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# Gait Parameters as Early Indicators: Exploring the Diagnostic Potential of Gait Analysis in Rare Diseases – A Preliminary Investigation on Mitochondrial Disorders

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ABSTRACT

**Background:** Instrumented gait analysis is now increasingly used in clinical decision-making scenarios, as a marker of disease progression, as an early indicator of motor dysfunction, as a differentiating feature for diseases with same phenotype presentation and as an outcome measure for effect of interventions. This is particularly relevant for motor dysfunction in rare inherited neurological disorders which often result in gait impairment.

**Purpose:** Several rare diseases have variable presenting features primarily manifesting as reduced quality of life and impaired function. We aim to investigate the role of gait analysis in the diagnosis of these disorders as it is often difficult and complex.

**Methods:** This is a retrospective observational analysis of quantitative gait parameters of a 15-year-old male presenting with features of mitochondrial dysfunction, and our analysis of gait-related parameters before exercise, post exercise and in recovery phase.

**Results:** The results depicted a few significant changes in gait analysis pattern post exercise which improved in recovery phase hinting at the potential use of gait analysis in such disorders particularly metabolic disorders. This study aims to bridge this gap by presenting three-dimensional gait parameters of a case with mitochondrial disorders and to explore its utility.

**Conclusions:** 3D gait analysis may prove to be an adjunct in the diagnosis, classification and prognosis of rare neuromuscular diseases. It holds potential for diagnosing subtle changes in gait and quantifying the effect of treatment and rehabilitation on gait and hence functional abilities of the patients.

## 1. Introduction

Several rare diseases have variable presenting features primarily manifesting as reduced quality of life and impaired function. Diagnosis is often delayed due to overlooking of the subtle changes in gait, early exhaustion, self-adaptation to functional deficits etc. For eg. among individuals with rare inherited neurological disorders most present with variable motor dysfunction, such as gait impairment, falls, weakness, tremors, dystonia, spasticity and rigidity, limited ambulation etc. The diagnosis of these is often difficult, given the overlapping symptoms with other neuromuscular disorders and variability in presentation. Symptoms associated with mitochondrial disorders range from progressive muscle weakness, respiratory complications, and exercise intolerance (Chinnery *et al.*, 2001). Typically, proximal weakness predominates resulting in waddling of gait (Koene *et al.*, 2018). While there are assumptions about gait patterns in these individuals, there is a lack of quantitative gait analysis parameters for objective data interpretation and classification. Previous studies throw light on spatiotemporal characteristics, revealing aspects such as slower walking speed and increased step widths in affected individuals.(Koene *et al.*, 2018; Delval *et al.*, 2011., Ramakers *et al.,* 2017) However, a comprehensive understanding of three-dimensional gait analysis in the context of rare genetic metabolic disorders remains elusive. Gait analysis studies in rare neurological disorders such as mitochondrial dysfunction are being used to quantify the severity of disease, as a prognostic marker and even as a differential investigation to diagnose a disease (Koene *et al.*, 2018; Chinnery *et al.*, 2001; Delval *et al.*, 2011; Indelicato *et al.*, 2022; Mindler *et al.*, 2020; Stephenson *et al.*, 2015; Maulet *et al.*, 2023; Pradhan *et al.*, 2015; MacWilliams *et al.*, 2022).

Previous studies have reported using gait analysis protocol including exercise in mitochondrial disorders (Koene *et al.*, 2018; Ramakers *et al.*, 2017). This study aims


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to bridge this gap by presenting three-dimensional gait parameters of cases with rare mitochondrial disorders. By quantifying and studying gait patterns in these individuals, this study aims to shed a light on common gait characteristics associated with these complex and heterogeneous disorders. This analysis is anticipated to give insights into the functional impact of rare genetic metabolic disorders on gait, paving the way for more individualised and targeted approaches in the rehabilitative management of these disorders. Human gait is a complex phenomenon which involves precise coordination of the neuromusculoskeletal system. A typical gait cycle consists of stance phase and swing phase where stance comprises approximately 60% of the cycle and the swing comprise remaining 40% (Figure 1). The unit of the gait cycle is Stride which is the distance between two successive placements of the heel/initial contact region of same foot (Pinzone *et al.*, 2016; Pau *et al.*, 2023).

| **Stance phase** | | | **Swing phase** | | |
|---|---|---|---|---|---|
| Initial contact | Loading response, Midstance, terminal stance | Preswing | Initial swing | Mid swing | Terminal swing |

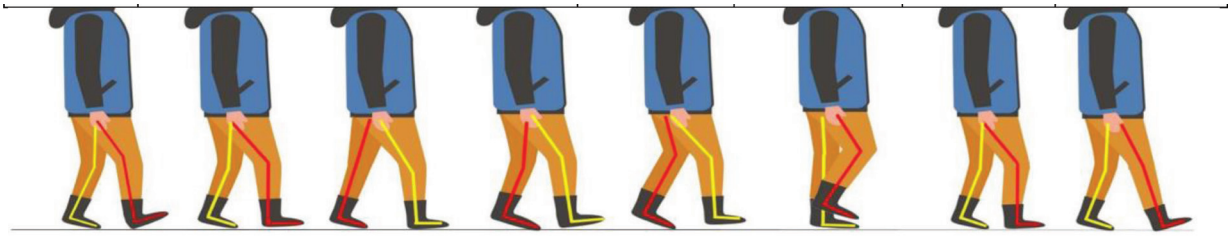

**Figure 1:** Gait cycle

## 2. Methodology

### *2.1. Study Design*

This is a retrospective observational analysis. In this study, quantitative gait analysis parameters (spatiotemporal, kinematic and kinetic parameters) are analysed for a single patient with suspected mitochondrial cytopathy. We assessed differences between pre exertion, post exertion and recovery gait of this patient and used these parameters to describe the gait of this patient.

### *2.2. Participant Selection*

We collected quantitative gait analysis data retrospectively and reviewed records of patients who underwent gait analysis between January 2020 and December 2023. The datasets were then analysed for their primary physician's diagnosis and findings noted in the records of the patient recorded by the examination during gait analysis. We excluded other datasets because of lack of sufficient interpretation from the studies to be included in this study. We only included data from this session of a single patient which was collected on a single day, and which was peculiar in its findings. It describes gait analysis features of a single patient presenting to department of Physical & Rehabilitation Medicine in a tertiary healthcare centre (PGIMER Chandigarh) in India. The diagnosis of this patient was done by the primary physician (neurologist) as per his clinical history and investigations.

### *2.3. Participant Characteristics*

This patient is a 15-year-old male presented to our OPD with the primary complaint of weakness of bilateral lower limbs which was progressive in nature and difficulty in daily activities. The patient had history of repeated seizures and motor and cognitive symptoms since 6 years. The patient reported progressive motor symptoms (difficulty in walking, difficulty in getting up from floor, difficulty climbing stairs). He reported worsening of motor symptoms after exertion. On examination he had significantly weak ankle plantar flexors, dorsiflexors, glutei (3/5) in both lower limbs. Tone was increased in both lower limbs and his feet were in cavovarus position during standing. The examination also revealed restricted dorsiflexion in both his feet.

### *2.4. Gait Data Recording and Acquisition*

The patient underwent a session of instrumented gait analysis under supervision of a medical doctor in the gait lab in the department of PMR in PGIMER Chandigarh. A complete 3D gait analysis was performed on BTS gait laboratory established in the department. System consisted of 6 infrared cameras (Smart-D, BTS Bioengineering, Italy), 16 force platforms and 2 video cameras. Complete anthropometric data was recorded for

the patient as per Halen Hayes Protocol, using measuring tape, pelvimeter, ruler, stadiometer and weight measuring machine. Halen Hayes Model is one of the widely used anatomical/biomechanical model for marker placement for motion analysis. It basically serves as a biomechanical model for algorithm for computing joint and anatomical segment motion. The anatomical segment position and orientation is defined by this marker placement model, to be read by the optoelectronic system. A total of eighteen reflective markers were placed at specified landmarks as per this model for gait analysis. Sites for anatomical marker placement on skin of the patient as per this prorocol are:

- Marker placement on Bony landmarks – trunk and pelvis segment (tip of spinous process of C7 vertebra, acromion processes, antero superior iliac spine (ASIS), Sacrum) lower limb segment (lateral femoral epicondyle, lateral malleolus of ankle, behind the calcaneum on both sides and between 2nd and 3rd metatarsal head).
- Strap marker placement- Mid thigh and mid calf (minimal movement of the marker with respect to limb movement).

This marker placement allows to record three dimensional motions of trunk, pelvis and lower limb joints by the infra-red sensing cameras and then further computation of quantitative gait analysis parameters.

The patient was first examined clinically, and then followed the following protocol for gait analysis:

The patient was made to walk on the force platforms as per our protocol and the baseline gait was recorded. Afterwards, patient was made to walk continuously for five minutes at a speed faster than self-selected speed and then another recording was performed. Finally, patient was asked to rest for five minutes and final recording was done to assess recovery gait. (Table 1).

**Table 1:** Gait Analysis Data Acquisition and processing process followed for the patient

| **Pre gait analysis procedure** |
|---|
| • Informed consent for the examination and testing<br>• Explanation and instructions to the patient for examination<br>• Anthropometric Examination relevant for Halen Hayes Protocol<br>• Body marker placement relevant for data acquisition according to the protocol |
| **Session 1 (Pre exercise)** |
| • Instructions to the patient about the standing and walking trials for session 1 (before exercise) – walk at self selected speed on the platform system, at least 2 steps before the walking pathway<br>• Standing trial acquisition (single trial)<br>• Walking trial acquisitions (8 trials) |
| Exercise: Patient was asked to walk for 5 minutes straight with our rest at a faster speed than self selected gait |
| **Session 2 (Post exercise)** |
| • Instructions same as session 1<br>• Standing trial acquisition<br>• Walking trial acquisition (8 trials) |
| Recovery: Patient was asked to lie down for 5 minutes |
| **Session 3 (Recovery)** |
| • Instructions same as session 1<br>• Standing trial acquisition<br>• Walking trial acquisition (8 trials) |
| Data processing and analysis<br>• Selection of best trials (minimum 3 trials)<br>• Processing of trials for quantitative gait analysis report generation by the gait expert<br>• Analysis and interpretation of the three sessions by the gait expert |

Data processing was done by a PMR specialist with experience in gait analysis. Three best trials were selected for each session and were analysed using the BTS software in the system available in gait lab. The data collected is represented in spatiotemporal parameters (numerical values), kinematic and kinetic parameters and ground reaction forces (graphical

data). The subjective interpretation of these findings is noted and explained in this article. All the recordings were processed through Smart analyser and Smart clinic software already installed in the system. The following parameters were analysed:

- Spatio-temporal parameters of gait (i.e. speed, stride length, cadence, step width and duration of stance, and swing and double support phase).
- Kinematics (i.e. hip and knee flexion and extension and ankle dorsiflexion and plantar flexion angle during the gait cycle).
- Kinetics (i.e. forces acting at hip knee and ankle joints during the gait cycle)
- Ground reaction force (i.e. trajectory through the gait cycle)

## 3. Results

### *3.1. Description of Baseline Gait Characteristics*

Spatiotemporal parameters e.g. stride time, stance time, swing time, stance phase and swing phase duration, single support and double support phase duration, mean velocity except cadence were normal. There was no significant reduction in step length. There was slight decrease in stride length, and significant increase in step width. Gait profile score didn't reflect much deviation from the normal score. Kinematic analysis parameters revealed near normal patterns in frontal plane trunk obliquity and pelvic obliquity graphs. Sagittal plane kinematics revealed normal graphs for trunk tilt, pelvic tilt, hip flexion – extension, knee flexion – extension graphs. Pattern of ankle Dorsiflexion and Plantar flexion kinematics was normal but there was decreased amplitude of peak plantar flexion. There was increased rotation in trunk, hip, knee and pelvic rotation in transverse plane. Foot progression graphs reflected in toeing progression. Kinetic analysis parameters showed significant change from normal in peak ankle dorsiflexion, peak knee extension moment, and reduced ankle power generation. Ground reaction forces: Antero posterior forces revealed much reduced forces. There was decreased lateral force during initial phase of gait cycle. Vertical force pattern and amplitude were near normal, except for slight delay in first peak, and slightly decreased second peak amplitude.

### *3.2. Comparison of Pre and post-exercise Parameters and Recovery Phase Parameters*

Spatio-temporal parameters: There was slight worsening in gait performance post exercise (which improved after a rest period (values are similar to pre exercise spatiotemporal parameters). Please refer to table 2 for details.

**Table 2:** Spatio-temporal parameters of gait

| | **Baseline** | | **Post exercise** | | **Recovery** | |
|---|---|---|---|---|---|---|
| | **Right** | **Left** | **Right** | **Left** | **Right** | **Left** |
| *Temporal parameters* | | | | | | |
| **Stride time (s)** | 1.06 | 1.06 | 1.1 | 1.11 | 1.08 | 1.09 |
| **Stance time (s)** | 0.63 | 0.64 | 0.68 | O.66 | 0.64 | 0.66 |
| **Swing time (s)** | 0.43 | 0.43 | 0.44 | 0.45 | 0.44 | 0.43 |
| **Stance phase (%)** | 59.38 | 60.42 | 61.79 | 59.74 | 59.57 | 60.12 |
| **Swing phase (%)** | 40.62 | 40.22 | 39.98 | 40.36 | 40.17 | 39.57 |
| **Single support phase (%)** | 40.07 | 40.78 | 40.67 | 39.68 | 39.76 | 39.76 |
| **Double support phase (%)** | 10.53 | 9.07 | 10.26 | 10.46 | 9.68 | 9.68 |
| **Mean velocity (m/s)** | 1.1 | | 1 | | 1.1 | |
| **Cadence (steps/min)** | 113 | | 108.6 | | 110.4 | |
| *Spatial parameters* | | | | | | |
| **Stride length (m)** | 1.16 | 1.17 | 1.14 | 1.13 | 1.16 | 1.18 |
| **Step length (m)** | 0.58 | 0.58 | 0.56 | 0.57 | 0.57 | 0.59 |
| **Step width (m)** | 0.17 | | 0.15 | | 0.17 | |

### *3.3. Kinematic Analysis*

Kinematic analysis parameters failed to elucidate any significant change in patterns due to exercise (Figure 2). There was significant reduction in amplitudes of vertical forces (first peak and second peak) in post exercise gait analysis, followed by a recovery pattern in recovery gait analysis (Figure 3).

**Baseline Gait Kinematics** **Post exertion GaitKinematics** **Recovery Gait kinematics**

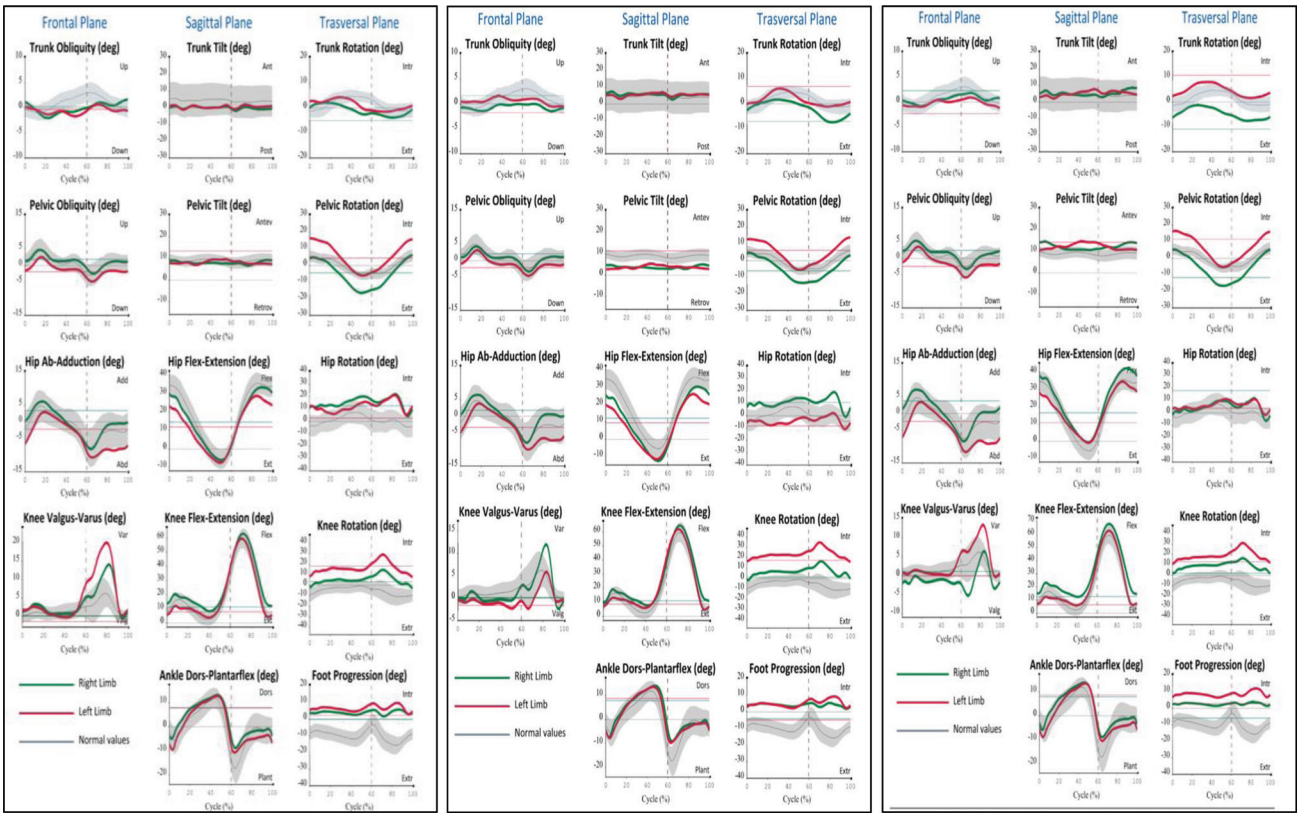


**Figure 2: Instrumented Gait Analysis Data:** Kinematic parameters in three dimensional planes - frontal, Sagittal and transverse planes for trunk, pelvis, hip, knee and ankle motions- Comparison of graphs between Baseline, post exercise and recovery Gait parameters. (Green lines in the graphs represent right limb, red lines represent left limb and gray line represent normative graphs)

**Baseline Gait Kinetics** **Post exertion Gait kinetics** **Recovery Gait kinetics**

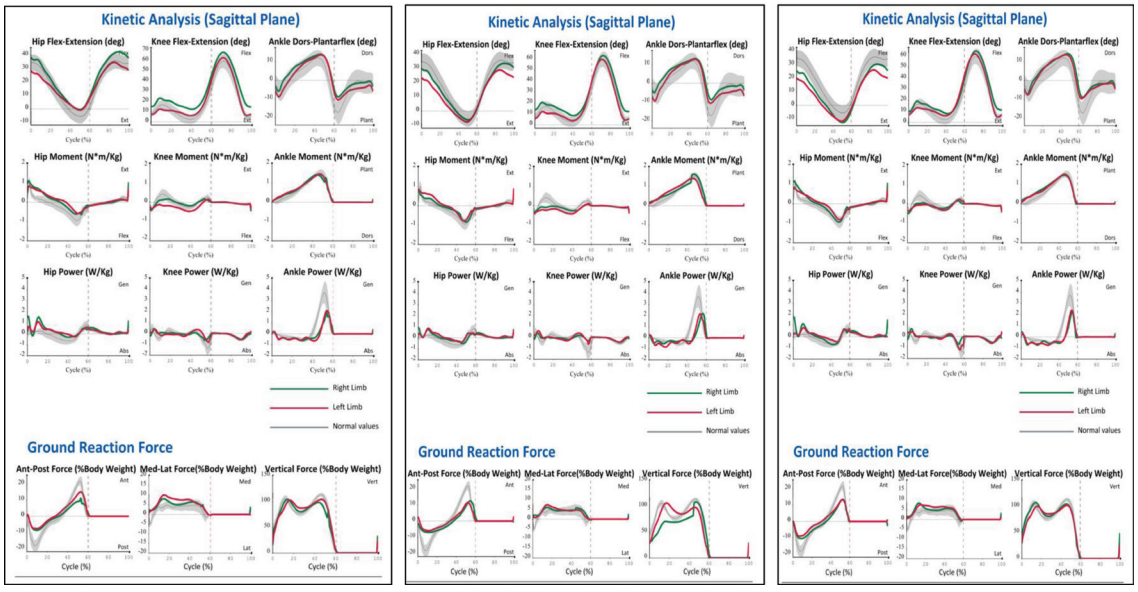


**Figure 3: Instrumented Gait Analysis Data:** Kinetic Analysis in Sagittal plane: Comparison between Baseline, post exercise and recovery Gait parameters (green lines in the graphs represent right limb, red lines represent left limb and gray line represent normative graphs)

### *3.4. Kinetic Analysis*

Kinetic analysis showed significant change from normal in peak ankle dorsiflexion, peak knee extension moment, and reduced ankle power generation.

## 4. Discussion

Patients with mitochondrial dysfunction have been reported to have shorter step length, reduced gait velocity and increased step width and increased variability in step time and step width (Koene *et al.*, 2018; Galna *et al.*, 2013).This study also depicted increased step width, reduced step length. The findings suggestive of balance dysfunction such as increase step width, decreased anterior posterior ground reaction forced, decreased ankle range of motion corroborate with the previous studies. However, in this case, decreased ankle plantar flexion could also be attributed to clinical finding of spasticity/dystonia in ankle. The exercise induced changes and then recovery patterns similar to pre-exercise gait parameters indicate metabolic nature of the disease.Increase in trunk, hip and pelvic rotation in transverse plane suggest proximal weakness (waddling gait), which is consistent with findings in previous studies (Koene *et al.*, 2018). However, it is difficult to point towards a specific diagnosis or phenotype based on these findings alone. These findings are only suggestive of metabolic disease with ataxic plus spastic paraplegic pattern of gait, with features suggestive of proximal weakness.

## 5. Conclusion

This is a single-centre limited depiction of our experience with a patient who presented with ambulatory difficulty in mitochondrial disease. Hence, it will be inappropriate to conclude out of it. But it surely provides an insight into probable deficits in the walking patterns of such patients as well as may help in developing protocols for testing and management of similar patients. Besides this, EMG evaluationwas not done in our study, which could have highlighted impaired individual muscle activity.

Future implications: 3D gait analysis may prove to be an adjunct in the diagnosis, classification and prognosis of rare neuromuscular diseases. It holds potential for diagnosing subtle changes in gait and quantifying theeffect of treatment and rehabilitation on gait and hence functional abilities of the patients.

## 6. Competing Interests

The author declares that there is no conflict of interest

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