Clinical Characteristics of Diabetes in People with Mitochondrial DNA 3243A>G Mutation in Korea

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Background/Aims: Maternally inherited diabetes and deafness (MIDD) is a rare mitochondrial genetic disorder most commonly caused by m.3243A>G mutation. The prevalence of MIDD varies by region and it is more frequently observed in East Asians compared to European. The clinical features of MIDD are also heterogeneous based on the affected organs. In this study, we aimed to describe the clinical features and investigate whether these are associated with level of m.3243A>G heteroplasmy.

Methods: This is a cross-sectional descriptive study including patients with confirmed m.3243A>G mutation and diabetes mellitus (DM) at Seoul National University Hospital. Through retrospective medical record analysis, we evaluated the clinical characteristics of the patients and analyzed the association between heteroplasmy level and various clinical features.

Results: A total of 40 patients were diagnosed with MIDD. Among them, 20 (50%) were male. Mean age at test was 33.3 ± 12.9yrs and mean heteroplasmy level in peripheral blood was 30.0 ± 14.6%. The most common comorbidity was hearing loss (90%), followed by albuminuria (61%), seizure (38%), stroke (33%), heart failure (15%), arrhythmia (13%). Maternal family history of diabetes was observed in 63% of the participants. All 40 patients were diagnosed with DM, of which 25 (63%) were treated with insulin. There were only 3 patients (8%) who did not receive any treatment for DM. Level of heteroplasmy showed no correlation with any other factors except age at DM diagnosis. A 10% increase in heteroplasmy was associated with 4.6 year earlier onset of diabetes (confidence interval 2.9 - 6.2, P-value <0.001).

Conclusions: MIDD was associated with early onset of diabetes, hearing loss, albuminuria, seizure and stroke and these characteristics warrants genetic testing for m.3243A>G mutation. However, only 57% of the participants had both typical feature of hearing loss and maternal family history of diabetes. Heteroplasmy level showed significant negative association with age at DM diagnosis.

Figure 1. Correlation between heteroplasmy and age at DM diagnosis

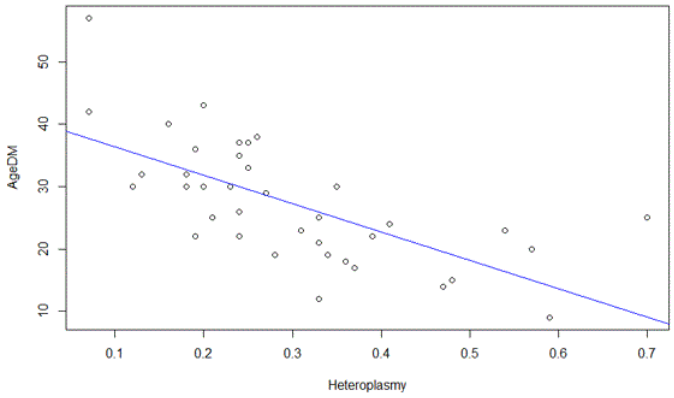

Table 1. Baseline characteristics

	Total (n=40)
Male/Female	20 / 20
Age at test	33.3 (± 12.9)
Age at DM Diagnosis	27.5 (± 9.7)
Family history of DM	63% (22/35)
Heteroplasmy (%)	30.0 (± 14.6)
Bwt. (kg)	
Male	50.1 (± 8.2)
Female	43.9 (± 6.6)
Ht. (cm)	
Male	164.4 (± 8.5)
Female	153.2 (± 5.0)
BMI (kg/m^2)	
Male	18.5 (± 2.5)
Female	18.7 (± 2.6)
HbA1c (%)	7.5 (6.5, 8.5)
C-peptide (ng/mL)	1.3 (0.8, 1.9)
Lactate (mmol/L)	4.2 (2.5, 6.2)

Table 2. Comorbidities

	Total (n=40)
Diabetes mellitus	100% (40/40)
Hearing loss	
Normal	10% (4/40)
Mild	15% (6/40)
Moderate	23% (9/40)
Moderately severe	13% (5/40)
Severe	7% (3/40)
Profound	7% (3/40)
Clinical	25% (10/40)
Stroke like episode	33% (13/40)
Seizure	38% (15/40)
Arrhythmia	13% (5/39)
Heart failure	15% (5/34)
Albuminuria	
Normal (<30mg/g)	39% (12/31)
Moderate (30-300mg/g)	45% (14/31)
Severe (>300mg/g)	16% (5/31)

Table 3. Diabetes mellitus treatment

	Total (n=40)
Insulin treatment	63% (25/40)
Number of insulin injection	2.32
Total daily dose of insulin	36 (19.5, 44.0)
Oral hypoglycemic agent	60% (24/40)
Metformin	63% (15/24)
Sulfonylurea	38% (9/24)
Thiazolidinedione	25% (6/24)
DPP-4 inhibitor	33% (8/24)
SGLT2 inhibitor	8% (2/24)
Insulin & OHA	33% (13/40)
No treatment	8% (3/40)