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Clinical and Genetic Characterizations of Maturity Onset Diabetes of The Young: Single Center Results

Ayla Güven[1,2], Canan Yıldırımoğlu[3]

[1]Göztepe Training and Research Hospital, Pediatric Endocrinology Clinic, Istanbul, [2]Health Science University, Medical Faculty, Women and Children Hospital, Pediatric Endocrinology Clinic,istanbul, [3]Numune Training and Research Hospital, Center of Genetic Diagnosis, Ankara, Turkey

Background: Maturity onset diabetes of the young (MODY) is a group of monogenic disorders classically presenting in adolescence or young adults before the age of 25 years. MODY is a rare cause of diabetes.

Methods: In this study, a panel of 23 MODY genes was screened. The Human Gene Mutation Database (HGMD), Clinvar, dbSNP and Exac database used for known or new variants causes MODY. Classification of variants performed according to ACMG 2015 Guidelines. We clinically evaluated 49 patients and 39 their relatives.

Results: Clinical, laboratory and genetic findings were given in Table.
BMI, BMI-SD, birth weight and fasting c-peptide were significantly different in MODY groups.
Mutations were detected in 27 out of 49 patients.
13 patients had **GCK** mutations. Four new variants were found in five patients: c.1265 G>C, p.Arg422 Pro in exon 10; c.128G>T, p.Arg431 Leu in exon 2; c.532 delG and c.C129Y. Two patients had de novo GCK mutations. Seven patients had **BLK** gene mutations. Two of them was siblings and they have new mutation in exon 9 (c.900C >A, p.Tyr300Ter).
Four patients had known **HNF4A** mutations in exon 8. Two patients were siblings.
Same **HNF1A** mutation was found in unrelated two patients, and **INS** gene mutation was identified in one.

MODY Subgroup	GCK	BLK	HNF1A	HNF4A	p
Patients number	13	7	2	4	
Age at the diagnosis, year	7.52±4	9.91±4.1	14.2±1.4	13.9±2.8	
Gestational Diabetes, n	7	3	-	4	0.026
Birth weight, gr	2816±633	3135±381	4500±707	4166±650	0.029
Height, cm	123±26	136±25	158±0.0	156±11	
BMI, kg/m^2	16.1±1.8	18.3±2.5	31.4±2.3	16.1±1.8	0.004
BMI-SDS	-0.37±1.0	0.52±1.1	2.0±0.3	-0.37±1.0	0.028
Prepubertal Pubertal	9 4	4 3	2 -	1 3	0.023
Fasting Glucose at diagnosis, mg/dL	175±137	142.8±65	134.5±12	138.2±88	
Fasting c-peptide, ng/mL	0.71±0.4	1.05±0.6	4.1±0	2.04(12)*	0.009
HbA1C, %	7.2±2.5	6.5±2.5	7.95±1.0	5.97±1	
G_0 at OGTT, mg/dL, (n:25)	118.3±44	91.6±13	136.5±43	113.5±54	
G_{120} at OGTT, mg/dL (n:25)	164.3±55	124.6±41	213±49	220±141	
Glucose increment in OGTT	110.2±29	67.8±39	146.5±50	113.5±77	
I_0 at OGTT, µIU/mL (n:25)	2.1(4.81)*	4.3(5.1)*	20.6±14	11.4±4	
I_{120} at OGTT, µIU/mL (n:25)	26.3±29	28.2±19	20.7±18	36.7±19	
Anti GAD Ab positive (n:24)	1	-	-	1	

Conclusion

Our study present four novel mutations in GCK, and one novel mutation in BLK gene. Although clinical findings were differing in each MODY group, laboratory results were similar.