

Pediatric Mitochondrial Disease: Clinical and Radiological profile, Experience from A Tertiary Care Hospital in Bangladesh

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Introduction

Mitochondrial diseases are rare group of heterogeneous, genetically determined disorders. These are caused due to defect in the electron transport chain within the mitochondria. Phenotypes vary from solely myopathy to multi organ involvement with variable age of onset, severity, and progression.

Common presentations are acute or chronic neuro regression, hypotonia, failure to thrive, seizures, cardiomyopathy, deafness, blindness, movement disorder, and lactic acidosis.

Most of them occur following febrile or infectious illness.

Objective

This study was aimed to describe the clinical, neuroimaging and genetic analysis of mitochondrial diseases.

Methodology

Study Design: Cross Sectional study Number of Patients: 16 admitted patients

Place: Department of Pediatric Neurology and Institute of Pediatric Neurodisorder and Autism (IPNA), Bangabandhu Sheikh Mujib Medical Universi-

Study duration: January 2016 to December 2023

Detailed history regarding the demographic profile, antecedent illness, age of onset, age at presentation, presenting clinical features were taken. Clinical examination including neurological examination was done in every patient. Basic metabolic screening, CSF study, EEG, MRI of brain with contrast and MRS were done in patients according to the indication. In every patient next generation sequencing including mitochondrial whole genome sequencing was advised.

Expert opinion from neuro-radiology and ophthalmology was taken.

Results

Table 1. Demographic cha	aracteristics of the studied subjects (n-16)	Table 2. Developmental status of the patients ,n=16							
Age at onset	1month-6.5 years	Developmental Impairment							
Age at diagnosis	3 months -8 years	Developmental	13 (81%) 11 (69%)						
Sex		delay							
Male	11 (69%)	Hypotonia							
Female	5(31%)								
Consanguinity		Developmental	9(56%)						
Present	6 (38%)	regression Microcephaly	2(12.5%)						
Absent	10(62%)	Hypertonia	2(12.5%)						

Ataxia 6 (38%) Tremor 3(19%) Choreiform movement 3(19%) Paroxysms of dyskinesia 1(6%) Table 5. Other features Table 6. Biochemical status of the studied patients. (n-16 Nystagmus 6(38%) NVESTIGATIONS PROFILE S. Lactate (increased) 9(56%) Increased CPK 4(25%) CSF lactate(increased) 3(19%) Hypertrichosis 1(6%) Hypoglycemia 2(12.5%) Urine ketone body(positive) TMS Carnitine deficiency-2 (12.5%) Table 7. Neuroimaging profile MRI OF BRAIN Basal gangia byperintensity 8(50%) Table 8. Genetic profile of the patients, n=16 MRI OF BRAIN Basal gangia byperintensity 8(50%) Coexic altopation within ming (38%) Midrotantin perintensity 5(11%) Cortical strophy 3(19%) Cortical strophy 3(19%) Cortical strophy 1(6%) Cortical strophy 1(6%) Cortical strophy 1(5%) Cortical strophy	Table J. W	oveille	nt disorder	Tabl	C 4. J	eizure	.5						
Tremor	Dystonia		8(50%)	Seizur	e 6 (38%	(0)							
Choreiform movement Solution Choreiform movement Solution Chore Choreiform movement	Ataxia		6 (38%)										
Paroxysms of dyskinesia 1(6%) GTCS 3(19%)	Choreiform movement		3(19%)	Myocl	Myoclonic			3(19%)					
Table 5. Other features Table 6. Biochemical status of the studied patients. (n-16 Nystagmus 6(38%) INVESTIGATIONS PROFILE S. Lactate (increased) 9(56%) Incraesed CPK 4(25%) CSF lactate(increased) 3(19%) Hypertrichosis 1(6%) Hypoglycemia 2(12.5%) Urine ketone body(positive) 1(6%) TMS Carmitine deficiency=2 (12.5%) Table 7. Neuroimaging profile Table 8. Genetic profile of the patients, n=16 MRI OF BRAIN Basal gauglia hyperintensity 8(50%) Dentate nuclei hyperintensity 5(31%) Cortical atrophy 5(31%) Cortical atrophy 3(19%) Cortical atrophy 3(19%) Cortical atrophy 2(12.5%) Cortical proprintensity 1(6%) Nermal 6(38%) Table 6. Biochemical status of the studied patients. (n-16 S. Lactate (increased) 9(56%) Increased CPK 4(25%) Carmitine deficiency=2 (12.5%) Carmitine			3(19%)										
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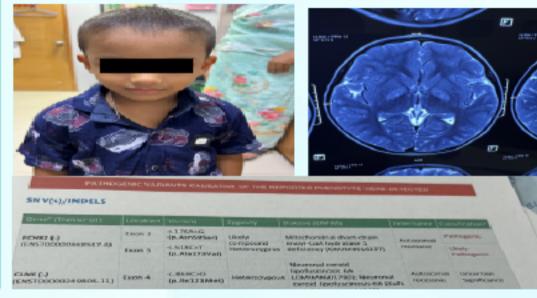
ears		C.1111C>A(p.Leu 371Met)	MT-CYB(+)	Homoplas mic	Mitochondrial	atrophy, Leigh syndrome, Mitochondrial Encephalopathy, lactic acidosis, stroke like episodes (MELAS) syndrome Leber hereditary optic atrophy, Leigh syndrome, Mitochondrial Encephalopathy, lactic acidosis, stroke like episodes (MELAS) syndrome	US	Case 6, Junayed ,3 years Case 7 Oishi, 3 Years Case 8 Ankita ,2 years 7 months Case 9 Arpon , 6	Years	Exone 5 Genetic study not gen	c.518C>T(p.Al a173Val) ot done	ECHS1(-)	Likely compou nd heteroz ygous	ARD	mitochondrial short chain enoyl co-A hydratase deficiency	LP
5 months			OPA 1 TARS 2+ve.	Heterozyg ous	ARD	Mitochondrial DNA depletion Syndrome	P	years								
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Mitochondrial complex US
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Mitochondrial DNA depletion syndrome

- Management of involuntary movement of involuntary movement of involuntary movement of the MRI showed Globus pallidus hyperintensity of ECHs1(-) mutation of mitochondrial short chain enoyl co-A hydratase deficiency

- MRI showed Globus pallidus hyperintensity of involuntary movement of the mitochondrial short chain enoyl co-A hydratase deficiency



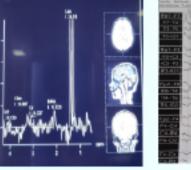
- 15 months old male child
 abnormal posturing for last 1year
 Jerky movement for 2 months
 developmental delay
- developmental delay
 opisthotonic posturing ,hypotonia exagin all 4 limbs with plantar extensor





Mitochondrial complex

IV deficiency, nuclear





INTERNATIONAL CHILD NEUROLOGY CONGRESS

Conclusion

c.694A>C(p.Thr2|NDUFv2(+) |Heterozyg |ARI

c.792 793del(p. |SURF1(-) |Homozygo|ARD

Mitochondrial Disease are a genetically and phenotypically diverse group of inherited energy deficiency disorders.

Neuroregression, Movement and tone abnormality and multisystem involvement are the key features.

MRI, MRS and some metabolic tests give clue for diagnosis.

Next-generation sequencing technologies have dramatically increased mitochondrial disease gene discovery.