Evaluation of Clinical, Laboratory and Therapeutic Features and Long Term Follow-up Results in 44 Cases with Genetic Diagnosis of MODY; Single Center Experience

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Introduction-Aim:
MODY;It is an autosomal dominant, rare type of diabetes that occurs in young people as a result of mutations of beta cell function and genes involved in insulin secretion(1,2). The cases may be misdiagnosed as Type 1 and Type 2 diabetes(3). Considering that MODY is clinically and genetically heterogeneous, the findings should be evaluated correctly. It is important to define the clinical-laboratory characteristics of diagnosis and follow-up of patients diagnosed genetically as MODY. The aim of this study was to investigate the clinical and laboratory features of patients with MODY and to investigate the relationship between genotype and phenotype.

Methods:
A total of 44 MODY cases were included in the study. Mutations in HNF4A,GCK,HNF1A, PDX1, HNF1B, NEUROD1, KLF11, CEL, PAX4, INS and BLK genes were studied by Sanger sequence analysis method. The cases who were treated a ccording to the MODY type and the follow-up data and were followed up for at least 3 years were included. Anthropometry, examination, blood glucose and HbA1C levels were evaluated at 3-month intervals.

Results:
The age of diagnosis of 44 patients with MODY (24 male) was 9.4±4.7(1-17) years. Except for three cases, the height and weight were normal. 55% of the patients were diagnosed as random hyperglycemia, 36% with symptomatic hyperglycemia and 9% with ketosis. All cases had a family history of diabetes. Blood glukoz levels (97-664mg/dl), HbA1C(5.2-15.6%), and C-peptide levels (0.2-5.9 ng/ml) were quite wide in the diagnosis. Only 2 of 44 cases had anti-GAD positivity and anti-insulin and islet-cell-antibodies were negative in allcases. The most common mutation was found in 55% GCK gene (5 new mutations) while the other distribution was; KLF11-MODY (n=7;16%), HNF1A-MODY (n=6;13%), NEUROD1-MODY (n=2), HNF4A-MODY (n=2), PDX1-MODY, CEL-MODY (new mutation) and HNF1B-MODY mutation were detected in one case. All cases of GCK, NEUROD1, PDX1 and CEL-MODY were treated only with diet, HNF1A-MODY sulfanylurea treatment, 1 of metformin in KLF11-MODY, 5 cases with intensive insulin,HNF4A and HNF1B-MODY.

Table 1. Clinical and Laboratory Characteristics of MODY Patients According to Genetic Mutations

MODY Type	Gender M/F	Age at diagnosis (year)	DM in 3rd generation	DM in 2ndgeneration	Type of presentation IH/SH/K**	Initial blood glucose level (mg/dl)	Initial Hba1c %	Initial c peptide ng/ml	DM Ab*	Treatment	Hba1c range in follow up	Duration of follow up (year)
GCK n=24	13/11	7.9±3.9 (1-16)	15	9	18/6/0	123±8.9 (111-138)	6.1±0.4 (5.1-6.8)	1,6±1.4 (0.3-5.9)	1 (Anti-GAD +)	Diyet	5.2-6.9	5,8
KLF11 n=7	4/3	11.7±1.6 (9-14)	6	1	1/3/3	345±221 (125-644)	10.9±3.8 (5.2-15.6)	2.4±2.08 (0,8-5,9)	1 (Anti-GAD +)	İnsülin-5 OAD-1 Diyet-1	5.2-9.8	4,9
HNF1A n=6	2/4	13.4±2.3 (11-17)	4	2	1/4/1	294± 146 (117-507)	11.3±3.3 (7.2-15.2)	0.96±0.75 (0.2-2.1)	0	Diyet-1 OAD-5	5.7-8.9	5,2
HNF4A n=2	2/0	12-15	1	1	1/1/0	257 – 273	10.9-12.9	0.5 - 4	0	İnsülin	5-10.3	3
NEUROD n=2	2/0	12-18	1	1	1/1/0	107- 106	5.5-6.3	0.9 -1.5	0	Diyet	5-6.4	4.7
PDX1 n=1	1/0	4	1	0	1/0/0	135	5.2	3.4	0	Diyet	5-6.4	5.1
HNF1B n=1	0/1	9	1	0	0/1/0	156	6.3	0.9	0	OAD-insülin	5.7-14.5	7.7
CEL n=1	0/1	6	0	1	1/0/0	137	4,8	0,7	0	Diyet	4.8-5.7	3.1

** DM antibodies; glutamic acid decarboxylase, islet cell and Insulin autoantibodies.*
***IH: Incidental hyperglycemia SH: Symptomatic hyperglycemia K:Ketosis*

Conclusion:
In this study, it was found that if the presenting form was hyperglycemia, there was diabetes in 2nd -3rd generations in the family, , anti-insulin and islet cell antibody negativity findings were strongly differentiated for MODY. Blood glucose, HbA1C and C-peptide levels were found to be in a wide range according to genetic heterogeneity. The most common GCK mutation was 55% of all cases. The cases with GCK, NEUROD1, PDX1 and CEL-MODY only with dietary treatment and HNF1A-MODY cases with sulfanilurea treatment, were found to be in good metabolic control during long-term follow-up. In other MODY types, required intensive insulin treatment according to their beta cell reserve.

References
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