Commentary: Heteroplasmy in maternally inherited diabetes and deafness

Maternally inherited diabetes and deafness (MIDD) is a mitochondrially inherited disease. Mitochondrial DNA is inherited from the mother and its defects affect organs that demand higher energy such as the eye, inner ear, central nervous system, skeletal, and cardiac muscle. MIDD is associated with early onset diabetes and sensorineural deafness. The various other systemic features reported include cardiomyopathy, renal problems, and neuropsychiatric symptoms. Pigmentary retinal dystrophy is the most common ophthalmic manifestation.[1]

The prevalence of MIDD ranges from 0.5% to 2.8%.[2] MIDD has been reported to be associated with mutations, such as MT-TL1 and MT-TK of which MT-TL1 is the most common.[3] Tripathy K *et al*. have noted A3243G mutation in MT-TL1 gene using Sanger sequencing in one of their subject.[4] The A3243G mitochondrial mutation is seen with a wide range of mitochondrial encephalomyopathies including MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke) or MELAS/MERRF (myoclonic epilepsy, red ragged fibers) overlap syndrome.[5] However, the same mutation can cause different phenotypes. The phenotypic variability is determined by the degree of heteroplasmy.[6] The authors too noted a difference in the phenotypes within the family members and related it to heteroplasmy.

Heteroplasmy is the presence of more than one type of organellar genome (mitochondrial DNA or plastid DNA) within a cell or individual. It is an important factor in considering the severity of mitochondrial diseases. The most frequent findings in A3243G mutation-positive participants was hearing loss and macular disturbance, with 95% of mutation-positive relatives having hearing loss.[5] Macular disturbance is in the form of a pattern dystrophy - an important clinical sign in the diagnosis of MIDD. There are three grades for this manifestation: Grade 1: Severe punctate pigment dots in the macula; Grade 2: A butterfly or reticular pattern; and Grade 3: Multifocal or a continuous perifoveal atrophy of the RPE.[5-8] The variability of the manifestations could be attributed to the heteroplasmy in MIDD.

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Conflicts of interest

There are no conflicts of interest.

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