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Letter to the Editor

Symptoms and Quality of Life of MELAS Patients Depend on Numerous Factors that must be Considered to Understand their Perspective

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We read with interest the article by Medrano *et al.* on the experience of mitochondrial encephalopathy, lactic acidosis and stroke-like episode (MELAS) patients with their disease as assessed by qualitative interviews of 16 patients and 5 treating physicians to identify, describe and substantiate relevant Symptoms, Signs, and health-related quality of life (HRQoL) Impact (S/S/I) concepts ^[1]. Physicians reported 44 S/S and 36 HRQoL impact concepts and patients reported 35 S/S concepts and 68 HRQoL impacts across 15 domains ^[1]. The most commonly reported S/S concepts were fatigue, hearing loss, mental fatigue, and exercise intolerance and the most commonly reported HRQoL impact domains were adaptive behaviour, work impacts, and emotional function ^[1]. The study is remarkable, but some points should be discussed.

The first point is that it is unclear whether truly all included patients met the criteria for diagnosing MELAS. MELAS is usually diagnosed according to the Hirano or Japanese criteria ^[2,3].

The second point is that the symptoms of MELAS can vary greatly depending on the stage of the disease, the heteroplasmy rate, the mtDNA copy number, the haplotype, the tissue distribution, and the influence of nuclear factors ^[4]. Therefore, it would be helpful to consider these determinants of the MELAS phenotype when interpreting the data collected by physicians and patients.

The third point is that MELAS patients may regularly take medications for symptomatic treatment ^[4]. Since medications can greatly affect well-being, quality of life, and symptoms of the underlying disease, it is crucial to include each patient's current medications in the analysis. It is particularly important to know how many patients were taking antiepileptic drugs, antidepressants, anxiolytics, neuroleptics, hypnotics, or sedatives. It is also important to report whether any of the medications caused side effects in any of the patients.

The fourth point is that fatigue, exhaustion, and stress intolerance can also be symptoms of depression. Therefore, depressed patients should be identified using one of the depression scores and excluded from the analysis.

The fifth point is that a patient cannot report "signs" ^[1]. "Signs" are recognized and assessed by the examining physician. They therefore represent an objective measure of whether or not a clinical neurological deficit is present. The individual patient can only report symptoms. If the patient reports "signs," these must come from the information that the physician has communicated to the patient about the results of their clinical neurological examination.

In summary, the index study has limitations that qualify the results and their interpretation. Taking these limitations into account could strengthen the conclusions and reinforce the message of the study. The symptoms, signs, and quality of life of MELAS patients depend on numerous influencing factors that must be taken into account in order to understand their perspective.

Declarations**Ethical Approval:** Not applicable.**Consent to Participation:** Not applicable.**Consent for Publication:** Not applicable.**Funding:** None received.**Availability of Data and Material:** All data are available from the corresponding author.**Completing Interests:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.**Author Contribution:** xx was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval.**Acknowledgements:** None.**Keywords:** MELAS, MT-TL1, Symptoms, Signs, Quality of Life**References**

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