment of type 2 diabetes in youth. Diabetes Care 2011;34(Supplement 2):S177.
[15] Vahlkamp T, Lł¼tjens A, Nauta E. The glucagon-stimulated C-peptide test: an aid in classification of patients with diabetes mellitus. Neth J Med 1990;36(3–4):196.
[16] Alanani K, Mohamed N, Alsulaimani AA. Epidemiological pattern of newly diagnosed children with type 1 diabetes mellitus, Taif, Saudi Arabia. Sci World J 2013;2013.
[17] Ahmadi A, Hasanzadeh J, Ghaem H, Khosravi S, Reisi R. The survey of family history of diabetes in patients with type 2 diabetes in Chaharmahal va Bakhteyari province, Iran, 2008. Journal of Shahrekord Uuniversity of Medical Sciences 2009;11(2):1–7.
[18] Olive JL, Ballard KD, Miller JJ, Milliner BA. Metabolic rate and vascular function are reduced in women with a family history of type 2 diabetes mellitus. Metabolism 2008;57(6):831–7.
[19] Park JW, Yun JE, Park T, Cho E, Jee SH, Jang Y, et al. Family history of diabetes and risk of atherosclerotic cardiovascular disease in Korean men and women. Atherosclerosis 2008;197(1):224–31.
[20] Naeem MA, Al-Alem HA, Al-Dubayee MS, Al-Juraibah FN, Omair A, Al-Ruwaili AS, et al. Characteristics of pediatric diabetic ketoacidosis patients in Saudi Arabia. Saudi Med J 2015;36(1):20.
[21] Szypowska A, Skórka A. The risk factors of ketoacidosis in children with newly diagnosed type 1 diabetes mellitus. Pediatr Diabetes 2011;12(4pt1):302–6.