Healthcare Studies, 3(2):24–25, 2025. DOI: 10.58612/hs323

Healthcare Studies

Journal homepage: https://www.fpub.org/journal-details.php?journal-id=42

ISSN (E): 2583-9802

Letter to the Editor

The frequency of pathogenic mtDNA variants in African L-haplogroups depends on the degree of clarification and definition of the healthy population

Josef Finsterer [1*]

[1] *Neurology Dpt., Neurology and Neurophysiology Center, Vienna, Austria.*
[*] *Corresponding author: fifigs1@yahoo.de*

Article Info

Keywords: *mtDNA, mitochondrial disorders, heteroplasmy, haplogroup, african population*

Received: *26.07.2025*
Accepted: *19.08.2025*
Published: *28.08.2025*

We read with interest the article by Meldau et al. on the frequency of pathogenic mtDNA variants in African L-haplogroups in patients with mitochondrial disorders (MIDs) from an African and a US center [1]. Haplogroup context was determined in 82 African and 165 US cases, 62 of which carried the L-haplogroup [1]. Unique L sub-haplogroups were identified in 11 families with the MELAS variant m.3243A>G, in 6 families with the LHON variant m.11778G>A, and in 20 cases with single large-scale mtDNA deletions [1]. The phenotypes of the included patients were similar to those described in other haplogroup cohorts [1]. The study is noteworthy, but several points should be discussed.

The first point is that the frequency of pathogenic variants in a cohort must be correlated with a defined collective of non-mutation carriers from the same defined population from which the diseased cohort originated in order to obtain reliable results. In addition, the entire cohort must be systematically and prospectively studied to truly determine a reliable frequency count of a particular mtDNA variant. A limited sample has the disadvantage that the resulting frequency figure may be unreliable.

The second point is that sub-Saharan African populations may not only be carriers of haplotype L, especially haplogroup L2, but that in the Y-DNA carriers (DNA found only in males and passed from father to son), haplogroup E, especially subclade E1b1a, is also dominant and associated with Bantu expansion [2]. We should know what haplotypes other than L were found in the two cohorts studied.

The third point is that heteroplasmy rates for individual mtDNA deletions were not reported [1]. Were they not determined? In addition, the heteroplasmy rates of the m.3460G>A and m.13513G>A variants in blood were low (14 and 45%, respectively), suggesting that their pathogenicity is questionable [1]. Were the heteroplasmy rates in these patients also determined in clinically affected tissues and were they higher there?

How To Cite: J. Finsterer. The frequency of pathogenic mtDNA variants in African L-haplogroups depends on the degree of clarification and definition of the healthy population. *Healthcare Studies*, 3(2):24–25, 2025. https://doi.org/10.58612/hs323

The fourth point is that the haplotype was not determined by mtDNA sequencing in each of the included patients according to the method section [1]. In "several cases", mtDNA sequence variants were determined by a query in MITOMASTER SNV [1]. As haplogroup determination by this approach may be less reliable than by mtDNA sequencing, it is recommended that haplogroup determination be repeated using more reliable methods.

The fifth point is that the reason for the limited data on MIDs in the African population, as mentioned in the introduction, has not been discussed in detail [1]. Is it conceivable that the lower number of MID patients in the African population is simply due to limited access to the healthcare system in various African countries [3], thus preventing individuals with symptoms suggestive of MID from undergoing specific diagnostic procedures and receiving appropriate treatment once diagnosed? It is known from African countries that only about half of the population has access to healthcare and usually has to pay for the service [3]. Who paid for the genetic testing in the African and US cohorts of the index study?

Overall, calculating the frequency of pathogenic mtDNA variants in African L-haplogroups requires extensive, comprehensive and complete clinical and genetic testing of a defined population.

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.
Competing 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: JF was responsible for the design and conception, discussed available data with coauthors, wrote the first draft, and gave final approval. xx: contributed to literature search, discussion, correction, and final approval.
Acknowledgments: None

References

[1] S. Meldau, E. M. McCormick, I. George-Sankoh, G. T. Riordan, K. Khan, L. E. MacMullen, S. Dawlat, D. Blackhurst, M. J. Falk, and J. L. Elson. Mitochondrial dna pathogenic variant prevalence in primary mitochondrial disease patients with african (l) mitochondrial genome haplogroups. *JIMD Rep.*, 66(4):e70036, July 2025. doi:10.1002/jmd2.70036.

[2] Wikipedia contributors. Y-dna haplogroups in populations of sub-saharan africa. In The Wikipedia, editor, *Free Encyclopedia*. 14, July 15, 2025, from, Retrieved 07, 2025. URL https://en.wikipedia.org/w/index.php?title=Y-DNA_haplogroups_in_populations_of_Sub-Saharan_Africa&oldid=1283398363.

[3] C. Cullinan. Universal health coverage: Only half of africans have access to health care. health policy watch independent global health reporting. *2021; Universal Health Coverage: Only Half Of Africans Have Access To Health Care - Health Policy Watch [last accessed*, 15th], July 2025.