The Spectrum of Renal Abnormalities in Mitochondrial Disorders Is Broad

To the Editor: We read with interest the article by Imasawa *et al*.[1] about a retrospective study of patients with a genetically confirmed mitochondrial disorder (MID) who also had proteinuria, reduced glomerular filtration rate, or Fanconi syndrome. The most common renal abnormality was proteinuria and the most common pathologic finding was focal segmental glomerular sclerosis.[1] Among 63 m.3243A>G carriers, diabetic nephropathy, nephrocalcinosis, and tubulo-interstitial nephropathy were the most frequent renal abnormalities.[1] The study is appealing but raises concerns that need to be discussed.

A limitation of the study is that heteroplasmy rates of patients carrying mitochondrial DNA variants were not included.[1] Because phenotype, disease course, genetic counseling, and outcome strongly depend on heteroplasmy rates in affected tissues, it is crucial to know this parameter. Mitochondrial DNA copy number is another parameter determining the phenotypic expression of a mitochondrial DNA variant; this is why it is essential to relate phenotype, disease course, and outcome with this feature as well.

Several renal manifestations of MIDs were not included in the discussion. These include, for example, nephrolithiasis, renal cysts, and neoplasms.[2] In various MIDs, nephrolithiasis has been reported as a phenotypic feature of the disease including patients carrying the variant m.3243A>G.[3] Cyst formation and neoplasms are generally more prevalent in MIDs than non-MID cohorts.[4]

For didactic reasons, it is recommended to delineate primary from secondary renal involvement in MIDs. Primary mitochondrial dysfunction originates from the kidney itself, whereas secondary dysfunction results from manifestations of the MIDs in organs other than the kidneys. For example, in the case of cardiac involvement, intracardiac thrombus formation may ensue leading to cardioembolism including the kidneys. Because MIDs frequently manifest with diabetes,[5] diabetic nephropathy may ensue. MIDs are most often complicated by lactic acidosis, which may secondarily damage renal tissue.

Not addressed was renal dysfunction due to the toxicity of drugs given to treat manifestations of the MID, particularly epilepsy, heart failure, arterial hypertension, psychosis, cognitive dysfunction, and depression.

Overall, the interesting study has limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could enhance the study.

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Ethics Approval

Ethics approval was in accordance with ethical guidelines. The study was approved by the institutional review board.

Consent to Participate

Consent to participate was obtained from the patient.

Consent for Publication

Consent for publication: was obtained from the patient.

Availability of Data

All data are available from the corresponding author.

AUTHOR CONTRIBUTIONS

JF: design, literature search, discussion, first draft, critical comments, and final approval.

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