



( 233 54.9%)  
 NDDG 2)  
 , 2  
 C-peptide 가 0.6 ng/ml ,  
 , , 가 24 kg/m2  
 , , GAD 가 가 ,

20 HLA-DR 276  
 HLA-DQA1 106 ,  
 HLA-DQB1 104 , 20  
 105

1 10  
 가 가  
 가  
 2.  
 1)

GAD 가 (immunoradio-  
 metric assay, IRMA; Elias, Osceola, WI, USA.)

(immunoprecipitation after *in vitro* translation) , IA-2 가

3) HLA-DR -DQ  
 11 International Histocompatibility Workshop  
 Conference

Ficoll-Hypaque  
 nylon column B  
 Terasaki tray .

rabbit (lym-  
 phocyte microcytotoxicity method; One Lamda Co.,  
 Stamford, CT, USA)

4) HLA-DQ  
 Genomic DNA

Taq DNA  
 polymerase 2.5units, HLA-DQA1  
 primer DQAS34 DQAA261 , HLA-DQB1  
 primer DQBS43 DQBA248(Table 1)  
 PCR cyler(Perkin Elmer Corp., Branchburg, NJ,  
 U.S.A.) (denaturation) 90-96 30 - 1  
 , 50-60 (annealing) 1 , 70-7  
 5 1 (extention) 35

**Table 1. Primer Sequences for HLA-DQA1 and -DQB1 PCR**

DQA1 gene	
DQAS34	5'-GGTGTAAACTTGTACCAG-3'
DQAA261	5'-ATTGGTAGCAGCGGTAGA-3'
DQB1 gene	
DQBS43	5'-TGCTACTTCACCAA(C/T)GGG-3'
DQBA249	5'-GTAGTTGTGTCTGCA(C/T)AC-3'

가  
 가  
 C-peptide  
 (hemoglobin A1c; HbA1c)  
 hexokinase  
 HbA1c ( : 5.5-8.4%)  
 C-peptide  
 (radioimmunoassay, Incstar Co., Stillwater, MN, USA.)

가. (restriction frag-  
 ment length polymorphism; RFLP) HLA-  
 DQA1  
 HLA-DQA1 Dde I  
 pattern , pattern  
 Rsa I 12% polyacrylamide

2) GAD 가 IA-2 가

**Table 2. Sequences Specific Oligonucleotide Probes for HLA-DQB1 Typing**

Probe	Sequence	Allele
QE2301	GACCGAGCTCGTGCGG	0401
QE2302	AACGGGACCGAGCGCGTG	03031,0305,0402
7007	AGGACCCGGGCGGCGGTG	0504,0401,0402
Q25	CGTGCGTTATGTGACCAGA	06011,06012,0301,0304
Q26	GTGCGTCTTGTGACCAGAT	0602,0302,03031,03032
Q27	GCGTGCGTCTTGTAAACCAGA	0603,0604,0605,0606,0607,0608
Q28	TGGTGTGAGCAGAAGCATC	0201
2606N	CTTGTAAACCAGATACATC	0605,0606
Q37	AGAGGAGTACGTGCGCTTC	0501,0502,05031,05032
Q68	CTGGAGGGGGCCCCGGGCG	0501,0502,05031
Q45	GACGTGGAGGTGTACCGGG	0301,0304
Q49	GGTGTACCGGGCAGTGACG	0501
Q51	CGCCTCTGGGGCTGCCTGC	0201
5701N	GCGGCCTGTTGCCGAGT	0501,0604,0605,0606,0608
5702NSK	GCGGCCTAGCGCCGAGTA	0502,0504
Q5703	GGGGCGGCCTGATGCCGAG	05032,0602,0603,0607
5706	GGGCCGCCTGACGCC	0301,03031,03032
5707	TGGGGCCGCCTGCCGCCG	0302,0304,0305
7107	GGAGGAGGACCGGGCG	0504,0401,0402
Q71	AGGACCCGAGCGGAGTTGG	06011,06012
Q72	CTGGAGGGGACCCGGGCGG	0602,0603,0608
Q77	CGTCGGTGGACAGAGTGT	0502,05031
UNIQ115	CGCTTCGACAGCGACGTG	0501,0502,05031,05032,0504,06011, 06012,0602,0603,0604,0605,0606,0607, 0608,0201,0301,0302,03031,03032,0304, 0305,0401,0402
E7007	AGGACCCGGGCGGCGGTG	0606

gel pattern, 80 2 DNA Mem-  
DQA1 23), brane 2 x SSC buffer probe가 가  
. SSO(sequence specific oligonucleotide) hybridization buffer(1 µl probe/1ml buffer, 3M TMAC,  
(dot blot hybridization) 0.1% SDS, 100 µg/ml herring sperm DNA)  
HLA-DQB1 46 1 ddUTP 3' end  
Genomic DNA, HLA-DQB1 labelling Sequence specific oligonucleotide probe  
DQB1 24가 oligonu- (Table 2) . Membrane 2 x SSC  
cleotide probe (hybridization) membrane TMAC  
allele 14). (50mM Tris-HCl, pH 8.0, 3.0M tetramethylammo-  
DNA 5 µl 0.4N NaOH Dot Blotter niumchloride, 2mM EDTA, 0.1% SDS) 56- 58  
(Bio- Rad) nylon membrane 2% blocking reagent/TN buffer mem-  
denatured DNA membrane brane TN buffer . Quick-  
Blotting membrane whatman 3MM light buffer(Dioxetane phosphate substrate buffer,

**Table 3. Clinical Characteristics of Childhood and Adult-Onset IDDM Patients**

	Childhood- onset (N=105)	Adult- onset (N=128)	p value
Age(years)	20.1 ± 8.7	45.0 ± 13.9	-
Sex(Male:Female)	43 : 62	58 : 70	NS
Age of onset(years)	12.4 ± 6.3	36.3 ± 11.8	-
Family history of diabetes(%)	24/96(25.0%)	46/128(35.9%)	NS
History of ketonuria(%)	65/94(69.2%)	67/123(54.5%)	0.04
BMI(kg/m <sup>2</sup> )	18.0 ± 2.4	20.4 ± 2.9	0.036
Duration of disease(years)	7.7 ± 5.5	8.8 ± 6.8	NS
Plasma glucose(mg/dl)			
fasting	167.4 ± 43.2	181.3 ± 38.1	NS
postprandial 2 hour	224.1 ± 55.6	234.1 ± 66.7	NS
Plasma C- peptide(ng/ml)			
fasting	0.53 ± 0.35	0.66 ± 0.43	0.047
postprandial 2 hour	0.68 ± 0.45	0.88 ± 0.77	0.0001
HbA1c(%)	9.29 ± 2.07	9.53 ± 1.8	NS
SPIDDM	1/99(1.0%)	35/128(27.3%)	0.00001

Values are means ± SD. NS: not significant, BMI: body mass index, HbA1C: hemoglobin A1c, SPIDDM: slowly progressive insulin dependent diabetes mellitus

**Table 4. Clinical Characteristics of SPIDDM and Acute-Onset Patients in Adult-Onset IDDM**

	SPIDDM (N=35)	Acute-onset adult IDDM (N=70)	p value
Age(years)	46.4 ± 13.5	41.1 ± 13.8	NS
Sex(Male:Female)	17 : 18	36 : 34	NS
Age of onset(years)	41.3 ± 13.4	33.5 ± 11.3	0.004
Family history of diabetes(%)	11/35(31.4%)	27/70(38.6%)	NS
History of ketonuria(%)	16/35(45.7%)	22/69(31.9%)	NS
BMI(kg/m <sup>2</sup> )	20.4 ± 3.3	20.3 ± 2.9	NS
Duration of disease(years)	5.1 ± 2.9	7.7 ± 6.1	NS
Plasma glucose(mg/dl)			
fasting	174.1 ± 42.8	169.2 ± 35.4	NS
postprandial 2 hour	211.0 ± 64.5	243.7 ± 64.5	NS
Plasma C- peptide(ng/ml)			
fasting	0.83 ± 0.58	0.55 ± 0.32	0.002
postprandial 2 hour	1.25 ± 1.21	0.43 ± 0.04	0.001
HbA1c(%)	9.0 ± 1.8	9.7 ± 1.9	NS

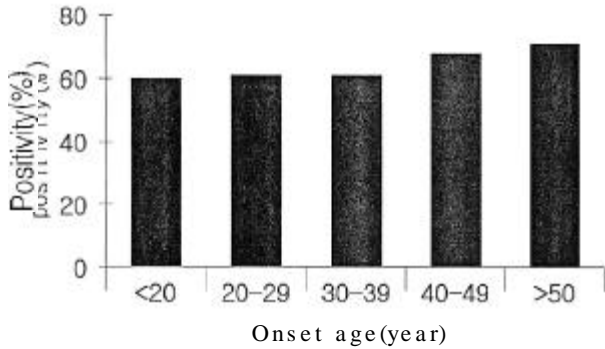
Values are means ± SD. NS: not significant, BMI: body mass index, HbA1C: hemoglobin A1c, SPIDDM: slowly progressive insulin dependent diabetes mellitus

alkaline substrate buffer) 5 CSPD allele .  
 developing folder membrane 5)  
 black bag 1 incubation  
 5 , 15 1 . SPSS version 7.0  
 ±

**Table 5. Prevalence of Autoantibodies in Childhood-Onset and Adult-Onset IDDM**

	Childhood-onset	Adult-onset	p value
Anti-thyroid antibody	4/62(6.5%)	5/32(15.6%)	NS
AntiMS antibody	11/60(18.3%)	10/31(32.3%)	NS
AntiGAD antibody	48/80(60.3%)	71/111(64.0%)	NS
IA-2 antibody	10/48(20.8%)	14/97(14.4%)	NS

NS: not significant, MS: microsomal, GAD: glutamic acid decarboxylase, IA-2: insulinoma-associated protein-2



**Fig. 1.** Distribution of Anti-GAD Antibody According to Onset Age of IDDM Patients

Unpaired Student's t test

Chi-square

가 5

Fisher's exact probability test

가

Phi

p

0.05

1.

가 가  
(67/123 vs. 65/94, p=0.04; 20.4 ± 2.9 vs. 18.0 ± 2.4kg/m<sup>2</sup>, p=0.036), 2 C-peptide

(0.66 ± 0.43 vs. 0.53 ± 0.35ng/ml, p=0.047; 0.88 ± 0.77 vs. 0.68 ± 0.45, p=0.0001). 가

가

(35/128 vs. 1/99, p=0.0001)(Table 3).

16.1% (36/224)  
(33.5 ± 11.3 vs. 41.3 ± 13.4 years, p=0.004)  
C-peptide 가 (0.55 ± 0.32 vs. 0.83 ± 0.58ng/ml, p=0.002; 0.43 ± 0.04 vs. 1.25 ± 1.21ng/ml, p=0.001)(Table 4).

**2. GAD 가 IA-2 가**

GAD 가

111 71

64.0%

62.3%

(119/191)

60.3% (47/78)

가 (Table 5),

가

(Fig. 1, 2). IA-2 가

16.6% (24/145)

20.8%,

14.4%

가

(Table 5),

(Fig. 2). 가

(Fig. 3).

가

51.6% (64/124) (Table 6) Phi

0.26(p=0.004)

GAD 가 가

72

GAD 가

(7.4 ± 6.7 vs.

10.4 ± 7.2years, p=0.034)

2

C-peptide

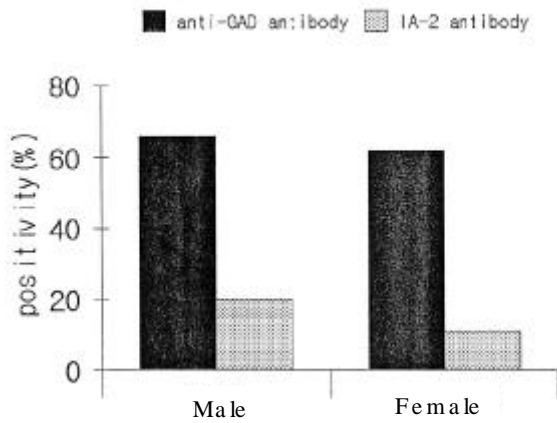


Fig. 2. Distribution of Anti-GAD and IA-2 Antibody According to Sex in Adult-Onset IDDM Patients

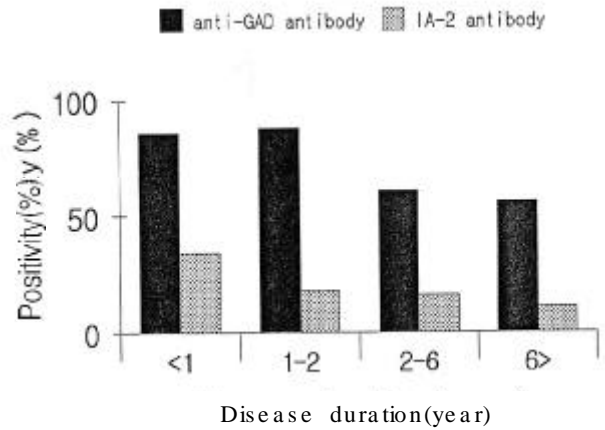


Fig. 3. Distribution of Anti-GAD and IA-2 Antibody According to Disease Duration of Adult-Onset IDDM Patients

Table 6. Concordance between Anti-GAD Antibody and IA-2 Antibody

	Anti-GAD antibody		Total
	(+)	(-)	
IA-2 antibody (+)	11(11.5%)	2(2.1%)	13
IA-2 antibody (-)	49(51.0%)	34(35.4%)	83
Total	60	36	96

Data are number(%) of patients.

GAD: glutamic acid decarboxylase, IA-2: insulinoma-associated protein-2

(0.74 ± 0.50 vs. 0.48 ± 0.22ng/ml, p=0.002; 1.02 ± 0.96 vs. 0.65 ± 0.40ng/ml, p=0.022)(Table 7).

3. HLA-DR -DQ HLA-DQ

DR4 DR9 (107/276 vs. 32/58, p=0.028; 44/276 vs. 19/58, p= 0.002) DR (Table 10).

가. HLA-DR -DQ

. HLA-DQ

DR9 DR3, DR4, DR4 DR9 (107/276 vs. 55/102, p=0.01; 44/276 vs. 26/102, p=0.038). DR3/4

DQA1 DQA1\*0301 DQA1\*0501 가, DQA1\*0601 (12/106 vs. 2/95, p=0.012)

DR9 DR3 DR4, DR3 DR9 DR4 (haplotype) (120/276 vs. 63/12, p=0.002; 4/276 vs. 10/102, p=0.001; 60/276 vs. 36/102, p=0.0001; 138/276 vs. 72/102, p=0.0001) DQ (Table 8, 9).

(Table 11). DQB1 DQB1\*0301, DQB1\*0301 DQB1\*0601 (31/104 vs. 13/94, p=0.017; 23/104 vs. 4/94, p=0.0001)(Table 12). GAD 가 DQA1\*0601, DQB1\*0301 DQB1\*0601 가 (12/106 vs. 0/52, p=0.009; 31/104 vs. 6/52, p=0.016;

HLA-DR

**Table 7. Clinical Characteristics of Adult-Onset IDDM According to Positivity of Anti-GAD Antibody**

	Anti-GAD antibody		p value
	Positive group (N=71)	Negative group (N=41)	
Age(years)	45.0 ± 14.4	45.7 ± 13.7	NS
Sex(Male:Female)	33 : 38	17 : 24	NS
Age of onset(years)	37.6 ± 12.3	35.5 ± 11.6	NS
Family history of diabetes(%)	20/71(24.2%)	19/41(46.3%)	NS
History of ketonuria(%)	37/69(53.6%)	25/41(61.0%)	NS
BMI(kg/m <sup>2</sup> )	20.6 ± 3.0	19.7 ± 2.2	NS
Duration of disease(years)	7.4 ± 6.7	10.4 ± 7.2	0.034
Plasma glucose(mg/dl)			
fasting	173.9 ± 40.1	162.7 ± 37.7	NS
postprandial 2 hour	248.5 ± 72.2	241.3 ± 58.4	NS
Plasma C- peptide(ng/ml)			
fasting	0.74 ± 0.50	0.48 ± 0.22	0.002
postprandial 2 hour	1.02 ± 0.96	0.65 ± 0.40	0.022
HbA1C(%)	9.5 ± 1.9	9.6 ± 1.7	NS
SPIDDM	24/60(40.0%)	10/33(30.3%)	NS
Positivity of other autoantibodies			
anti-thyroid antibody	5/18(27.8%)	0/11(0%)	NS
anti-MS antibody	9/18(50.0%)	1/10(10.0%)	0.048
antiIA-2 antibody	12/61(19.7%)	2/36(5.6%)	NS

Values are means ± SD. NS: not significant, BMI: body mass index, HbA1C: hemoglobin A1C, SPIDDM: slowly progressive insulin dependent diabetes mellitus, MS: microsomal, GAD: glutamic acid decarboxylase, IA-2: insulinoma-associated protein-2

**Table 8. Frequencies of HLA DR Serotypes in Childhood-Onset and Adult-Onset IDDM Patients**

HLA-DR	Control (N=276)	Childhood-onset IDDM (N=87)		Adult-onset IDDM (N=102)			
	No.(%)	No.(%)	p	OR	No.(%)	p	OR
1	25(9.1)	5(5.7)	NS		13(12.7)	NS	
2	53(19.2)	6(6.9)	0.007	0.82	12(11.8)	NS	
3	17(6.1)	22(25.3)	0.0001	1.83	12(11.8)	NS	
4	107(38.8)	45(51.7)	0.035	1.14	55(53.9)	0.01	1.19
5	52(18.8)	10(11.5)	NS	17(16.7)	NS		
6	56(20.3)	9(10.3)	0.037	0.88	22(21.6)	NS	
7	56(20.3)	10(11.5)	NS	15(14.7)	NS		
8	34(12.3)	12(13.8)	NS	9(8.8)	NS		
9	44(15.9)	26(29.9)	0.008	1.26	26(25.5)	0.038	1.19
10	7(2.5)	4(4.6)	NS	3(2.9)	NS		
3 or 4	120(43.5)	58(66.7)	0.0001	1.25	63(61.8)	0.002	1.22
3/4	4(1.4)	10(11.5)	0.0001	2.73	10(9.8)	0.001	2.61
3 or 9	60(21.7)	44(50.6)	0.001	2.95	36(35.3)	0.0001	2.39
3/9	1(0.4)	5(5.7)	0.004	4.62	2(2.0)	NS	
4 or 9	138(50.0)	65(74.7)	0.0001	1.27	72(70.6)	0.0001	1.25
4/9	13(4.7)	6(6.9)	NS	9(8.8)	NS		

Data are number(%) of patients and control subjects. P values vs. control subjects  
OD: odds ratio, NS: not significant

**Table 9. Comparison of HLA DQ Serotypes between Control and Adult-Onset IDDM Patients**

	Control(N=87)	Adult-onset IDDM(N=99)	p value
	No.(%)	No.(%)	
DQ 1(5,6)	50(57.5)	46(46.5)	NS
2	17(19.5)	21(21.2)	NS
3(7,8,9)	50(57.5)	63(63.6)	NS
4	23(26.4)	30(30.3)	NS

Data are number(%) of patients and control subjects. NS: not significant

**Table 10. Frequencies of HLA DR Serotypes in Adult-Onset IDDM Patients Carrying Anti-GAD Antibody**

HLA - DR	Control (N=276)	AntiGAD- positive adult-onset IDDM (N=58)		
	No.(%)	No.(%)	p	OR
3	17(6.1)	5(8.6)	NS	
4	107(38.8)	32(55.2)	0.028	1.13
6	56(20.3)	13(22.4)	NS	
9	44(15.9)	19(32.8)	0.005	1.23

Data are number(%) of patients and control subjects. P values vs. control subjects  
OR: odds ratio, NS: not significant

**Table 11. Frequencies of HLA DQA1 Genotypes in Childhood-Onset and Adult-Onset IDDM Patients**

HLA - DQA1	Control (N=106)	Childhood-onset IDDM (N=52)			Adult-onset IDDM (N=95)		
	No.(%)	No.(%)	p	OD	No.(%)	p	OD
0101,2	43(40.6)	14(26.9)	NS		32(33.7)	NS	
0103	13(12.3)	2(3.8)	NS		8(8.4)	NS	
0201	17(12.3)	4(7.7)	NS		14(14.7)	NS	
0301	64(60.4)	42(80.8)	0.012	1.34	65(68.4)	NS	
0501	29(27.4)	24(46.2)	0.021	1.34	21(22.1)	NS	
0601	12(11.3)	0(0.0)	0.009	0.64	2(2.1)	0.012	0.59

Data are number(%) of patients and control subjects. P values vs. control subjects  
OD: odds ratio, NS: not significant, R: Arg 52, nR: non-Arg-52

17/104 vs. 3/52, p=0.01)(Table 13, 14).

vs. 28/94, p=0.009)(Table 15).

DQA1 DQB1 Arg 52/ HLA-DQA1 -DQB1 가  
non-Arg 52 Asp 57/non-Asp 57 DQA1\*Arg-52  
DQ A1 Arg 52 DQB1\*nonAsp-57  
가 1.4,  
(44/106 vs. 32/52, p=0.027) 1.3 (odds ratio, OR) 가  
가 DQB1 non-Asp 57 DQA1\*nonArg  
가 DQB1\*nonAsp-57  
가 (15/104 vs. 17/52, p=0.006; 15/104 가 2.4



**Table 12. Frequencies of HLA DQB1 Genotypes in Childhood-Onset and Adult-Onset IDDM Patients**

HLA - DQB1	Control	Childhood-onset IDDM			Adult-onset IDDM		
	(N=104)	(N=50)			(N=94)		
	No.(%)	No.(%)	p	OR	No.(%)	p	OR
0201	20(19.2)	19(38.0)	0.017	1.42	20(21.3)	NS	
0301	31(29.8)	4(8.0)	0.002	0.69	13(13.8)	0.017	0.69
0302	28(26.9)	20(40.0)	NS		26(27.7)	NS	
0303	20(19.2)	15(30.0)	NS		24(25.5)	NS	
0401	18(17.3)	14(28.0)	NS		21(22.3)	NS	
0402	8(7.7)	0(0.0)	0.05	0.66	5(5.3)	NS	
0501	13(12.5)	3(6.0)	NS		12(12.8)	NS	
0502	7(6.7)	0(0.0)	NS		5(5.3)	NS	
0503	7(6.7)	4(8.0)	NS		3(3.2)	NS	
0601	23(22.1)	0(0.0)	0.001	0.63	4(4.3)	0.0001	0.59
0602	7(6.7)	1(2.0)	NS		9(9.6)	NS	
0603	1(9.6)	1(2.0)		NS	4(4.3)	NS	
0604	17(16.3)	10(20.0)	NS		9(9.6)	NS	

Data are number(%) of patients and control subjects. P values vs. control subjects  
 OD: odds ratio, NS: not significant, D: Asp-57, nD: non-Asp-57

**Table 13. Frequencies of HLA DQA1 Genotypes in Adult-Onset IDDM Patients Carrying Anti-GAD Antibody**

HLA - DQA1	Control	AntiGAD-positive adult-onset IDDM		
	(N=106)	(N=52)		
	No.(%)	No.(%)	p	OR
0101,2	43(40.6)	21(40.4)	NS	
0301	64(60.4)	37(71.2)	NS	
0501	30(28.3)	11(21.2)	NS	
0601	12(11.3)	0(0.0)	0.009	0.64

Data are number(%) of patients and control subjects. P values vs. control subjects  
 OR: odds ratio, NS: not significant

**Table 14. Frequencies of HLA DQB1 Genotypes in Adult-Onset IDDM Carrying Anti-GAD Antibody**

HLA - DQB1	Control	AntiGAD-positive adult-onset IDDM		
	(N=104)	(N=52)		
	No.(%)	No.(%)	p	OD
0201	20(19.2)	11(21.2)	NS	
0301	31(29.8)	6(11.5)	0.016	0.73
0302	28(26.9)	11(21.2)	NS	
0303	20(19.2)	15(28.8)	NS	
0401	18(17.3)	11(21.2)	NS	
0601	23(22.1)	3(5.8)	0.01	0.70
0604	17(16.3)	7(13.5)	NS	

Data are number(%) of patients and control subjects. P values vs. control subjects  
 OD: odds ratio, NS: not significant

**Table 15. Comparison in the Distribution of HLA DQA1 and DQB1 Genotype in Childhood-Onset and Adult-Onset IDDM Patients**

Genotype	Control	Childhood-onset			IDDM Adult-onset IDDM		
	N=106 No.(%)	N=52			N=95		
DQA1		No.(%)	p	OD	No.(%)	p	OD
Arg-52/Arg-52	44(41.5)	32(61.5)	0.027	1.31	42(44.2)	NS	
Arg-52/nonArg-52	46(43.4)	17(32.7)	NS		37(38.9)	NS	
nonArg-52/nonArg-52	16(15.1)	3(5.8)	NS		16(16.8)	NS	
DQB1	N=104 No.(%)	N=52			N=94		
		No.(%)	p	OD	No.(%)	p	OD
nonAsp-57/nonAsp-57	15(14.4)	17(34.0)	0.006	1.57	29(30.9)	0.006	1.71
nonAsp-57/Asp-57	55(52.9)	4(8.0)	NS		42(44.7)	NS	
Asp-57/Asp-57	34(32.9)	9(18.0)	NS		23(24.5)	NS	

Data are number(%) of patients and control subjects. P values vs. control subjects  
OD: odds ratio, NS: not significant

(p=0.04)(Table 16). DQA1-DQB1 (p=0.044) DR  
DQA1\*0301-DQB1\*0201 DQ (Table 19).  
가 [8/103(7.8%) vs. 13/47 (27.7%), p=0.002] 4. GAD 가 HLA  
(Table 17), GAD 가 HLA  
가 (Table 18). HLA  
DR3, DR4 DR9 DQ GAD 가 DQA1\*  
DR3 DQA1\*0301-DQB1\* 0501-DQB1\*0201 가  
0201 DQA1\*0501-DQB1\*0201 (0/97 vs. 11/46, p= (9/1 vs. 10/25, p=0.031), HLA  
0.0001; 1/97 vs. 11/46, p=0.0001) DR4 DQA1\*0301- GAD 가  
DQB1\*0201 (3/97 vs. 8/46, p=0.005) DR9 (Table 20).  
DQA1\*0301-DQB1\*0303 (7/97 vs. 9/46, DR4 DR9

**Table 16. Distribution of HLA DQA1(position 52) and DQB1(position 57) Genotypes in Childhood-Onset and Adult-Onset IDDM Patients**

HLA-DQ Susceptible Heterodimers	Control (N=105) No.(%)	Childhood-onset IDDM (N=47)			Adult-onset IDDM (N=91)		
		No.(%)	p	OR	No.(%)	p	OR
SS SS 4	5(4.8)	5(10.6)	NS	1.4	7(7.7)	NS	1.3
SP SS 2	9(8.6)	4(8.5)	NS	1.0	12(13.2)	NS	1.3
SS SP 2	25(23.8)	14(29.8)	NS	1.1	21(23.1)	NS	0.9
SP SP 1	22(20.9)	9(19.1)	NS	1.0	15(16.5)	NS	0.9
PP SS 0	3(2.9)	0(0.0)	NS	0.7	10(10.9)	0.04	2.4
SS PP 0	13(12.4)	10(21.3)	NS	1.3	12(13.2)	NS	1.0
SP PP 0	15(14.3)	2(4.3)	NS	0.8	8(8.8)	NS	0.8
PP SP 0	7(6.7)	1(2.1)	NS	0.8	3(3.3)	NS	0.8
PP PP 0	6(5.7)	2(4.3)	NS	0.9	3(3.3)	NS	0.8

Data are number(%) of patients and control subjects. P values vs. control subjects  
OD: odds ratio, NS: not significant, S: susceptible chain, P: protective chain

**Table 17. Frequencies of HLA DQA1-DQB1 Heterodimers in Childhood-Onset and Adult-Onset IDDM Patients**

DQA1-DQB1	Control (N=103)	Childhood-onset IDDM (N=47)		Adult-onset IDDM (N=91)			
	No.(%)	No.(%)	p	OR	No.(%)	p	OR
0301-0201	8(7.8)	13(27.7)	0.002	1.93	11(12.1)	NS	
0301-0302	24(23.3)	19(40.4)	NS	22(24.2)	NS		
0301-0303	17(16.5)	15(31.9)	0.029	1.42	23(25.3)	NS	
0301-0401	17(16.5)	13(27.7)	NS	21(23.1)	NS		
0501-0201	8(7.8)	12(25.5)	0.008	1.83	11(12.1)	NS	
0501-0302	4(3.9)	11(23.4)	0.004	2.07	5(5.5)	NS	
0501-0303	2(1.9)	4(8.5)	0.009	3.39	3(3.3)	NS	
0102-0601	10(9.7)	0(0.0)	NS	1(1.1)	NS		

Data are number(%) of patients and control subjects. P values vs. control subjects  
OD: odds ratio, NS: not significant

**Table 18. Frequencies of HLA DQA1-DQB1 Heterodimers in Adult-Onset IDDM Carrying Anti-GAD Antibody**

DQA1-DQB1	Control (N=103)	AntiGAD- positive adult-onset IDDM (N=52)	
	No.(%)	No.(%)	p
0301-0201	8(7.8)	5(9.6)	NS
0301-0302	24(23.3)	11(21.2)	NS
0301-0401	17(16.5)	10(19.2)	NS
0501-0201	8(7.8)	5(9.6)	NS
0501-0302	4(3.9)	1(1.9)	NS

Data are number(%) of patients and control subjects. NS: not significant

**Table 19. Frequencies of HLA DQA1-DQB1 Heterodimers Associated with Specific DR Serotype in Childhood-Onset and Adult-Onset IDDM Patients**

DR-DQA1-DQB1	Control (N=97)	Childhood-onset (N=46)		IDDM Adult-onset IDDM (N=91)			
	No.(%)	No.(%)	p	OR	No.(%)	p	OR
3-0301-0201	0(0.0)	11(23.9)	0.0001	3.7	4(4.4)	NS	
3-0501-0201	1(1.0)	11(23.9)	0.0001	8.79	6(6.6)	NS	
4-0301-0201	3(3.1)	8(17.4)	0.005	2.61	8(8.8)	NS	
4-0301-0302	17(17.5)	15(32.6)	NS		15(16.5)	NS	
4-0301-0401	16(16.5)	13(28.3)	NS		19(20.9)	NS	
9-0301-0302	6(6.2)	3(6.5)	NS		9(9.9)	NS	
9-0301-0303	7(7.2)	9(19.6)	0.044	1.62	13(14.3)	NS	

Data are number(%) of patients and control subjects. P values vs. control subjects  
OD: odds ratio, NS: not significant

DR4-DQA1\*0301-DQB1\*0401 (DR4-DQ4)

DR9-DQA1\*0301-DQB1\*0303 (DR9-DQ9)

가 , 20

GAD 가 DR4-DQ4 DR9-DQ9 50% 24)

(13/24 vs. 15/16, p=0.002) (Table 21). 233 128

**Table 20. Prevalence of Anti- GAD Antibody in IDDM Patients Carrying HLA- DQ Risk Haplotypes**

HLA- DQ alleles	Childhood- onset	Adult- onset
DQA 1* - DQB1*	anti- GAD antibody	anti- GAD antibody
0301- 0201	8/11(72.7% )	5/11(45.5% )
Non(0301- 0201)	13/27(48.1% )	47/77(61.0% )
p value	NS	NS
0501- 0201	9/11(81.8% )	5/10(50.0% )
Non(0501- 0201)	10/25(40.0% )	47/78(60.3% )
p value	0.031	NS
0501- 0302	6/8(75.0% )	1/4(25.0% )
Non(0501- 0302)	15/30(50.0% )	51/84(60.7% )
p value	NS	NS
0501- 0303	3/4(75.0% )	2/3(66.7% )
Non(0501- 0303)	18/34(52.9% )	50/85(58.8% )
p value	NS	NS

NS: not significant, GAD: glutamic acid decarboxylase

**Table 21. Comparison of Clinical and Immunological Characteristics between DR4- DQ4 Group and DR9- DQ9 Group**

	DR4- DQ4 group (N=24)	DR9- DQ9 group (N=16)	p value
Age(years)	50.5 ± 12.7	45.8 ± 17.3	NS
Sex(Male:Female)	12 : 12	5 : 11	NS
Age of onset(years)	41.3 ± 12.2	37.1 ± 12.7	NS
Family history of diabetes(%)	8/24(33.3% )	3/16(18.8% )	NS
History of ketonuria(%)	17/24(70.8% )	9/16(56.3% )	NS
BMI(kg/m <sup>2</sup> )	19.5 ± 1.9	19.7 ± 1.3	NS
Duration of disease(years)	9.2 ± 1.9	9.9 ± 1.9	NS
Plasma glucose(mg/dl)			
fasting	163.0 ± 35.7	158.4 ± 37.1	NS
postprandial 2 hour	217.6 ± 63.2	220.1 ± 51.4	NS
Plasma C- peptide(ng/ml)			
fasting	0.47 ± 0.29	0.55 ± 0.26	NS
postprandial 2 hour	0.51 ± 0.33	0.73 ± 0.50	NS
HbA1C(%)	9.9 ± 1.9	9.8 ± 1.7	NS
Positivity of autoantibodies			
anti- GAD antibody	13/24(54.2% )	15/16(93.8% )	0.002
IA- 2 antibody	5/22(22.7% )	2/11(18.2% )	NS

Values are means ± SD. NS: not significant, BMI: body mass index, HbA1C: hemoglobin A1C, GAD: glutamic acid decarboxylase, IA- 2: insulinoma- associated protein- 2

54.9%

가

C- peptide 가

25.

가 C- peptide

7 :  
16.1% 20% GAD 가 가 64%  
26) , 1 80% 가  
. GAD 가 20  
가 20.4kg/m2 60.3% 20 62%  
41  
C-peptide 가 ICA가 70- 80% 가  
가가 5 15%  
19, 35) GAD 가  
29)  
, IA- 2 가  
가 65- 75% 36, 37)  
48%  
가 90% 가 25  
.38)  
27) 16.1%  
가 14.4% , 20.8%  
가 IA- 2  
가 가 GAD 가  
1 6  
70- 80% 33.3%  
, 1 1  
50%  
가 ICA GAD 가 가  
28), HLA- DR HLA- DR3, DR4 DR9가 가  
60- 80% , 3- 42 59% DR4 DR9 DR3  
29, 30) GAD 가 가 가 DR4가 가 가 6 39).  
GAD 가 50% , 33, 40, 41) DR3 DR9 가  
39% , 5- 30% 42)  
31, 32). 가 DR9 가  
가 가 가  
33), 가 .34) GAD 가 HLA- DR  
GAD 가 HLA- DR4, DR9

가 HLA-DQA1  
DQA1\*0301 \*0501 가 DQA1 DQB1  
DQA1\*0601 가  
DQA1\*0601 cis trans DQ  
DQB1 DQB1 DR  
DQB1\*0201 가 DQB1\* 0301, \*0402, \*0601 DR DQA1, DQB1  
가 가  
DQB1 DQB1 \*0301, \*0601 가  
GAD 가 DR4가 DQA1\*  
0301- DQB1\*0302 , DR4 DQA1\*0301-  
가 DQB1\* 0303 DQB1\*0401 48). cis trans  
가 DQA1 DQB1  
DQA1\*0301  
DQB1 \*0201, \*0303  
가 , DQA1\*0501 DQB1\*0201, 0302, 0303  
HLA 가 가 (odds  
가 ratio)가 DQA1\*0501- DQB1\*0303 가 3.4 가  
DQ Arg 52 가 가  
DQA1\*0301, 0401, 0501 0601 DQ Asp  
57 가 DQB1\*0201, 0302, 0304,  
0501, 0502, 0504 0604 DQA1 DQB1 가  
43-45).  
46, 47). DR  
Arg 52 DR3 DQA1  
Asp 57 \*0301- DQB1\*0201 DQA1\*0501- DQB1\*0201 , DR4  
가 DQA1\*0301- DQB1\*0201 , DR9 DQA1 \*0301-  
Arg 52 가 DQB1\*0303 가  
Asp 57 DR DQ  
가 Asp 57가 DQ 가  
가  
DQA1\*0301, 0501 DQB1\*0201 DR 가 DQ DQ  
가 가 DR 가  
HLA 가  
가 HLA- DR ICA  
HLA 가 GAD 가 33, 49) HLA- DQ  
가 가 GAD 가  
DQ IA- 2 가 .50)  
10  
DQ Asp57 DQA1\*0301- DQB1\*0302

ICA 가가 10 가 5), 가 가

가 5), .

DR4- DQ4 가 20

가 DR9- DQ9 가 ,

DR9- DQ9 가 C- peptide 가

2 가 . 20

GAD 가 가가

DR9- DQ9 가 가

T , 가 HLA- DR, - DQ

12).

가

DQA1- DQB1 GAD 가 : 128 105

DQA1 DQB1 233

GAD 가 GAD 가 IA- 2 가

DQA1\*0501- HLA- DR - DQ ,

DQB1\*0201 .

가 : 1)

가

DR4 DR9 ,

DR4- DQ4

DR9- DQ9 가

GAD 가 가

C- peptide 2) GAD 가

64.0% 60.3% 가

IA- 2 가

GAD 가 20.0% , 14.4% .

3) HLA- DR DR4

HLA DR9 HLA- DQA1 - DQB1

DQA1\*0601, DQB1\*0301, DQB1\*0601 .

가 HLA DR3, DR4, DR9 DQA1\*0301, HLA-

HLA DQA1\*0501, DQB1\*0201 HLA-

가 가 DQA1 - DQB1 DR

가

4) HLA- DR4

- DR9

: HLA- DQ DR9- DQ9

DR4-DQ4 GAD 가  
 :  
 GAD 가  
 , HLA-DR HLA- DQ  
 가  
 HLA  
 가  
 :  
 GAD 가 , HLA,

= Abstract =

**The Clinical and Immunogenetic Characteristics of Adult-Onset Insulin-Dependent Diabetes Mellitus in Korea**

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**Background** : Insulin-dependent diabetes mellitus (IDDM) is an autoimmune disease occurring among genetically susceptible individuals. Although the HLA class II genes and immunological abnormalities are clearly associated with IDDM in all racial groups, there are considerable variations in associated genotypes and prevalence of autoantibodies. Especially, it seems that adult-onset IDDM is somewhat different from childhood-onset IDDM in clinical and immunogenetic aspect. In order to determine the characteristics of the immunogenetic patterns and to use these results as an early diagnostic tool and a guideline of the therapeutic plan in Korean adult-onset IDDM, we investigated the clinical and immunogenetic characteristics in adult-onset IDDM patients.

**Methods** : We investigated the clinical and biochemical characteristics, and measured anti-GAD antibody by immunoradiometric assay or immunoprecipitation after in vitro translation of human GAD cDNA and IA-2 antibody

by immunoprecipitation after in vitro translation of human IA-2cDNA. The distribution of HLA-DR serotypes by lymphocyte microcytotoxicity method, HLA-DQA1 genotypes by restriction fragment length polymorphism and HLA-DQB1 genotypes by dot-blotting analysis using sequence specific oligonucleotide probe were analysed in 233 IDDM patients and controls.

**Results** :

1) Adult-onset patients had more preserved beta cell functions and slowly evolving form of clinical pattern rather than childhood-onset cases.

2) Each prevalences of anti-GAD and IA-2 antibody were 64% and 14.4% in adult-onset patients. Among them, the group with DR9-DQ9 had higher prevalence of antiGAD antibody rather than DR4-DQ4 group.

3) There were increased frequencies of HLA-DR4 and -DR9 in adult-onset patients. Considering the frequency of HLA-DQA1 and -DQB1 and the distribution of DQ heterodimers, they had no significantly increased genotypes or haplotypes. But childhood-onset cases had high frequencies in HLA DR3, -DR4, -DR9 serotypes and DQA1\*0301, DQA1\*0501, DQB1\*0201 genotypes.

**Conclusion** : Korean adult-onset IDDM patients have relatively higher prevalence of anti-GAD antibody implicating autoimmune pathogenesis. HLA genetic markers in adult-onset IDDM were somewhat different from those in childhood-onset cases. This pathogenetic heterogeneity according to age of onset may be due to the influences of other genetic markers and environmental factors involved in the etiology of Korean IDDM.

**Key Words** : Korean adult-onset IDDM, antiGAD antibody, HLA, pathogenetic heterogeneity

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