Journal Homepage: - www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI: 10.21474/IJAR01/1299
DOI URL: http://dx.doi.org/10.21474/IJAR01/1299
ISSN NO. 2320-5407

RESEARCH ARTICLE

DIAGNOSIS OF LATENT AUTOIMMUNE DIABETES IN ADULTS (LADA).

Dr Preeti Samir Pachpute, Dr. Z.G. Badade, Dr Sandeep Rai and Dr Samir Pachpute.
Department of Biochemistry, MGM Medical College and Hospital, Kamothe, Navi Mumbai.

Manuscript Info

Manuscript History

Received: 15 June 2016
Final Accepted: 19 July 2016
Published: August 2016

Key words:-
LADA, GAD- 65 antibodies, diabetes mellitus.

Abstract

Aims & Objectives: To study the prevalence of LADA in Diabetic patients. To study the association of GAD -65 antibodies as marker in the diagnosis of LADA. Methods: we studied 41 persons aged between 18 to 45 years diagnosed as type 2 Diabetes by FPG>126mg/dl and C-peptide >0.6 ng/ml. Results: 14.6% type 2 Diabetic individuals were GAD- 65 antibody positive. 4 were males and 2 were females. 83.3% of GAD-65 antibody positive diabetes individuals had BMI <25 kg/sqmt and age of onset of diabetes <45 years.

Conclusions—Prevalence of GAD antibody positivity is 14.6% in type 2 Diabetes individuals. It is necessary to test for GAD antibodies as early insulin therapy can be initiated to prevent further beta cell damage in LADA patients.

This study done in one centre so it gives only an approximate prevalence of LADA in diabetes. It is necessary to do a large multicentre study all over India to find out the exact prevalence of LADA.

Introduction:-

The global prevalence of diabetes mellitus (DM) was estimated to be 2.8% in the year 2000 and is expected to rise to 4.4% in 2030[1]. Latent autoimmune diabetes in adults (LADA) accounts for 2%-12% of all cases of diabetes. Patients are typically diagnosed after 35 years of age and are often misdiagnosed as type II Diabetes Mellitus (DM). Glycemic control is initially achieved with sulfonylureas but patients eventually become insulin dependent more rapidly than with type II DM patients. Although they have a type II DM phenotype, patients have circulating beta (β) cell autoantibodies, a hallmark of type I DM. Alternative terms that have been used to describe this condition include type 1.5 diabetes, latent type I diabetes, slowly progressive Insulin Dependent Diabetes Mellitus, or youth onset diabetes of maturity. With regards to its autoimmune basis and rapid requirement for insulin, it has been suggested that LADA is a slowly progressive form of type I DM. However, recent work has revealed genetic and immunological differences between LADA and type I DM. This review deals with the contribution of the genetic, immunological and metabolic components involved in the pathophysiology of LADA and recent approaches in screening of this distinct but heterogeneous clinical entity.[1]

Corresponding Author:- Dr Preeti Samir Pachpute
Address:- Department of Biochemistry, MGM Medical College and Hospital, Kamothe, Navi Mumbai.

Aims And Objectives:-

- To study the association of GAD-65 autoantibodies as a marker in the diagnosis of LADA.
- Our study attempts to separate LADA from IDDM and NIDDM more clearly & accurately to aid investigators & clinicians in diagnosing & treating diabetes more efficiently.

Materials and methods:-

- **Period of study:-** April 2015 to April 2016
- **Place of Study:-** Biochemistry Department, Medicine & Diabetology Department MGM Hospital in Navi Mumbai.
- **Study Design:-** Observational & Prospective study

The Study was carried out on all the patients presenting to Diabetology OPD, having any type of diabetes as per the Study Protocol approved by the Ethics Committee.

Inclusion criteria:-

- Patients attending OPD confirmed as diabetic as per WHO criteria will be included in the epidemiological study.
- Adult patients above the age of 18 yrs.

Exclusion Criteria:-

- Patients having gestational diabetes/IGT/alcoholic pancreatitis/steroid or drug induced Pancreatitis.
- Patients who are seriously ill
- Patients who have any specific objection for undergoing the tests for estimation of GAD auto antibodies will be excluded from the study.

All patients were given a Patient information sheet and an informed consent form. Blood (10 ml) were collected for determination of various biochemical parameters.

Study Procedure:-

The diagnosis of LADA is currently based on three criteria: (1) adult age at onset of diabetes; (2) the presence of circulating islet autoantibodies; and (3) lack of a requirement for insulin for at least 6 months after diagnosis. Islet autoantibodies are markers of beta cell autoimmunity that distinguish LADA from type 2 diabetes. A period of insulin independence after diagnosis is meant to distinguish LADA from classic type 1 diabetes.

Various parameters evaluated for the study are:-

- Present age;
- Gender;
- Age at onset of diabetes;
- Duration of diabetes;
- Family history of diabetes, if any;
- Diet and lifestyle;
- Basal metabolic index (BMI);
- Fasting & Post prandial blood glucose levels, HbA1c levels;
- Cholesterol levels;
- Type of diabetes;
- Medical complications;
- The current treatment regimen that the patient was following.
- GAD Autoantibodies.

Observation & Results:-

Table 1:- Distribution according to age (in years).

	Diabetic Patients	
Age	**No. of diabetics**	**%**
18-25	1	2.4%
26-35	24	58.5%
36-45	16	39.1%
Total	41	100.0%
	Diabetic Patients	
Age	**No. of LADA**	**%**
18-25	1	16.7%
26-35	4	66.6%
36-45	1	16.7%
Total	6	100.0%

Maximum patients diagnosed with diabetes were in the age group of 26-35 yrs (58.5%).And in case of LADA diagnosed cases, 26-35 was the significant age group (66.6%).

Table 2:- Duration of Diabetes &Age at Onset of Diabetes in diabetic patients.

	Diabetic Patients	
Age of onset of Diabetes	**No. of diabetics**	**%**
18-25	4	9.7
26-30	10	24.3
31-35	27	66
Total	41	100.0%
	LADA Patients	
Duration of Diabetes	**No.of LADA**	**%**
<1 year	2	5
1-5	30	73
6-10	5	12
>10	4	10
Total	41	100.0%

Table 3:- Out of total 41 patients with diabetes, 19 were males and 22 females.

	Diabetic Patients	
Sex	**No. of Diabetics**	**%**
Male	19	46.3
Female	22	53.7
Total	41	100.0%
	LADA Patients	
Sex	**No. of LADA**	**%**
Male	4	66.6
Female	2	33.4
Total	6	100.0%

66.6% of LADA patients were males and 33.4 % were females.

Table 4 : Relation of BMI with diabetes

	Diabetic Patients	
BMI	**No. of diabetics**	**%**
Normal	30	73
Overweight	11	27
Obese	0	0
Total	41	100.0%
	LADA Patients	
BMI	**No. of LADA**	**%**
Normal	5	83.3
Overweight	1	16.7
Obese	0	0
Total	6	100

83% of LADA patients(GAD-65 positive) had normal BMI(<25).

Table 5:- Association of Family History in Diabetes

	Diabetic Patients	
Family history	**No.of diabetics**	**%**
Yes	7	17
No	34	83
Total	41	100
	Diabetic Patients	
Family history	**No.of LADA**	**%**
Yes	4	66.7
No	2	33.3
Total	6	100.0%

66.7% of LADA subjects had family history of Diabetes

Table 6:- Diabetic control using HbA1C in diabetic patients.

	Diabetic Patients	
HbA1c control	**No. of diabetics**	**%**
</=7	12	29%
>7	29	71%
Total	41	100.0%
	LADA Patients	
HbA1c control	**No. of LADA**	**%**
</=7	2	33.6
>7	4	66.7
Total	6	100.0%

33.3% of LADA patients had uncontrolled diabetes.

Table 7:- Cholesterol Levels in Diabetic patients.

	Diabetic Patients	
Cholesterol levels	**No. of diabetics**	**%**
< /=200	18	44
>200	23	56
Total	41	100.0%
	LADA Patients	
Cholesterol levels	**No. of LADA**	**%**
< /=200	2	33.6
>200	4	66.7
Total	6	100.0%

66.7% of LADA patients had high cholesterol

Table 8:- GAD -65 Results in Diabetic patients.

	Diabetic Patients	
GAD- 65 results	**No. of diabetics**	**%**
GAD 65 Positive	6	14.6%
GAD 65 negative	32	84%
Total	41	100.0%

Our results showed that out of 41 diabetic patients, 6 (14.6%) were positive for GAD- 65 antibodies. These 6 GAD-65 positive patients were considered as Latent Autoimmune Diabetes in Adults.

Discussion:-

Spiros fourlanos in diabetes care 2006 has published a retrospective study and formulated a LADA clinical risk score.[2]

1. Age of onset<50 years.
2. Acute symptoms of hyperglycemia.
3. BMI < 25 kg/sqmt.
4. Personal history of autoimmune disease.
5. Family history of autoimmune disease.

The presence of at least two of these distinguishing clinical features that is LADA risk score ≥2 had 90% sensitivity for identifying LADA. In the present study all the 6 GAD-65 Positive had LADA risk score ≥2.

In our study, Maximum patients diagnosed with diabetes were in the age group of 26-35 yrs (58.5%). And in case of LADA diagnosed cases, 26-35(66.6%) was the significant age group. 66.6% of LADA patients were males and 33.4 % were females.83% of LADA patients(GAD-65 positive) had normal BMI(<25). 66.7% of LADA subjects had family history of Diabetes. 33.3% of LADA patients had uncontrolled diabetes. 66.7% of LADA patients had high cholesterol.

In USA, 103 of 2,212 (4.7%) were GAD antibody positive, whereas in Europe 71 of 1,922 (3.7%) were GADAb positive. Although there is a paucity of information regarding the prevalence of GAD antibodies in subjects with diabetes in North America, two smaller studies, each with <200 subjects, have found somewhat conflicting data in that the prevalence rate in one was 16% and in the other was 3.4%.[4] A Tasmanian study of 1232 patients with adult-onset diabetes reported that 36% of the men and 34% of the women were GAD antibody positive.[5] In a New Zealand study of 1,148 subjects with what was presumed to be type 2 diabetes, 14.4% were GAD positive within one year of diagnosis and of these 83% required insulin within a year of diagnosis.[5]Tuomi et al showed that the prevalence of GAD+ was 9.3% among 1,122 type 2 diabetic patients, 3.6% among 558 impaired glucose tolerance (IGT) subjects, and 4.4% among 383 non diabetic control subjects.[6] The prevalence of GAD positivity was 17.7% in Latakia in Syria.[7]In our study the prevalence of GAD positivity is 17% with 7% having low titres of <20IU/ml, 82.4% of type2 diabetes subjects had BMI <25 and age of onset is <50 years and all subjects had symptoms of hyperglycemia, so it is absolutely necessary to test for GAD antibodies in selected type 2 diabetes persons with age of onset <50years,

BMI <25 and acute symptoms of hyperglycemia. If they are GAD positive with high titres insulin therapy can be started early to prevent progression of beta cell damage.

Conclusions:-

Prevalence of LADA is 14.6% of type 2 diabetes subject using GAD-65 antibodies. It is absolutely necessary to test for GAD antibodies in individuals selected by using LADA risk score so that early insulin therapy can be initiated and prevent further beta cell damage in LADA patients. This is a small study done in one diabetic centre so it gives only an approximate prevalence of LADA in diabetes. It is necessary to do a large multicentre study all over India to find out the correct prevalence of LADA subjects.

References:-

1. Global status report on noncommunicable diseases 2014. Geneva, World Health Organization
2. Fourlanos S1, Perry C, Stein MS, Stankovich J, Harrison LC, Colman PG.A clinical screening tool identifies autoimmune diabetes in adults.Diabetes Care. 2006 May;29(5):970-5
3. Rosario PW, Reis JS, Fagundes TA, Calsolari MR, Amim R, Silva SC, Purisch S.Latent autoimmune diabetes in adults (LADA): usefulness of anti-GAD antibody titers and benefit of early insulinization. Arq Bras EndocrinolMetabol. 2007 Feb;51(1):52-8
4. Bernard Zinman; Steven E. Kahn; Steven M. Haffner; M. Colleen O'Neill; Mark A. Heise; Martin I. Phenotypic Characteristics of GAD Antibody-Positive Recently Diagnosed Patients With Type 2 Diabetes in North America and Europe. Freed Diabetes. 2004;53(12) c 2004 American Diabetes Association, Inc
5. Dr D Bell. Latent autoimmune diabetes in adults. CLI April 2005
6. Tuomi T, Carlsson A, Li H, Isomaa B, Miettinen A, Nilsson A, Nissen M, Ehrnstrom BO, Forsen B, Snickars B, Lahti K, Forsblom C, Saloranta C, Taskinen MR, Groop LC.GAD antibody clinical and genetic characteristics of type 2 diabetes with and without GAD antibodies. Diabetes. 1999 Jan;48(1):150-7.
7. AI Farwi et al. Latent autoimmune diabetes in adults in latakia, Syria International journal of endocrinology and metabolism, January 2010.
8. Takino H, Yamasaki H, Abiru N, Sera Y, Abe T, Kawasaki E, Yamaguchi Y, Eguchi K, Kanazawa Y, Nagataki S. Antibodies to GAD in Japanese patients classified as Type 2 diabetes at diagnosis. High titre of GAD Ab is a predictive marker for early insulin treatment--report of west Japan (Kyushu, Yamaguchi, Osaka) study for GAD Ab(+) diabetes.Diabet Med. 2002 Sep;19(9):730-4.
9. Sanjeevi,**CB**.Balaji, M, Balaji, V and Seshiah. Autoantibodies to GAD65 and IA-2 antibodies are increased but not tissue transglutaminase 9TTG-Ab) in type 2 diabetes mellitus patients from South India. V Ann NY Acad Med Sci1005; 387-389 2003.98
10. Sima et.al Latent autoimmune diabetes in adults. Alexandra TMJ 2003.