MITOCHONDRIAL DISEASES IN PEDIATRIC NEUROLOGY PRACTICE: A SINGLE CENTER EXPERIENCE

İlknur Erol[1] , **Elif Perihan Öncel[1]** , Şeyda Besen[1] , Sevcan Tug Bozdoğan[2], Serdar Ceylaner[3]

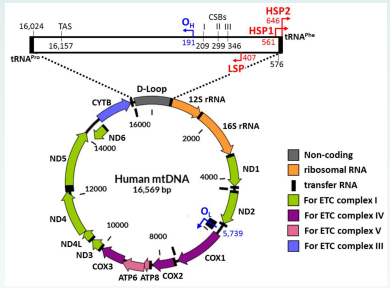
[1]Baskent University Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center, Department of Pediatric Neurology

[2]Cukurova University AGENTEM (Adana Genetic Diseases Diagnosis and Treatment Center) and Medical Genetics Department of Medical Faculty

[3]Intergen Genetics and Rare Diseases Diagnosis Research & Application Center, Clinical Genetics

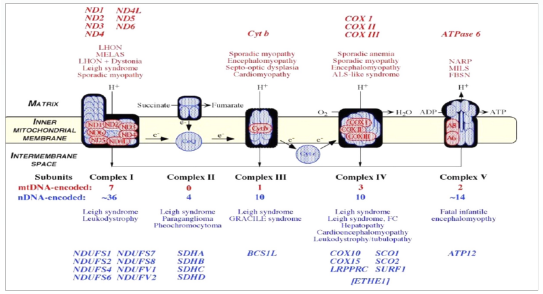
INTRODUCTION

Disorders of mitochondrial energy metabolism can show all inheritance patterns and new genes and associated mitochondrial disorders continue to be identified. In the absence of definitive pathognomic clinical features, elevated mitochondrial biomarkers or neuroimaging findings can be diagnostic clues. However, a diagnosis of mitochondrial disease often cannot be confirmed until potential pathogenic variants associated with mitochondrial disease are defined by an exome or genome analysis. Approximately 85-90% of primary mitochondrial diseases in childhood are associated with nuclear gene mutations.



OBJECTIVES

We aimed to reveal the genetic, clinical, and geographical differences in mitochondrial diseases seen in children in the Eastern Mediterranean region of Turkey.

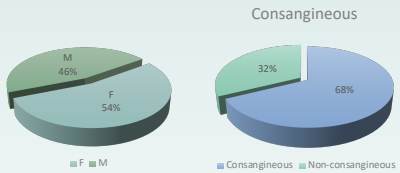


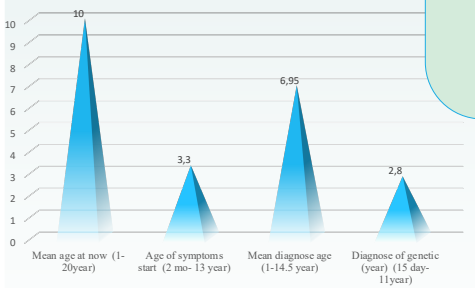
METHODS

We retrospectively analyzed the symptoms, laboratory investigations, imaging, and mutations of 34 patients with a consecutively confirmed genetic diagnosis of mitochondrial disease between 2011 and 2022.

RESULTS

The most common complaint was gait disturbance presenting 19 males (55.8%) aged between 5 months and 17 years. Other common symptoms were flaccidity, decline in motor skills, and visual impairment, respectively. The patients' plasma lactate and CK levels were elevated at 40% (n:14) and 31.4% (n:11), respectively. Mitochondrial disease-compatible appearance on brain MR imaging was observed in 19 patients. Mitochondrial disease associated with nuclear DNA mutation was detected in 76.4% (n:26) of the patients. The most common mutations were MFN2, OPA1, RMND1, SUCLA2 and SLCA193, respectively.





Systemic findings

✓1 & proteinuria
✓3 & Transaminase elevation
✓2 & Hepatic findings
✓3 & mild cardiac problems

✓6 patient multisystemic findings (%17.6)

✓13 patient (%38) Lactat/pyruvate ratio > 20:1

24 & Pathological MRI
6 & Normal
4 & No MRI
(Clinical findings related to HSMN)
12 & MRS'de lactate peak
1 & Succinate peak
11 & Normal

Polyneuropathy & 8 patient
Myopathy & 2 patient
PNP+MYP & 1 patient
Normal & 7 patient

WES	Mitochondrial genome analyses	Monogenic analyses	CES	Panels
21 (%61.7)	8 (%23.5)	3 (%8.8)	1 (%3)	1 (%3)

26 (%76.4) patient nuclear DNA
8 (%23.6) patient mtDNA

MFN2 (n:5;%14.7) 4 heterozygous 1 homozygous	SLC19A3 (n:3; %8.8) homozygous	RMND1 (n:2; %5.8) homozygous	ETFDH (n:2; %5.8) homozygous	SUCLA2 (n:2; %5.8) homozygous
OPA1 (n:2; %5.8) homozygous	INF2 heterozygous/ de Novo	MICU1 homozygous	CHKB homozygous	NDUFV1 homozygous
SLC25A19 homozygous	SORD homozygous	MPV17 homozygous	PDHA1 1 Heterozygous 1 X kalıtım	SDHA (compound heterozygous)
SDHB homozygous	mt.3316G>A Mt-ND1	mt.6109T>C Mt-COX1	mt.c133T>C Mt-ND3	mt.3229-3230 INSA (%100) Mt-RNR2-TRNL1
mt.8344A>G related tRNA gene	mt.7569A>G Mt-TRND	mt.3020C>T Mt-RNR2	mt.13066T>A Mt-ND5	

19 & OR
6 & OD
1 & XLD
8 & mt patern

7 patient & Newly defined variant

SLC19A3
RMND1
SORD
MT-TRND
SDHA
MT-COX1
MT-ND5

CONCLUSION

We emphasized that planning genetic studies based on the most common inheritance pattern is important rather than relying solely on mitochondrial genome analysis. It is important to keep in mind that these diseases are more common in childhood and that nuclear DNA transmission and OR inheritance are more frequent.

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ACKNOWLEDGEMENTS

Elif Perihan ONCEL, MD, peri_elif@Hotmail.com
Prof. Dr. İlknur EROL , ilknur_erol@yahoo.com