
**“PROSPECTIVE STUDY OF PREVALENCE AND
CLINICO-ETIOLOGICAL PROFILE OF MOVEMENT
DISORDERS IN CHILDREN”**

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LIST OF ABBREVIATIONS:

AADC	-	Aromatic l-amino acid decarboxylase
ACOX1	-	Acyl-CoA oxidase 1
ADHD	-	Attention-deficit/hyperactivity disorder
ADGRV1	-	Adhesion G protein-coupled receptor V1
ALERD	-	Acute leukoencephalopathy with restricted diffusion
ATP8A2	-	ATPase phospholipid transporting 8A2
BIND	-	Bilirubin induced neurologic dysfunction
CNS	-	central nervous system
CDG	-	Congenital Disorders of Glycosylation
COQ8A	-	Coenzyme Q8A
CNNM2	-	Cyclin M2
CACNA1A	-	Calcium channel subunit alpha1 A
DNA	-	Deoxyribonucleic acid
DYN	-	Dynorphin
ENK	-	Enkephalin
EIF2AK2	-	Eukaryotic translation initiation factor 2 alpha kinase 2;
GABAergic	-	Gamma-aminobutyric acid
GCDH	-	Glutaryl-CoA dehydrogenase
HIE	-	Hypoxic-ischemic encephalopathy
KMT2B	-	Lysine methyl transferase 2B;
LSS	-	Lumbar spinal stenosis;
MRI	-	Magnetic resonance imaging
MRC	-	Medical Research centre
MD	-	Mediodorsal nucleus

MR	-	Mental retardation
MAPT	-	Microtubule-associated protein tau
MECR	-	Mitochondrial Enoyl CoA Reductase Protein
MD	-	Movement disorder
NCL	-	Neuronal ceroid lipofuscinoses
NBIA	-	Neurodegeneration with brain iron accumulation
NHBI	-	Neonatal hypoglycemic brain injury
NMDAR	-	Anti-N-methyl-D-aspartate receptor encephalitis
NKX2-1	-	Homeobox protein
OMAS	-	Opsoclonus-myoclonus-ataxia syndrome
OMD	-	Oro-motor dyskinesia
OPD	-	out patient department
PANK 2	-	Pantothenate kinase 2
PPA	-	pedunculopontine area
PLC β 1	-	Phospholipase C- β 1
Poly-EMG	-	Polygraphic electromyography
PROM	-	preterm or premature rupture of membrane
PCDH12	-	Protocadherin 12
RHOBTB 1	-	Rho-related BTB domain-containing protein
RNASEHC	-	Ribonuclease H subunit C
SD	-	standard deviation
SSPE	-	Subacute sclerosing panencephalitis
SC	-	superior colliculus
SMA	-	supplementary motor area
SNpc	-	Sub-stantia nigra pars compacta

SNpr	-	Substantia nigra pars reticulata
SP	-	Substance P
STN	-	Subthalamic nucleus
TTC19	-	Tetratricopeptide;
VA	-	Ventral anterior nucleus
VL	-	Ventral lateral nucleus
WES	-	Whole Exome Sequencing

ABSTRACT

Background: Movement disorders in children represent a complex spectrum of neurological abnormalities manifesting as hyperkinetic, or hypokinetic movements. Often linked to basal ganglia dysfunction, these disorders stem from diverse etiologies, including genetic, metabolic, or acquired factors. Despite their clinical and socioeconomic burden, data on pediatric movement disorders, particularly from resource-limited regions, remain sparse.

Objectives: Primary objective: To estimate the prevalence of movement disorders in children between 1 month to 18 years of age.

Secondary Objective: To evaluate the underlying aetiology and clinical spectrum and correlate the neuroimaging findings in children with movement disorders.

Methods: A hospital-based cross-sectional study was conducted from July 2022 to July 2023, involving 148 children aged 1 month to 18 years diagnosed with movement disorders. Comprehensive clinical evaluations, detailed video-based movement assessments, neuroimaging (MRI), and genetic analyses, including whole exome sequencing, were performed. Disorders were classified phenomenologically, and etiological associations were analyzed using advanced statistical methods.

Results: Hyperkinetic movement disorders predominated (98%), with dystonia (77.7%) as the most prevalent phenotype, followed by chorea (23.6%), athetosis (11.5%), myoclonus (10.1%), tremor (4.1%), stereotypes (2%), tics (0.7%) and ballism, catatonia, myorhythmia each constitutes 1.4%. Hypokinetic disorders accounted for only 2% of cases. Acquired etiologies, including cerebral palsy (54.4%), infections (32.9%), vascular (5.1%), nutritional (3.8%) contributed to 53.4% of cases. Genetic disorders accounted for 46.6%, with inborn errors of metabolism

and neurotransmitter diseases being prominent. Neuroimaging identified basal ganglia lesions in 32.8% and cortical abnormalities in 26.5%. High rates of consanguinity (60.8%) highlighted the genetic burden in this population.

Discussion: This study underscores dystonia as the predominant phenotype, reflecting a dual burden of acquired and genetic factors. The integration of neuroimaging and advanced molecular diagnostics provided critical insights, emphasizing their indispensability in comprehensive evaluations. Findings also advocate for early intervention strategies tailored to regional genetic and socio-environmental contexts.

Conclusion: This first-of-its-kind regional analysis bridges the gap in understanding pediatric movement disorders in India. It advocates for collaborative research, robust neurogenetic diagnostics, and personalized management approaches to optimize outcomes in resource-constrained settings.

Keywords: Pediatric neurology, dystonia, movement disorders, genetic etiology, neuroimaging, cerebral palsy, consanguinity.

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INTRODUCTION

Movement disorders in children represent a diverse group of neurological conditions characterized by abnormal motor activity, including involuntary movements, excessive motor function, or deficits in motor control¹. Voluntary movements require complex interaction of the corticospinal (pyramidal) tracts, basal ganglia, and cerebellum to ensure smooth and purposeful movements. The basal ganglia forms the extrapyramidal system and most movement disorders are attributed to dysfunction of the basal ganglia, their connections, or associated structures².

Paediatric movement disorders must be differentiated from developmental involuntary movements such as jitteriness in neonates, rapid eye movement, sleep myoclonus seen in young infants, ritualistic behaviours seen in infants and young children, and shivering and shuddering movements in infants and young children. Children can also present with physiologic involuntary movements such as jerks, fragmentary myoclonus, hiccups, bruxism and masturbatory movements. Transient pathological disorders can be present with involuntary movements, such as dystonia associated with gastroesophageal reflux in infants³.

The prevalence of movement abnormalities in children and their percentage of paediatric manifestations are not estimated globally. These disorders impact a considerable segment of the paediatric population, with prevalence estimates differing according to type, spectrum, aetiology of PMD, and diagnostic criteria across various geographical areas. For example, tics and Tourette syndrome are estimated to affect 1-2% of children globally⁴. The prevalence of dystonia is around 0.1-0.2%, while

chorea and myoclonus are less common but still present considerable clinical challenges.

Movement disorders in childhood may present acutely, sub-acutely or in a more chronic manner. The underlying aetiologies for childhood movement disorders are diverse, and include both acquired and genetic conditions. Movement disorders in children are more often secondary than primary, that is, they are more often associated with lesions of the brain such as cerebral palsy, traumatic brain injury, or stroke than occurring as a primary disorder³. Significant advances in genetic technologies have facilitated the discovery of several novel disease-causing genes and movement disorder syndromes in childhood in recent years⁵.

The pathophysiology of childhood movement disorders can be attributed to various factors, including genetics, neuroimmunology, structural abnormalities, and psychogenic reasons. Neuroimaging can be used to identify structural abnormalities or lesions of the central nervous system and of the basal ganglia's connecting components in certain situations of aberrant involuntary movements⁶.

The spectrum and aetiology of movement disorders are likely to differ in different geographic areas of the world⁵. There are very few studies on the spectrum, types, and aetiology of childhood movement disorders from India⁶ and other developing countries, with most studies excluding cerebral palsy, which contributes to a significant proportion of movement disorders in children³. The physiological type of CP a child develops depends on the cause and the areas of the brain that are predominantly affected due to the etiological factor. Like in developed countries, because of improved obstetric and perinatal care, prematurity is an important cause of CP (>75% of children with CP), and thus, spastic type is the most common type of

CP. However, in developing countries like ours, where we still have perinatal asphyxia, hyperbilirubinemia, and perinatal infections, dyskinetic CP is the most common type, contributing to a significant proportion of children with movement disorders in this part of the world⁷.

Marriage between close biological kin is not common in the western world, but in developing countries like ours, consanguineous unions persist which in turn increases the prevalence of recessive disorders making it further important to study the autosomal recessive conditions with movement disorders⁷.

Hence we conducted this study to determine the prevalence of movement disorders in children and also study the clinic etiological profile of movement disorders in children from this part of Karnataka.

AIMS AND OBJECTIVES

Primary objective: To study the prevalence of movement disorders in children between 1 month to 18 years of age.

Secondary Objective: To evaluate the underlying aetiology and clinical spectrum and correlate the neuroimaging findings in children with movement disorders.

REVIEW OF LITERATURE

Movement disorders definition:

Movement disorders are defined as neurologic syndromes in which there is either an excess of movement or a paucity of voluntary and automatic movements, unrelated to weakness or spasticity¹. Movement disorders involve impaired performance of voluntary movements, dysfunction of posture, the presence of abnormal involuntary movements, or the performance of normal-appearing movements at inappropriate or unintended times. The abnormalities of movement are not due to weakness or abnormal muscle tone but may be accompanied by weakness or abnormal tone⁸.

The term movement disorders came into existence in July 1968 when Prof Stanley Fahn joined the faculty of the Department of Neurology at the University of Pennsylvania and started the clinic with a mission expanded to cover hyperkinetic diseases as well as parkinsonian disorders¹. Before that, the term 'extrapyramidal disorders' was used, which was originally coined by Wilson to describe neurological ailments secondary to disorders of the basal ganglia and its pathways. However, this term was not widely acceptable considering the intimate connections of basal ganglia with the pyramidal tract; and, some movement disorders, such as myoclonus and ataxia were not associated with a basal ganglia pathology⁹. The department's chairman, Lewis P. Rowland and Fahn discussed various terminologies and came up with the term Movement Disorders which included all the above disorders being studied¹. The first organization formed to bring together clinical investigators who were involved in the study of these disorders was the Research Group on Extrapyramidal Disorders, which was one of the research groups in the World

Federation of Neurology. Melvin D. Yahr founded the group, and it organized international symposia, mostly about Parkinson's disease.

In November 1977, Chairman Yahr appointed an adhoc committee to develop a glossary of terms, clinical classification of disorders of the extrapyramidal system, and to suggest standard rating scales for abnormal involuntary movements and postures. The committee classified the disorders into 2 major groups: (I) Disorders of movement and (II) Disorders of posture and tone. In group I, the subdivisions were hypokinesias and hyperkinesias (various tremor phenomenologies, tics, myoclonus, chorea, ballism, athetosis, and akathisia). Group II was subdivided into dystonia, torsion spasm, cogwheel phenomenon, rigidity, Gegenhalten, and hypotonia.

Pathophysiology of movement disorders

The pathophysiology of childhood movement disorders can be attributed to various factors, including genetics, neuroimmunologic factors, structural abnormalities, and psychogenic reasons. To understand it, neuroimaging can be used to identify structural abnormalities or lesions of the CNS. Recent research suggests that movement disorders can have a neuroimmunologic (such as Tourette syndrome and Sydenham's chorea) or genetic basis (e.g., Huntington's disease)¹⁰.

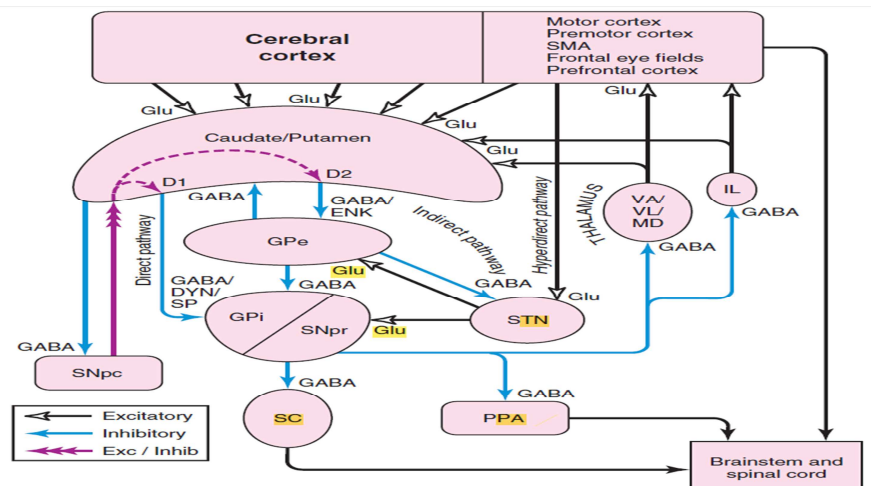
Basal Ganglia Pathophysiology in Movement Disorders

The majority of movement disorders can be attributed to Basal ganglia dysfunction. However, "Basal ganglia disorders" and "Movement disorders" are not synonymous. Some movement disorders (e.g., tremor and myoclonus) may have little to do with the basal ganglia. Conversely, basal ganglia lesions may cause cognitive or affective symptoms with minimal or no motor impairment. Nonetheless, because most

movement disorders involve the basal ganglia, it is useful to understand how this system is organized.

The basal ganglia are subcortical structures comprising several interconnected nuclei in the forebrain, midbrain, and diencephalon (Fig 1). They include the striatum (caudate, putamen, nucleus accumbens); the subthalamic nucleus (STN); the globus pallidus (internal segment [GPi]; external segment [GPe]); the ventral pallidum; and the substantia nigra (pars compacta [SNpc] and pars reticulata [SNpr]). The striatum and STN are the primary input structures of the basal ganglia, receiving excitatory input from the cerebral cortex. The GPi and SNpr are the primary output nuclei, sending inhibitory output to thalamic and brainstem targets. Acting through the thalamus, the basal ganglia output influences frontal lobe cortical neurons. By virtue of the inhibitory output from the basal ganglia, conditions associated with destruction of the output nuclei may be associated with unwanted and nonspecific overactivity of thalamocortical and brainstem targets. The striatum receives excitatory input from virtually all of the cerebral cortex. In addition to the cortical input, the striatum receives a dense input from dopamine-containing neurons in the SNpc¹¹.

Figure 1 : Schematic diagram of basal ganglia circuitry



Excitatory connections are indicated by black arrows, inhibitory connections by blue arrows, and the modulatory dopamine projection is indicated by a red three-headed arrow. DYN, dynorphin; ENK, enkephalin; thalamic nuclei; MD, mediodorsal nucleus; PPA, pedunculopontine area; SC, superior colliculus; SMA, supplementary motor area; SNpc, sub-stantia nigra pars compacta; SNpr, substantia nigra pars reticulata; SP, substance P; STN, subthalamic nucleus; VA, ventral anterior nucleus; VL, ventral lateral nucleus.

Basal ganglia dysfunction can occur on many levels. Destructive lesions of specific nuclei (e.g., infarction, haemorrhage, metabolic disorders) may result in particular movement disorders. There also can be injury to multiple nuclei that results in single or multiple movement disorders (e.g., hypoxia, carbon monoxide poisoning, metabolic disorders). Movement disorders also can be caused by loss of specific neuron types (e.g., Huntington's disease, Parkinson disease) or by cellular dysfunction without neuronal death (e.g., DYT1 dystonia). As in other areas of neurology, lesion localization is important in assessing movement disorders and may provide important clues to guide an efficient evaluation and treatment plan¹¹.

Lesions in the striatum produce variable results that depend in part on the location of the lesion, in part on the lesion mechanism, and in part on what is measured. Lesions in the caudate nucleus most commonly cause behavioural disturbance, such as abulia, but also may cause chorea or dystonia. Lesions in the putamen are likely to produce movement deficits and typically cause dystonia (most common) or parkinsonism. Smaller amplitude chorea can result from STN lesions. When bilateral, STN lesions cause bilateral chorea or ballism. Most commonly, the chorea or hemiballism occurs in extremities and can persist for days to months. The intensity of hemiballism usually diminishes over time. Globus pallidus lesions usually

involve GPe and GPi, GPe and putamen, or GPi and SNpr. Such lesions can cause dystonia, parkinsonism, or both. Chorea rarely accompanies globus pallidus lesions. Focal lesions of SNpr can cause involuntary eye movements. Lesions of SNpc dopamine neurons cause dopamine depletion in the striatum, resulting in parkinsonism, dystonia, or both. Movement disorders in children are more likely to result from global dysfunction of basal ganglia circuits¹¹.

Classification of Movement disorders

Jorg Baumann attempted the first formal classification of extrapyramidal disorders in 1963, which was based on anatomic localization of the pathology. Fahn, Marsden and Jankovic first classified the movement disorders into two groups, hypokinetic (paucity of movements) and hyperkinetic (excess movements)⁹.

By convention, Movement disorders are divided into two major categories.

The first is Hyperkinetic Movement disorders, sometimes referred to as Dyskinesias. This term refers to abnormal, repetitive involuntary movements and encompasses most of the childhood movement disorders, including tics, chorea/ballismus, dystonia, myoclonus, stereotypies, and tremor.

The second category is hypokinetic movement disorders, sometimes referred to as akinetic/rigid disorders. The primary movement disorder in this category is bradykinesia, manifested primarily in adulthood as Parkinson disease or one of many forms of secondary parkinsonism. Hypokinetic disorders are relatively uncommon in children⁸.

A group of movement disorders with a different phenomenology caused by underlying psychological factors are referred to as psychogenic or functional movement disorders.

There is no specific diagnostic test to differentiate between movement disorders. Categorizing these movement disorders help in localizing the pathologic process, whereas the age, onset, and degree of abnormal motor activity and associated neurologic features assist in organizing the relevant investigations¹².

When faced with a movement disorder, the following key questions need to be asked⁸:

- Is the pattern of movements normal or abnormal?
- Is the number of movements excessive or diminished?
- Is the movement paroxysmal (sudden onset and offset), continual (repeated again and again), or continuous (without stop)?
- Has the movement disorder changed over time?
- Do environmental stimuli or emotional states modulate the movement disorder?
- Can the movements be suppressed voluntarily?
- Is the abnormal movement heralded by a premonitory sensation or urge?
- Are there findings on the examination suggestive of focal neurologic deficit or systemic disease?
- Is there a family history of a similar or related condition?
- Does the movement disorder abate with sleep?

In clinical practice, the diagnosis of a movement disorder requires a qualitative appreciation of the movement type and context. Abnormal movements can be difficult to define. To best classify the disorder phenomenologically, one should describe the characteristics of the movements. Even under the best circumstances, movement disorders may be difficult to characterize. However, careful observation of the spatial and temporal properties of the movement, can usually lead to appropriate identification of the phenomenology. Movements in some contexts may be normal and in others may indicate underlying pathology, some which are worrisome for a degenerative disorder in adolescents (myoclonus) may be completely normal in an infant (benign neonatal myoclonus). It is difficult to specifically diagnose a movement disorder without seeing the abnormal movements. Thus, obtaining video examples of the child's movement may be essential to making a correct diagnosis¹³.

Many classification schemes have been used to provide a taxonomy for various movement disorders. Disorders can be classified by phenomenology, based on the observed temporal and spatial features of the movements themselves, along with characteristic clinical features. They can also be classified based on presumed aetiology, anatomic localization, or neuropathological features, by disease course, by genetic or molecular criteria, or by other biological factors¹⁴. In response to advances in genetics, the Movement Disorders Society proposed a new classification of movement disorders but the nomenclature is constantly evolving. Even in the era of "Next generation DNA sequencing, the classification of movement disorders according to phenomenology provides an important framework for diagnostic interpretation, therapeutic decisions, and the development of new treatments¹³.

Table 1: Phenomenological classification of Movement disorders:

HYPERKINESIAS	HYPOKINESIAS
Dystonia	Akinesia/bradykinesia (Parkinsonism)
Athetosis	Apraxia
Chorea	Catatonia, psychomotor depression
Ballism	Cataplexy and drop attacks
Paroxysmal dyskinesias	Hypothyroid slowness
Myorhythmia	Rigidity
Myoclonus	
Stereotypies	
Tics	
Tremors	
Hemifacial spasm	
Hyperekplexia	
Restless legs	

HYPERKINETIC MOVEMENT DISORDERS:

1) Dystonia:

The term “dystonia” appears to have been first used when Oppenheim applied the description “dystonia musculorum deformans” in 1911 to a progressive childhood-onset syndrome characterized by twisted postures, muscle spasms, bizarre walking with bending and twisting of the trunk, and eventually fixed postural deformities.¹³ In 2013, an international consensus committee was established by the Dystonia Medical Research Foundation, the Dystonia Coalition, and the European Dystonia COST Action to review and revise the definition. The resulting, and current, International Consensus definition is as follows:

Dystonia is defined as a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both. These movements are typically patterned, twisting, and may be tremulous. It is often initiated or worsened by voluntary action and associated with overflow muscle activation¹³.

It is classified as primary, which is pure dystonia without any associated neurological or pathological abnormality, while secondary is associated with non-primary dystonia. A consensus update by Albanese et al¹⁵, showed that dystonia to be classified into two axis based on clinical and etiological conditions which aids in diagnosis and treatment. Axis 1: clinical characteristics (including age at onset, body distribution, temporal pattern and associated features) and Axis 2: aetiology (including nervous system pathology and inheritance).

One of the most important characteristics of dystonia that differentiates this movement disorder from other hyperkinesia is the patterned nature of the contractions, meaning the same muscles or groups of muscles contract consistently throughout the disease in that particular individual. Sometimes dystonia may overflow when adjacent muscles become recruited and/or the opposite side of the body may become involved when a patient performs voluntary movement on one side of the body, the so-called mirror dystonia.

Two important associated characteristic features of dystonia are task specificity and the so-called geste antagoniste, sensory trick, or an alleviating maneuver. Examples of alleviating maneuvers include touching near the lateral canthus may relieve the eyelid squeezing of blepharospasm; a straw in the mouth may reduce jaw and tongue dystonia; and touching the side of the chin may decrease torticollis associated with cervical dystonia. Even in generalized dystonia, light touch to the neck or an affected limb may transiently reduce dystonic contractions or walking backwards may improve leg dystonia, truncal flexion (camptocormia) or dystonic scoliosis. Task-specificity manifests as dystonic posturing occurring only with selected movements and paradoxically not with others that may use the same muscles. For example, a patient with writer's cramp may have dystonia only while writing, but not while knitting, typing, or using a screwdriver. In cranial dystonia, lower facial grimacing may occur only when talking and not when eating. The 2013 revised classification scheme identifies two distinct axes: clinical features and aetiology. A combination of these two axes provides meaningful information on any dystonia patient that can serve to guide diagnosis and to develop research and treatment strategies¹⁵.

Axis I: Clinical Characteristics

Five elements specify the key clinical characteristics: age at onset, body distribution, temporal pattern, coexistence of other movement disorders, and other neurological manifestations.

Table 2: Showing Axis I classification of dystonia

<i>Clinical Characteristics of Dystonia</i>	
• Age at onset	<ul style="list-style-type: none"> • Infancy (birth to 2 years) • Childhood (3–12 years) • Adolescence (13–20 years) • Early adulthood (21–40 years) • Late adulthood (>40 years)
• Body distribution	<ul style="list-style-type: none"> • Focal • Segmental • Multifocal • Generalized (with or without leg involvement) • Hemidystonia
• Temporal patterns	<ul style="list-style-type: none"> • Disease course <ul style="list-style-type: none"> ◦ Static ◦ Progressive • Variability <ul style="list-style-type: none"> ◦ Persistent ◦ Action-specific ◦ Diurnal ◦ Paroxysmal
<i>Associated Features</i>	
• Isolated dystonia or combined with another movement disorder	<ul style="list-style-type: none"> • Isolated dystonia • Combined dystonia
• Occurrence of other neurological or systemic manifestations	<ul style="list-style-type: none"> • List of cooccurring neurological manifestations

Axis II: Aetiology

The second axis addresses aetiology under two broad elements: anatomically identifiable nervous system pathology and pattern of inheritance. Anatomical causes may be identified using brain imaging or by pathology. Inherited is differentiated from acquired conditions employing genetic, metabolic, or other tests. These two elements, nervous system pathology and pattern of inheritance, are complementary for etiological classification.

Table 3: Showing Axis II classification of dystonia

<ul style="list-style-type: none"> • Nervous system pathology • Inherited or acquired 	<ul style="list-style-type: none"> • Evidence of degeneration • Evidence of static lesions • No evidence of degeneration or structural lesion • Inherited <ul style="list-style-type: none"> • Autosomal dominant • Autosomal recessive • X-linked recessive • Mitochondrial • Acquired <ul style="list-style-type: none"> • Perinatal brain injury • Infection • Drug • Toxic • Vascular • Neoplastic • Brain injury • Functional • Idiopathic <ul style="list-style-type: none"> • Sporadic • Familial
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Aetiology of Dystonia:

The causes of dystonia in children are varied and can be either acquired or genetic (Table 3). In many conditions, dystonia appears as just one of several neurological signs or symptoms. In other cases, dystonia may be the primary or even the sole manifestation of the disorder¹¹. Recent advancements in molecular and genetic research, along with improved diagnostic tools, have enabled the identification of specific causes of dystonia that were once thought to be idiopathic. Many genetic forms of dystonia have been assigned genetic loci labelled as DYT_x, where 'x' denotes the order in which the locus was identified^{11,15}.

Table 4: Aetiology of paediatric dystonia

<p>STATIC INJURY/STRUCTURAL DISORDERS</p> <ul style="list-style-type: none"> • Cerebral palsy • Hypoxic-ischemic injury • Kernicterus • Head trauma • Encephalitis • Tumors • Stroke in the basal ganglia (which may be due to vascular abnormalities or varicella) • Congenital malformations affecting basal ganglia <p>HEREDITARY/DEGENERATIVE DISORDERS</p> <ul style="list-style-type: none"> • DYT1 (autosomal dominant, TorsinA) • DYT2 (autosomal-recessive, Hippocalcin) • DYT4 (autosomal dominant, β-tubulin 4a) • DYT5 (autosomal dominant, GTP cyclohydrolase 1) • DYT6 (autosomal dominant, THAP1) • DYT8 (autosomal dominant, Myofibrillogenesis regulator 1) • DYT9 (autosomal dominant, GLUT1) • DYT10 (autosomal dominant, PRRT2) • DYT11 (autosomal dominant [maternal imprinting], ϵ-Sarcoglycan) • DYT12 (autosomal dominant, Na⁺/K⁺ ATPase α3 subunit) • DYT15 (autosomal dominant, unknown) • DYT16 (autosomal recessive, Protein kinase activator PRKRA) • Pantothenate kinase-associated neurodegeneration (PKAN; neuronal brain iron accumulation type 1, due to mutations in PANK2) • PLA2G6-associated neurodegeneration (PLAN) • Huntington disease (Westphal variant, IT15-4p16.3) • Spinocerebellar ataxias (SCAs, particularly SCA3/Machado-Joseph disease) • Striatal necrosis • Leigh syndrome • Neuroacanthocytosis 	<ul style="list-style-type: none"> • HARP syndrome (hypoprebetalipoproteinemia, acanthocytosis, retinitis pigmentosa, and pallidal degeneration) • Tay-Sachs disease • Sandhoff disease • Niemann-Pick type C <p>METABOLIC DISEASE</p> <ul style="list-style-type: none"> • Glutaric aciduria types 1 and 2 • Acyl-CoA dehydrogenase deficiencies • Neurotransmitter disorders • Mitochondrial disorders • GM, gangliosidosis • Lesch-Nyhan disease • Wilson disease • Vitamin E deficiency • Methylmalonic aciduria • Tyrosinemia <p>DRUGS/TOXINS</p> <ul style="list-style-type: none"> • Neuroleptic and neuroleptic-like antiemetic medications (haloperidol, chlorpromazine, olanzapine, risperidone, prochlorperazine) • Calcium channel blockers • Stimulants (amphetamine, cocaine, ergot alkaloids) • Anticonvulsants (carbamazepine, phenytoin) • Thallium • Manganese • Carbon monoxide • Ethylene glycol • Cyanide • Methanol <p>PAROXYSMAL DISORDERS</p> <ul style="list-style-type: none"> • Paroxysmal kinesigenic dyskinesia (PKD) • Paroxysmal nonkinesigenic dyskinesia (PNKD) • Exercise-induced dyskinesia (PED)
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2) CHOREA

Chorea refers to involuntary, irregular, non-repetitive dance-like movements of the body parts that appear to flow from one muscle group to another without following any pattern¹³. It commonly affects children, causing hyperactivity and fidgety, with unimpaired voluntary movements. It can be inherited or caused by genetics, infections, injuries, or immune-mediated disorders. Patients may transform choreiform movements into voluntary acts, resulting in motor impersistence and it disappears during sleep¹³.

Chorea is characterized by random, unpredictable movements that occur continuously, in contrast to dystonia, which features more predictable and stereotyped

movements or postures. The movements associated with chorea are usually faster than those seen in dystonia. Unlike dystonia, chorea can occur even when a person is at rest, although it may worsen with voluntary movement. Children with chorea may exhibit "Parakinesia," where they attempt to incorporate the involuntary movements into more purposeful actions to disguise the disorder. Interestingly, despite the involuntary movements, children with chorea can often maintain the accuracy of their reaching movements, as they seem to compensate well when trying to approach a target^{11,13}. Choreic movements can occur in both proximal and distal muscles¹³.

Chorea can be differentiated from tremor because it lacks rhythmicity and predictability. Unlike myoclonus, where all movements are quick and involve simple shock-like contractions of individual muscles, chorea consists of more complex and varied movements. Additionally, myoclonic movements tend to follow a consistent pattern, engaging the same set of muscles repeatedly.

Chorea also differs from tics in that it cannot be voluntarily suppressed and is not preceded by an urge. Furthermore, chorea does not consist of repeated stereotyped movements. In chorea, movement fragments frequently overlap, and multiple fragments can occur simultaneously. In contrast, when tics are present, each tic usually completes before the next one begins¹¹.

Pathophysiology of chorea

The loop model that describes the function and connection between the cortex and basal ganglia indicates that there is a decrease in inhibitory GABAergic projections from the globus pallidus internus (GPi) to the thalamus in individuals with chorea. This reduction allows for an increase in excitatory glutamatergic output from the thalamus to the motor, premotor, and supplementary motor cortices. This thalamic

disinhibition may arise from either: (1) increased activity of the GABAergic projections or (2) decreased activity of the subthalamic nucleus (STN) in the “indirect” pathway, although the latter typically results in hemiballismus. Additionally, pre- and postsynaptic molecular abnormalities (Fig.2) appear to create an imbalance between the “direct” and “indirect” pathways, leading to chorea.¹⁶

Figure 2: Direct and Indirect pathways of chorea

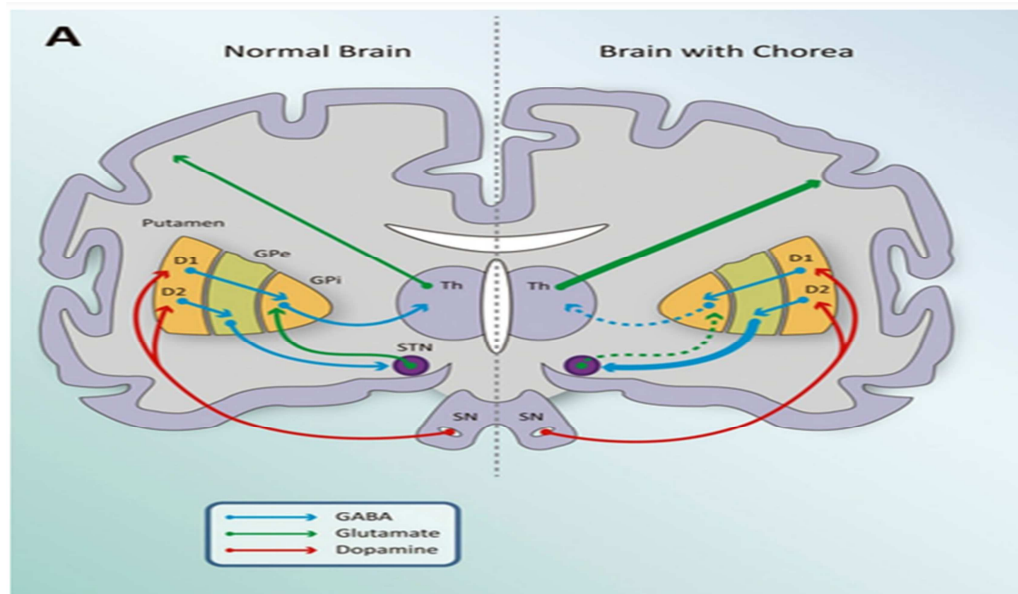


Figure 2 shows: Basal ganglia projections to the thalamus and cortex; the direct pathway mediated by D1 dopaminergic receptors is composed by GABAergic striatal projections to the GPi; whereas the “indirect pathway” mediated by D2 receptors projects to the GPe, STN, and ultimately the GPi; a bilateral imbalance between both pathways likely explains the choreic movement.

Aetiology of chorea

Choreiform movements can be benign or can emerge as a consequence of autoimmune diseases, genetic and metabolic diseases, cerebrovascular disease, infections, trauma, toxins, or neoplasms. The cells and structures in the basal ganglia are vulnerable to a wide variety of pathologies. In many of these diseases, hyperkinetic movement disorder is not the sole or predominant neurologic problem^{16,17}.

Table 5: Showing key etiologic categories of chorea and important diagnoses.

<p>STATIC INJURY/STRUCTURAL DISORDERS</p> <ul style="list-style-type: none"> • Cerebral palsy • Stroke • Trauma • Moyamoya disease • Vasculitis • Tumors • Congenital malformations • Joubert syndrome <p>HEREDITARY/DEGENERATIVE DISORDERS</p> <ul style="list-style-type: none"> • Ataxia-telangiectasia (A-T), and Ataxia-Telangiectasia-Like Disorder (ATLD) • Ataxia oculomotor apraxia (AOA) (includes AOA-1, AOA-2, and early onset cerebellar ataxia and hypoalbuminemia [EOCA-HA]) • Fahr disease • Pantothenate kinase-associated neurodegeneration (PKAN, associated with mutations in <i>PANK-2</i>, pantothenate kinase-2 gene), and other causes of Neuronal Brain Iron Accumulation (NBIA) <p>METABOLIC DISORDERS</p> <ul style="list-style-type: none"> • Acyl-coA dehydrogenase deficiencies • Mitochondrial disorders, including Leigh syndrome • GM1 gangliosidosis • Lesch-Nyhan disease • Niemann-Pick type C • Methylmalonic aciduria • Nonketotic hyperglycemia • Kernicterus • Hypoparathyroidism • Propionic acidemia • Hyponatremia • Hypomagnesemia • Hypocalcemia • Hypo- or hyperglycemia • Vitamin E deficiency or malabsorption • Bassen-Kornzweig disease • Complications of cardiac bypass <p>INFECTIOUS/PARAINFECTIOUS DISEASE</p> <ul style="list-style-type: none"> • Encephalitis/postencephalitis 	<p>IMMUNE-MEDIATED/DEMYELINATING DISORDERS</p> <ul style="list-style-type: none"> • Sydenham chorea • Lupus erythematosus • Henoch-Schönlein purpura • Anticardiolipin or antiphospholipid antibody syndrome • Anti-NMDA antibody syndrome <p>DRUGS/TOXINS</p> <ul style="list-style-type: none"> • Neuroleptic medications, and neuroleptic-like antiemetics (haloperidol, chlorpromazine, pimozide, prochlorperazine, metoclopramide) • Calcium channel blockers (flunarizine, cinnarizine) • Antiseizure medications (phenytoin, carbamazepine, valproate, phenobarbital) • Anticholinergic medications (trihexyphenidyl, benztrapine) • Antihistamines • Tricyclic antidepressants • Clomipramine • Stimulants (including methylphenidate, dexamphetamine, pemoline, and bronchodilators) • Clonidine • L-dopa • Cocaine • Bismuth • Lithium • Manganese • Ethanol • Carbon monoxide • Oral contraceptives • General anesthesia (including propofol)—during induction or emergence <p>PAROXYSMAL DISORDERS</p> <ul style="list-style-type: none"> • Complex migraine • Alternating hemiplegia of childhood • Paroxysmal kinesigenic dyskinesia (PKD) • Paroxysmal nonkinesigenic dyskinesia (PNKD) • Paroxysmal exercise-induced dyskinesia (PED) <p>ENDOCRINE DISORDERS</p> <ul style="list-style-type: none"> • Hyperthyroidism • Pheochromocytoma
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3) MYOCLONUS:

Myoclonus refers to quick, shock-like jerks due to sudden involuntary contraction of one or more muscles. The term is usually applied to describe positive myoclonus. Negative myoclonus refers to a sudden, brief interruption or relaxation of

contraction in active postural muscles. Asterixis, a flapping hand tremor with the wrist extended, occurs because of negative myoclonus.

Both negative myoclonus and positive myoclonus occur in children.

In Paediatric neurology, myoclonus rarely occurs in isolation. Most cases of myoclonus in children are seen in those who have epilepsy as their primary diagnosis. Conditions that cause myoclonus in children frequently have a negative impact on cognitive development or are linked to cognitive decline.

Startle disorders, which resemble myoclonus, less commonly present with additional movement disorders. Acquired neurological diseases that include myoclonus often also exhibit signs of encephalopathy. Additionally, functional jerks that mimic myoclonus may be referred to Pediatric neurologists, and these may be associated with other functional symptoms¹³.

Localization and Neurophysiology of myoclonus

Myoclonus can originate at multiple levels of the neuroaxis. There are anatomic and neurophysiological features that tend to differ between these levels. In certain situations, knowing these distinctions might assist focus diagnostic testing and guide symptomatic treatment.¹³

Table 6: Shows Type of Myoclonus and Neuroanatomic Localization

Neuroanatomic substrate	Type of myoclonus
Cortical—cerebral	Focal Multifocal Generalized Reflex/stimulus-evoked
Subcortical	Focal Generalized Reflex
Brainstem	Reticular/generalized Startle
Spinal	Segmental
Peripheral	Focal

Cortical Myoclonus

Usually, cortical myoclonus affects the muscles in the face and distal limbs, likely due to these areas having extensive cortical representation. Myoclonic jerks from the cortex often happen spontaneously, but they can also be triggered by tactile or other sensory stimuli. Polygraphic electromyography (Poly-EMG) reveals bursts in agonist and antagonist muscle pairs, with a burst duration of less than 50 milliseconds.

Brainstem (Reticular) Myoclonus

Brainstem-generated myoclonus involves the entire body. This type of myoclonus can happen on its own or be brought on by somatosensory inputs to the distal limbs. Both flexors and extensors may be involved. The site of origin is believed to be the medulla.

Subcortical Myoclonus

It is still unknown where subcortical myoclonus originates, and its symptoms can include both positive and negative myoclonus, with burst times longer than 100 ms. Other criteria for different myoclonus types are not fulfilled.

Segmental Myoclonus

Segmental myoclonus is a rare condition in children. It may affect the cranial-branchial structures due to lesions in the diencephalon or brainstem, leading to rhythmic contractions of the posterior pharyngeal muscles (e.g., palatal myoclonus), neck muscles, and even the diaphragm.

Table 7: Displaying the aetiology of Myoclonus:

Categories	Characteristic features	Disorders and diseases
Physiologic/benign	Occurs in healthy persons in certain settings or during phases of development	Sleep myoclonus Benign myoclonus of infancy Hereditary chin myoclonus
Genetic diseases with prominent myoclonus and not epilepsy	Myoclonus is the primary symptom Myoclonus with additional features of phenotype	Myoclonus dystonia syndrome Familial myoclonus 1 and 2 Accompanying other predominant motor phenomenologies In skeletal malformation syndromes
Myoclonus in epilepsy without encephalopathy	Myoclonus as seizure-type or accompanying generalized seizures in an epilepsy syndrome	Juvenile myoclonic epilepsy Eyelid myoclonia with generalized epilepsy
Myoclonus ataxia syndromes/ progressive myoclonic epilepsies, with encephalopathy	Myoclonus in the context of a progressive neurological disease with cognitive problems and other movement disorders, particularly ataxia	Myoclonic epilepsy associated with ragged-red fibers (MERRF) Myoclonic epilepsy of Unverricht and Lundborg (EPM1) LaFora disease (EPM2A, EPM2B) North Sea progressive myoclonus epilepsy (EPM6) Myoclonus epilepsy and ataxia (MEAK) due to potassium channel mutation Sialidosis/Neuraminidase deficiency 1 Ceroid lipofuscinoses, neuronal: for example, CLN1, CLN2, CLN7, CLN8, CLN14 Angelman syndrome Rett syndrome
Genetic diseases causing other movement disorders, sometimes with myoclonus	One or more other movement disorders is more prominent, but myoclonus may occur	Ataxia telangiectasia Dystonia 24 (DYT-ANO3) Dyskinesia, familial, with facial myokymia (DYT-ADCY5) Glucose transporter 1 deficiency syndrome

4) TREMORS

Tremor refers to a rhythmic, relatively symmetric oscillatory involuntary movement about a joint axis. Usually this involves rhythmic alternating contractions of antagonistic muscles and produces an oscillatory, sinusoidal-appearing movement. Myoclonus involves jerk-and-release and is therefore distinguished from tremor in part by its lack of both symmetry and midpoint.

A recent consensus document on the classification of tremors, which involves phenomenology and various clinical features, has been established by a task force from the International Parkinson and Movement Disorder Society. This classification system proposes the use of two axes^{13,18}.

Axis 1 codifies clinical features important for any comprehensive neurological assessment, adding tremor characteristics. These characteristics combine in recurring patterns in individuals affected with tremor.

Axis 2 designates the cause¹³.

Table 8: Shows Task Force Consensus Statement: Tremor Classification:

Axis 1: Clinical Features

Historical features

- Age at onset
- Temporal onset and time course
- Past medical history
- Family history/inheritance pattern
(Alcohol, drug sensitivity)

Tremor characteristics

- Body distribution
- Activating conditions
- Frequency of tremor

Associated signs

- Systemic illness
- Neurological signs
- Subtle motor signs

Additional diagnostic tests

- Serum (tissue) biomarkers
- Structural imaging
- Receptor imaging
- Electrophysiological testing

Axis 2: Etiology

Acquired

Genetic

Idiopathic

- Familial
- Sporadic

Localization and Pathophysiology:

Tremor involves alternating, relatively symmetric contractions of agonist and antagonist muscles that lead to movement around a fixed point, axis, or plane. The movements are visually oscillatory and may appear either regular or irregular and jerky¹³.

Tremor can be conceptualized as abnormal movement resulting from the insufficient inhibition of or excessive facilitation of oscillatory activity in the central nervous system, transmitted out to muscles. This central oscillatory activity involves motor control networks through the cortical-cerebellar-thalamo-cortical circuits or less commonly the cortical-striatal-pallidal-thalamo-cortical circuits.

The frequency of the various tremors may thus have some localizing value, corresponding in some cases to pathological firing frequencies and altered desynchronization patterns while performing movements. Tremors of various frequencies appear, based on lesioning studies and clinical-pathologic correlations, to have characteristic anatomic locations. For example, cerebellar hemispheric lesion tremors vary from 5 to 11 Hz, and dentate nucleus lesion results in slower, 6-8 Hz tremor. Midbrain tremors are slower at 2-3 Hz, high brainstem lesions have 5-7 Hz tremor, and low brainstem lesions have 8-11 Hz tremor. In addition to anatomic location, the type of lesion may also be important, with destructive or multifocal processes causing lower frequency tremors than compressive lesions.

5) ATHETOSIS AND BALLISMUS:

Athetosis literally means “without position or place.” It is defined as slow, writhing, continuous, involuntary movements. In athetosis, the same regions of the body are repeatedly involved, unlike chorea where individual involuntary movements appear to move from one body part to another. Athetosis may worsen with attempts at movement or posture, but it can also occur at rest. Athetosis typically involves the distal extremities (hands or feet) more than the proximal extremities and it can also involve the face, neck, and trunk^{11,19}.

Athetosis is distinguished from dystonia by the lack of sustained postures, although it may accompany dystonia. Athetosis differs from chorea by the lack of identifiable movement fragments. Athetosis is not rhythmic or stereotyped. There is some debate as to whether athetosis should be considered as a discrete entity, or whether it is part of the spectrum of dystonia or simply a form of “slow chorea.” Although cerebral palsy is one of the most common causes of childhood athetosis, athetosis may be associated with multiple etiologies¹³.

Ballismus or ballism refers to involuntary, high amplitude, flinging movements typically occurring proximally. These movements may be brief or continual and may occur in conjunction with chorea. Often, one side of the body is affected, that is, hemiballism. In many cases, hemiballism gets milder with time and evolves into chorea. It has been suggested that because the same lesions can produce both ballismus and chorea, ballismus is likely to part of the spectrum of chorea and not a separate entity¹³.

6) TICS:

Tics are sudden, rapid, and repetitive movements or vocalizations that can be either simple or complex. They are divided into two main categories: motor tics (involving movements) and phonic tics (involving sounds). Each category can be further classified into simple and complex types. Tics are typically preceded by an uncomfortable feeling or urge, known as a premonitory sensation, which is relieved by performing the tic.

These movements have predictable characteristics, both in their nature and onset. They often worsen in response to stress or excitement, but individuals can temporarily suppress them voluntarily. Both the person experiencing the tics and

observers can usually predict the movements, as there are typically a limited number of distinct tics present at any given time. The duration of each tic remains consistent, even when repeated.

Tics may wax and wane over weeks, months, or years, with different tics emerging or disappearing at various times, often varying in severity. The frequency of tics can change throughout the day, and they tend to occur more often during periods of stress, fatigue, anxiety, or excitement.

Tics may also manifest as brief, sudden jerky movements, known as "clonic tics," or as briefly sustained postures, referred to as "dystonic tics" or "tonic tics." It is important to note that while dystonia is often triggered by voluntary movement and can interfere with it, tics are typically suppressed without obstructing voluntary movements^{4,13}.

7) STEREOTYPIES

Stereotypies are broadly defined as involuntary, patterned, coordinated, repetitive, nonreflexive movements that occur in the same fashion with each repetition. Stereotypies are typically rhythmic simple movements such as waving or flapping the hands or arms. Still, they may consist of more complex sequences or movement fragments. Stereotypies can affect the fingers, wrists, or other parts of the upper extremities. In contrast, involvement of the lower extremities is less common, especially in children. These movements can occur on one side (unilateral) or both sides (bilateral) but are more frequently bilateral. No premonitory urge is associated with these movements, and they typically arise when a child is stressed, excited, distracted, or deeply engaged in an activity. Stereotypies can be interrupted by distraction or by beginning another activity. Generally, they do not interfere with the

child's ability to perform tasks. A stereotype involves repeating a single movement multiple times, rather than a set of different recognizable movements. Each movement has a clear beginning and ending, but the duration of the stereotypy is variable and can continue for many minutes at a time¹³.

Table 9 - Key features of Hyperkinetic Disorders.

	Rhythmic	Repeated posture	Repeated stereotyped movement
Dystonia	Rarely	Yes	Sometimes
Chorea	No	No	Rarely
Athetosis	No	No	No
Myoclonus	Sometimes	Sometimes	Usually
Tremor	Yes	No	Yes
Tics	No	Yes	Yes
Stereotypies	Yes	Sometimes	Yes

Sanger et al.

Table 10 - Elements of the Clinical Examination of Hyperkinetic Disorders^{13,20}.

	Dystonia	Chorea	Athetosis	Myoclonus	Tremor	Tics	Stereotypies
Distractibility	No	No	No	No	No	Yes	Yes
Suppressibility	Partial	No	No	No	Briefly	Usually	Yes
Duration	Variable	Ongoing	Ongoing	Shock-like	Ongoing	Variable	Variable
Speed	Variable	Medium – fast	Slow – medium	Very fast (<1 s)	2- 14 Hz	Variable	2 – 6 Hz
Jerkiness	Sometimes	Sometimes	No	Very	Sometimes	Sometimes	Rarely
Stereotyped	Often	No	No	Usually	Yes	Yes	Yes
Rhythmic	Sometimes	No	No	Sometimes	Yes	Usually not	Yes
Intermittent	Sometimes	Sometimes	No	Sometimes	Sometimes	Yes	Yes
Ongoing	Sometimes	Yes	Yes	Sometimes	Yes	No	Yes
Flowing	No	Yes	Yes	No	No	Sometimes	Sometimes
Submovements	No	Yes	Maybe	No	No	Sometimes	No
Context	Movement > rest	Movement > rest	Rest > movement	All	Variable	Rest	Rest
Predictable	Sometimes	No	No	No	No	Yes	Often not aware
Normal pattern	Sometimes	Yes	Yes	No	Yes	Yes	Yes

Sanger et al.

Developmental Movement Disorders:

In the event that a child has a movement issue, it often raises concerns about the possibility of a serious underlying issue, such as a progressive, degenerative, or metabolic disease. Nonetheless, a large number of childhood movement abnormalities are benign and associated with typical growth phases.

The developing nervous system can produce various motor patterns that, while pathological in older individuals and youngsters, are simply signs of central nervous system (CNS) immaturity in young children. Similar to many neonatal reflexes—such as grasping, rooting, placing, and tonic neck reflexes—these motor patterns typically disappear as neuronal network connectivity and myelination progress.

Table 11: Transient, Developmental Movement disorders of Infancy & Childhood

Disorder	Age at onset	Age at resolution	Treatment
Benign neonatal sleep myoclonus	Less than 1 month	Six months	Reassurance
Benign myoclonus of early infancy	3-9 months	Typically by 15 months	Reassurance
Jitteriness	1 st week of life	Typically before 6 months	Reassurance
Shuddering	Infancy, early childhood	Unknown	Reassurance
Paroxysmal tonic Upgaze (downgaze) of infancy	Typically the first year of life	Usually age 1-4 years	Levodopa may be effective
Spasmus nutans	3-12 months	In a couple months, but subtle nystagmus may persists for years	Reassurance
Head nodding	Before age 3 years	May persist for years	Reassurance
Benign paroxysmal Torticollis	First year of life	By 5 years	Topiramate may be effective
Benign idiopathic Dystonia of infancy	Before 5 months	By 1 year	Reassurance
Infantile masturbation	Before 3 years	Becomes more covert	Reassurance

Table 12: Salient features from earlier research on childhood movement disorders:

Study	Year	Place	Total Enrolled Cases and type of study	Age Group	Phenomenology	Etiology	Neuroimaging	ExclusionCriteria
Dale et al ²²	2006	Sydney, Australia	52 patients; prospective study	2 months-15 years	<ol style="list-style-type: none"> 1. Chorea (20 cases) 2. Dystonia (17 cases) 3. Tremor (12 cases) 4. Myoclonus (10 cases) 5. Parkinsonism (10 cases) 	<ol style="list-style-type: none"> 1. inflammatory or autoimmune disorders (n=22) <ol style="list-style-type: none"> a. N-methyl-D-aspartate receptor encephalitis (n=5), b. opsoclonus–myoclonus syndrome (n=4), c. Sydenham chorea (n=3), d. systemic lupus erythematosus (n=3), e. acute necrotizing encephalopathy (n=3), f. other types of encephalitis (n=4) 2. non-inflammatory disorders (n=18), <ol style="list-style-type: none"> a. drug-induced movement disorder (n=6), b. post-pump chorea (n=5), c. metabolic (n=3) d. vascular (n=2) disease 3. psychogenic disorders (n=12) 	Basal ganglia lesions (globus pallidum and putamen) as the hallmark features of dystonia	<ol style="list-style-type: none"> 1. Tics, paroxysmal movement disorder, genetic or metabolic causes, and acquired brain injuries 2. Neonates and infants with transient or benign movement disorders, 3. acute-onset cerebellar syndromes (postinfectious cerebellar ataxia and cerebellitis)

<p>Baumer et al⁶⁶</p>	<p>2004 to 2013</p>	<p>Germany</p>	<p>606 consecutive patients; cohort study</p>	<p>Below 18 years</p>	<ol style="list-style-type: none"> 1. tic disorders (57%) 2. dystonia (12%), 3. psychogenic movement disorders (4%) 4. paroxysmal movement disorder (4%) 5. stereotypies (3%) 6. chorea (3%) 7. ataxia (3%) 8. myoclonus (2%) 9. tremor (2%) 10. hypokinetic (2%) 	<ol style="list-style-type: none"> 1. dystonia syndromes(12%) <ol style="list-style-type: none"> i. DYT-TOR1A (early-onset generalized dystonia)- 7 cases ii. DYT-GCH1 (dopa-responsive dystonia) 3 cases iii. DYT-THAP1 (adolescent-onset dystonia of mixed type) 1 case iv. DYT-MR-1 (paroxysmal nonkinesigenic dyskinesia) 2 cases v. DYT-PRRT2 (paroxysmal kinesigenic dyskinesia) 4 cases vi. DYT-SGCE (myoclonus dystonia) vii. DYT-SLC2A1 (paroxysmal exertion-induced dyskinesia) 1 case 2. psychogenic (4%) 3. ADHD related (3%) 4. Genetic causes (17%) (ataxia teleangiectasia, Neimann Pick type C, glutaric aciduria, Friedreich ataxia) 	<p>No imaging done</p>	<p>Cerebral palsy</p>
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Goraya et al⁷	2010-2014	Punjab	92 children; retrospective study	Up to 18 years	<ol style="list-style-type: none"> 1. Myoclonus (25 cases), 2. dystonia (21 cases), 3. Choreoathetosis (19 cases), 4. Tremors (15 cases), 5. Tics (2 cases), 6. Parkinsonism (3 cases) 	<ol style="list-style-type: none"> 1. inflammatory aetiology- 32 cases. <ol style="list-style-type: none"> i. Autoimmune – 17 cases ii. Infectious- 13 cases 2. Non-inflammatory aetiology- 60 cases <ol style="list-style-type: none"> i. Physiological – 17 children ii. Nutritional/ metabolic – 25 children (infantile tremor syndrome- 13 cases and hypocalcemia- 3 cases) iii. inborn error of metabolism-8 case (Leigh disease, PKAN, MELAS, glutaric aciduria) iv. psychogenic- 4 cases v. drugs- 3 cases. 	white matter and basal ganglia lesions in chorea and myoclonus	cerebellar syndromes such as cerebellitis, paroxysmal dyskinesias, and nonepileptic seizures were excluded
Param-eshwarappa NN et al⁶⁸	2018 to 2019	South India	100 cases; prospective study	2 months – 18 years	<ol style="list-style-type: none"> 1. dystonia (39%), 2. choreoathetosis (29%) 3. tremors (22%) 4. gratification reaction (7%), 5. shuddering attacks (4%), 6. tremors (22%), 7. ballismus (3%), 8. myoclonu 3% 9. tics, stereotypes, and 	<ol style="list-style-type: none"> 1. Prenatal insult (27%); HIE (19%) followed by BIND (5%) 2. Infectious/ immune (22%)- NMDAR encephalitis 7%, rheumatic chorea and infection each 5%, SSPE 3%. 3. Metabolic/hereditary/genetic were 25% (Leigh's disease 6%, glutaric aciduria and Wilson's each 4%, NCL 3%) 	The basal ganglia and the white matter changes in the brain are the key contributors.	epilepsy patients were excluded

					hypokinesia 2% each	4. Psychogenic causes (8%) 5. Miscellaneous (18%)- Infantile tremor syndrome 16%, tic disorder 2%		
Ahirrao et al ¹⁴	2015	Dhule, India	64 patients, prospective study	Under 15 years of age	1. Tremors (38.23%), 2. Hemiballismus (16.20%). 3. Ataxia (13.23%), 4. Tics (10.29%), 5. Dystonia (7.35%), 6. Choreoathetosis (4.41%), 7. Myoclonus (2.94%), 8. chorea (2.94%), 9. Psychogenic movement disorders (6.25%).	1. Infectious etiology (71.87%) a. CNS tuberculosis (65.38%), b. Post varicella (7.69%), c. Post measles (7.69%), d. Viral meningoencephalitis (7.69%), e. Brain abscess (7.69%), f. Pyogenic meningitis (3.86%). 2. Non-infectious etiologies (43.48%), a. Cerebral palsy (40%), b. Delayed milestones with MR (15%) c. Post traumatic (10%) d. Congenital causes 3. Non-neurological etiology (28.13%), a. Drug toxicity (55.56%) b. Psychogenic (6.24%) c. Nutritional recovery syndrome (3.12%) d. Sydenham's chorea (1.56%)	CT scan done in 27 cases (58.70%). Most frequently, hydrocephalus was discovered followed by tuberculomas (23.52%), basal exudates, and infarcts. MRI done in 19 cases (41.30%) - cystic encephalomalacia 7 cases (36.8%) periventricular leukomalacia 4 cases (21%), hyperintense basal ganglia 1 case.	Non availability of consent

Limitations of previous studies

Previous studies on movement disorders have had certain limitations including small sample sizes and a lack of accuracy in defining the movement disorders. Children with cerebral palsy, a major contributor to movement abnormalities in children, have not been included in the majority of the studies. Neuroimaging data and correlation with the movement disorders was only available for a subset of the patients, and most studies did not include genetic evaluations. Furthermore, standard guidelines for analysing exome sequencing data were often not employed, and some studies relied on retrospective data collection.

Very few studies specifically focus on cohorts within the Pediatric age group. Most of the existing research data has come from Western countries, with limited studies available from South Asia.

Clinical implications of studying the clinical spectrum of movement disorders:

Identifying the phenomenology and studying the clinic etiological range of childhood movement problems has several important advantages:

1. Targeted Treatment: Accurate diagnosis allows for developing tailored treatment plans that address the specific type of movement disorder. Different disorders, such as tics, stereotypies, or chorea, may respond better to certain therapies, whether pharmacological or behavioural.
2. Improved Outcomes: More effective interventions may result from early and accurate identification, which may enhance general functioning and lessen the influence of the movement disorder on the child's day-to-day activities. Their

capacity to engage in activities and their quality of life may both be improved by this.

3. **Avoidance of Misdiagnosis:** Misidentifying a movement disorder can lead to inappropriate treatments, which may exacerbate the child's symptoms or create new challenges. Understanding the specifics of the disorder helps prevent unnecessary interventions that may not be beneficial.
4. **Informing Prognosis:** Understanding the particular kind of movement disorder can provide valuable prognostic information, helping families and caregivers understand potential developmental trajectories and long-term implications.
5. **Interdisciplinary Management:** Correctly categorizing the disorder can facilitate collaboration among healthcare professionals, including neurologists, paediatricians, occupational therapists, and psychologists, ensuring a comprehensive approach to care.
6. **Educational Support:** Identifying the nature of a child's movement disorder can assist educators in creating appropriate support strategies within the school environment, accommodating the child's needs, and enhancing learning experiences.
7. **Research Contributions:** Understanding childhood movement disorders contributes to broader research efforts to discover more effective treatments and understand underlying mechanisms, ultimately benefiting future patients.

NEED FOR THE STUDY

1. Childhood movement disorders are most often secondary than primary; that is, they are more often associated with lesions of the brain such as cerebral palsy, traumatic brain injury, or stroke as opposed to being a primary condition.
2. Many movement disorders are difficult to treat completely, so treatment can just control or reduce the movements. Because of limited studies, evidence-based therapeutic options are difficult to identify.
3. The spectrum and etiology of movement disorders are likely to differ in different geographic areas of the world.
4. The range, forms, and causes of childhood movement disorders in India and other developing nations are the subject of relatively few investigations.
5. Most studies excluded cerebral palsy, but it contributes to the majority of movement-related disorders. So, in this research, we plan to include cerebral palsy children.

MATERIALS AND METHODS

This study was conducted from July 2022 to July 2023 in the department of Paediatrics at Jawaharlal Nehru Medical College and the KLES Dr Prabhakar Kore Hospital and Medical Research centre (MRC), a 2400 bedded hospital located in Belagavi, Karnataka, India.

Study Design: Hospital based cross sectional study.

Source of data: Children with movement disorders (less than or equal to 18 years old) attending Paediatric Neurology OPD or admitted in Pediatric ward at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi

Sample Size: Sample size was calculated to be 148. Considering the proportion of 24.9% of patients with involuntary movement along with other symptoms studied by Ahirrao M et al,¹⁴ with 95% as type I error, the power of 80% with precision as 7, the sample size calculated was 148. The formula used to calculate was

$$n = \frac{Z^2 pq}{d^2}$$

where Z (95% confidence or 5% alpha error) – 1.96; d (Margin of error) – 7; p (Prevalence of dystonia) – 24.9%; q (alternative prevalence) – 75.3%.

Inclusion Criteria

1. Patients with any form of movement disorder between the age 1 month to 18 years of age attending Paediatric Neurology outpatient department or admitted at KLE's Prabhakar Kore hospital and research centre.

Exclusion Criteria

1. Newborns
2. Those who denied consent for Neuroimaging or any other relevant investigations.

Ethical clearance: The institutional ethical committee of Jawaharlal Nehru Medical College, Belagavi, approved the study before it started (**REF No. MDC/JNMCIEC/211**).

Informed Consent: The study's nature was explained to the child and/or the parents of children with movement disorders who met the eligibility criteria. Written informed consent was also collected prior to enrolment in a language that they were familiar with (Annexure I).

Study Protocol: Informed consent was taken from parent/guardian of all patients.

Based on the verbal and cognitive ability of the child, if possible, verbal assent was taken for children aged 7-12 years and written assent was taken from children aged 13-18 years. Children with any kind of movement disorder who presented to outpatient department were evaluated with a detailed history including birth history, developmental history, family history, type of movement disorder, time of onset of symptoms, progression (if any) and associated history of seizures, sensory abnormalities, feeding difficulties, hearing deficits, visual deficits, musculoskeletal problems and behavioural problems.

Clinical examination including a detailed neurological examination was done by the same Paediatric neurologists. The children with movement disorder were examined, atleast 1min video of the abnormal movements was recorded and assessed

by two Pediatric neurologists and the phenomenological classification was assigned. Relevant diagnostic evaluation including MRI brain was performed. The clinical data like demographics, clinical features, aetiology and neuroimaging correlation was recorded. Whenever required, children with movement disorders who were suspected to have a genetic aetiology, were subjected to Whole Exome Sequencing (WES) by Next Generation sequencing on a peripheral blood sample. Genetic test results were reported based on the recommendations of American College of Medical Genetics. Test results of Next generation sequencing were clinically correlated and interpreted. In case of clinical phenotype match in variants of unknown significance, sanger sequencing of parents was attempted wherever consent was given, reclassification was checked in online databases such as ClinVar to re-categorize as pathogenic or likely pathogenic cases.

Statistical Analysis:

The data was entered in MS EXCEL (Ver_2007) software. Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) (Version 24.0, developed by IBM Corp, Armonk, New York) software. To minimize the errors in data entry, data cleaning for the variables were done. To know the presence of any blank or null data in the datasheet as a missing or not applicable data, separate numbers '99' were assigned and '00' for others respectively. The legal values were decided for categorical variables, not for continuous variables.

Before performing the analysis, an inspection of each field of variables in the data set was done for missing values, blank values, and typographical errors. In case of any uncertainties, the unique identifying code created for each respondent was used to trace the questionnaires and the information was cross-checked and re-entered.

Descriptive statistics were calculated for all categorical variables were added in the study were distribution of age, gender, classification and spectrum of MD, clinical neurological presentation (CP, epilepsy), etiology and subcategory of etiological cause, were measured in terms of frequencies and percentages. Continuous variables such as age were calculated and presented as mean and standard deviation (SD) based on the distribution of the variable.

Inferential statistics used in the study were Pearson's chi-square test, and correlation. The type of variables used to analyse the data and the normal distribution between two groups, males and females. Categorical variables which follow nonparametric distribution were analyzed using Pearson's Chi-square test or two-tailed Fisher's exact test. Variables include age categorization, birth history, neurological findings, classification of MD, etiology of MD. Added to this, odds ratio (OR) was calculated for the risk factors to assess the risk for developing dystonia among the study participants.

Statistical significance was considered as a p value of <0.05 for the data analyzed.

RESULTS

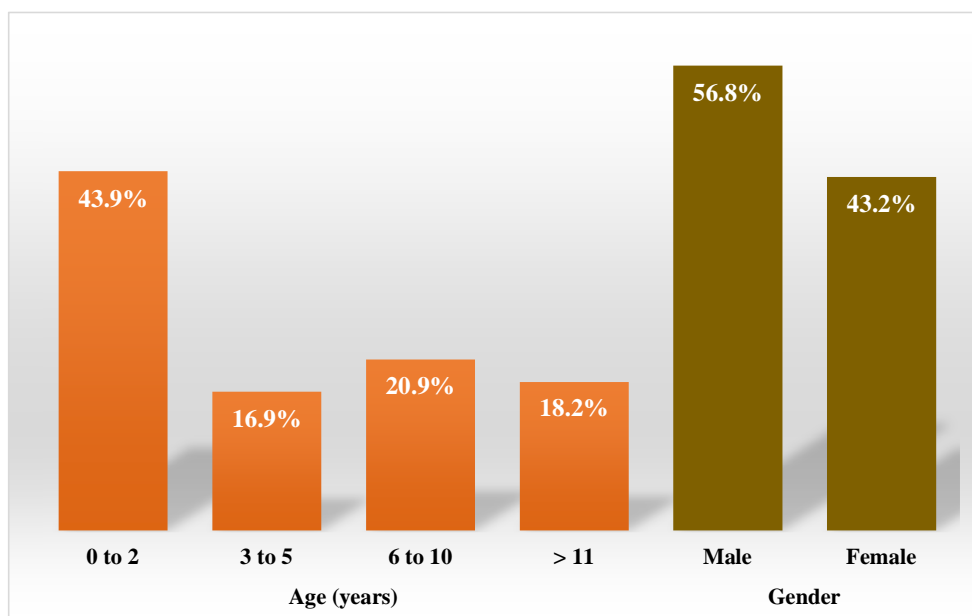
During the study period, 148 children with movement disorders (age of less than 18 years) attending the Paediatric Neurology OPD or admitted in the Pediatric ward, KLE s Dr Prabhakar Kore hospital were enrolled into the study and detailed clinical history, examination, movement disorder phenomenology and neuroimaging findings were documented. One minute video of the abnormal movements was recorded and analysed by two Pediatric Neurologists.

Table 13: Descriptive analysis of age and sex of the study population (N = 148)

Variables	n (%)
Age (in years)	
0 – 2	65 (43.9)
3 – 5	25 (16.9)
6 – 10	31 (20.9)
> 11	27 (18.2)
Mean \pm SD	5.43 \pm 4.86
Gender	
Male	84 (56.8)
Female	64 (43.2)

The children's presentation age was 5.43 years on average, with a standard deviation of 4.86 years. Among the participants, 84 (56.8%) were male, while 64 (43.2%) were female.

Figure 3: Bar chart showing Age and gender distribution among the study participants



Among the participants, 65 children (43.9%) were under two years old. Of the children, 25 (16.9%) were between the ages of three and five, and 31 (20.9%) were between the ages of six and ten. The remaining 27 children (18.2%) were older than eleven years.

Table 14: Age of onset of the movement disorder (N = 148)

Variables	Mean \pm SD
Overall age of onset (years)	2.70 \pm 3.87

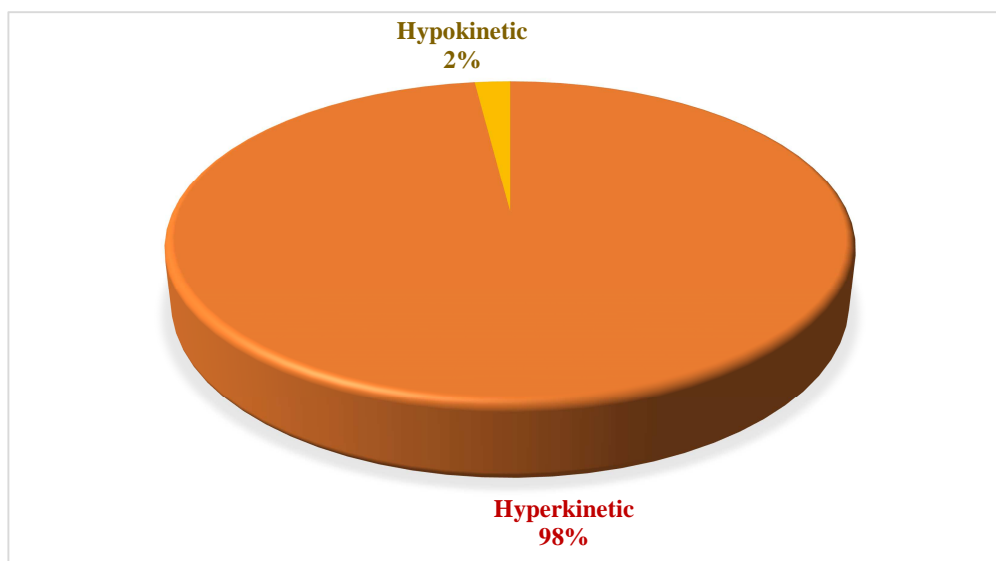
The mean age of onset of movement disorder observed in our study population is 2.70 \pm 3.87 years.

Table 15: Classification of movement disorders among the study participants (N = 148)

Variables	Total (N = 148)	p value
Hyperkinetic	145 (98.0)	0.726
Hypokinetic	3 (2.0)	

Pearson's chi-square; Nominal and non-parametric; p value <0.05 is statistically significant indicated by boldface. Values given in brackets were percentage

Figure 4: Pie-chart representing the classification of the movement disorder (N = 148)

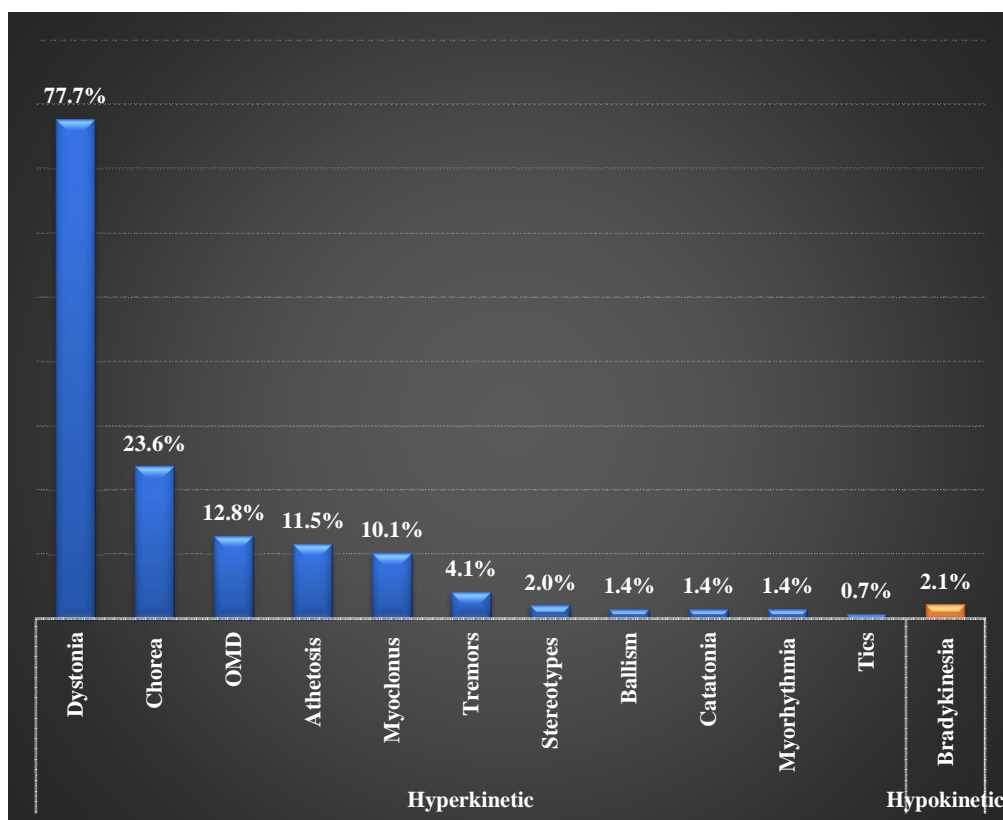


Among the 148 study participants, 98% (145 children) exhibited hyperkinetic movement disorders, while the remaining three patients (2%) had hypokinetic movement disorders.

Table 16: Phenomenology of the movement disorder among the study participants (N = 148)

Variables	Total (N = 148)
Hyperkinetic movement disorder	145 (98.0)
Dystonia	115 (77.7)
Chorea	35 (23.6)
Oro-motor dyskinesia	19 (12.8)
Athetosis	17 (11.5)
Myoclonus	15 (10.1)
Tremors	6 (4.1)
Stereotypes	3 (2.0)
Ballism	2 (1.4)
Catatonia	2 (1.4)
Myorhythmia	2 (1.4)
Tics	1 (0.7)
Hypokinetic movement disorder	3 (2.1)
Bradykinesia	3 (2.1)

Figure 5: Bar-chart representing the phenomenology of the movement disorder among the study participants (N = 148)



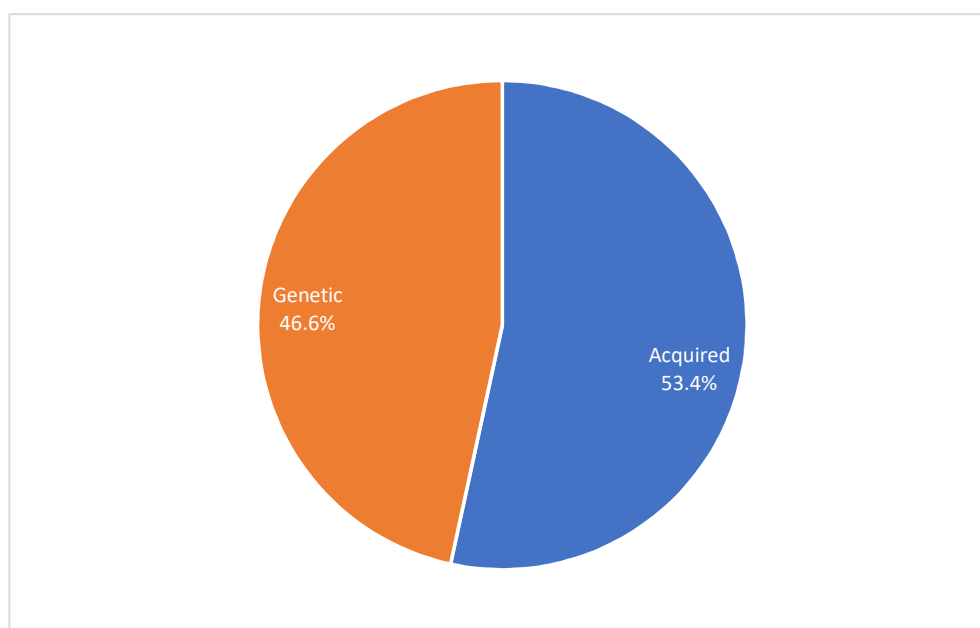
In participants with hyperkinetic movement abnormalities, 115 (77.7%) had dystonia. Chorea was seen in 35 patients (23.6%), oro-motor dyskinesia in 19 patients (12.8%), athetosis in 17 children (11.5%), and myoclonus in 15 children (10.1%). Additionally, tremors were present in six patients (4.1%), stereotypes were noted in three patients (2%), and two patients (1.4%) had ballism. Two patients (1.4%) presented with catatonia, while myorhythmia in two children (1.4%). One had tics (0.7%). Bradykinesia was observed in three children (2.1%), which is classified under hypokinetic movement disorder.

Table 17: Aetiology of the movement disorder among the study participants (N = 148)

Variables	Total (N = 148)	p value
Acquired	79 (53.4)	0.041
Genetic	69 (46.6)	

Pearson's chi-square; Nominal and non-parametric; p value <0.05 is statistically significant indicated by boldface. Values given in brackets were percentage

Figure 6: Pie chart showing aetiology of the movement disorders.



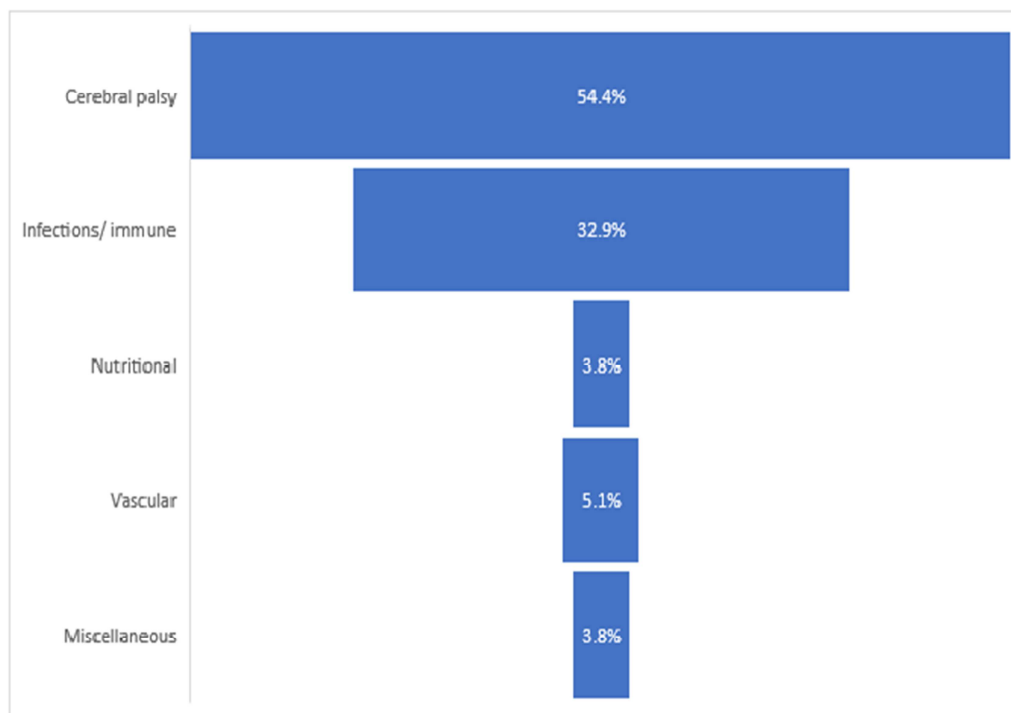
About 53.4% of the patients (79 out of 148) had a movement disorder caused by acquired aetiology and 46.6% (69 out of 148) had a movement disorder due to genetic aetiology.

Table 18: Acquired etiological profile of movement disorders among the study participants.

Variables	Total	p value
Subcategory of the acquired etiological cause of movement disorder (n = 79)		
Cerebral palsy	43 (54.4)	0.713
Infections/ immune	26 (32.9)	
Nutritional	3 (3.8)	
Vascular	4 (5.1)	
Miscellaneous	3 (3.8)	

Pearson's chi-square; Nominal and non-parametric; p value <0.05 is statistically significant indicated by boldface. Values given in brackets were percentage

Figure 7: Bar chart representing acquired etiological profile of movement disorders among the study participants. (N = 79)



Out of 79 patients with acquired conditions, 43 children (54.4%) had cerebral palsy. Furthermore, 26 patients (32.9%) had conditions associated with infections or immune-related causes. Nutritional factors accounted for 3 children (3.8%), 4 children (5.1%) were identified with vascular conditions, and 3 patients (3.8%) were categorized under miscellaneous conditions.

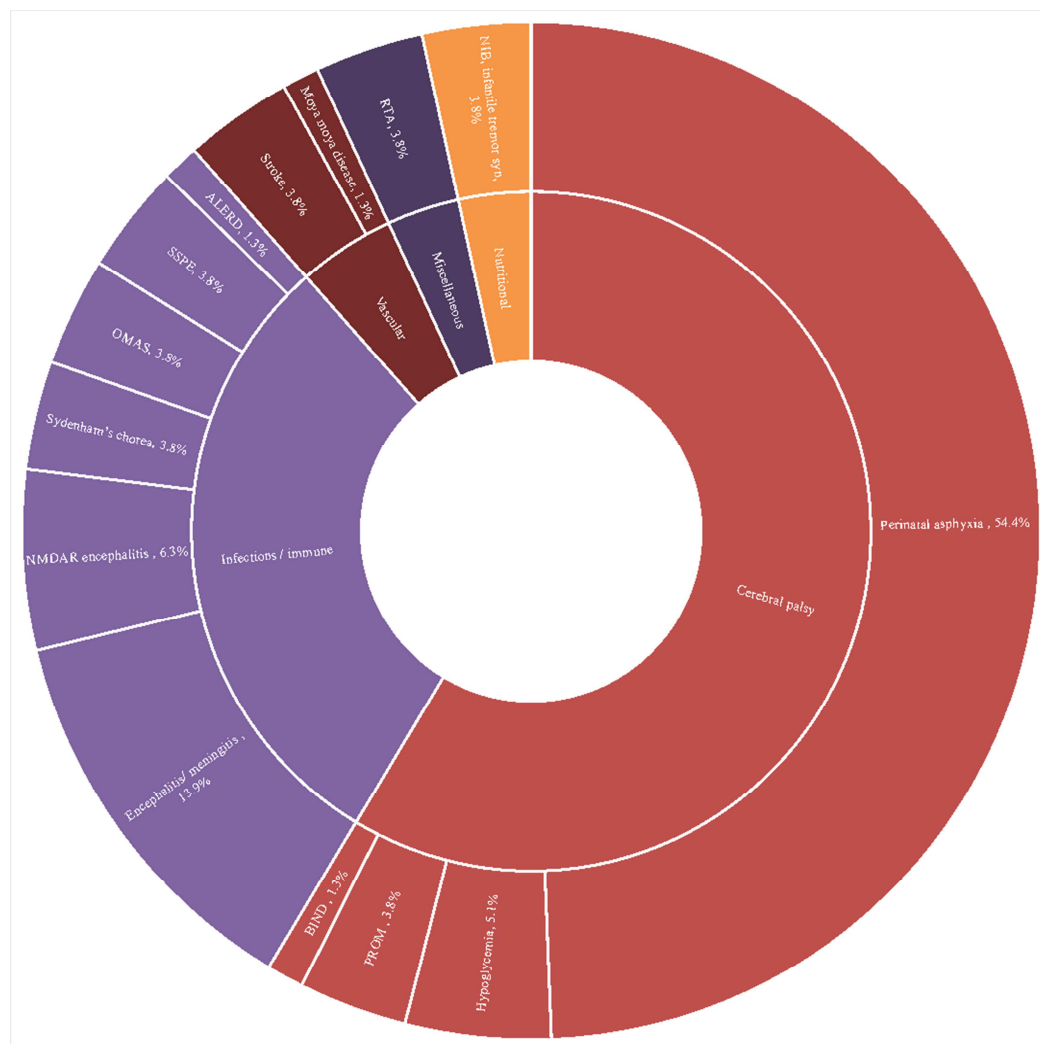
Table 19: Sub-categorization of acquired aetiology among the study participants

(n = 79)

Variables	Total (n = 79)
Acquired etiology	
Sub-category 1: cerebral palsy	43 (54.4)
Perinatal asphyxia	35 (44.3)
BIND	1 (1.3)
Hypoglycemia	4 (5.1)
PROM	3 (3.8)
Sub-category 2: Infections/immune	26 (32.9)
Encephalitis/ meningitis	11 (13.9)
NMDAR encephalitis	5 (6.3)
Subacute sclerosing Panencephalitis	3 (3.8)
Opsoclonus myoclonus ataxia syndrome	3 (3.8)
Sydenham's chorea	3 (3.8)
ALERD	1 (1.3)
Sub-category 3: Nutritional	3 (3.8)
Infantile tremor syndrome/ Neurocutaneous Infantile B12 deficiency (NIB)	3 (3.8)
Sub-category 4: Vascular origin	4 (5.1)
Stroke	3 (3.8)
Moya Moya disease	1 (1.3)
Sub-category 5: Miscellaneous	3 (3.8)
Road-traffic accident	3 (3.8)

Values given in brackets were percentage. BIND – Bilirubin induced neurologic dysfunction; PROM – preterm or premature rupture of membrane; NMDAR - Anti-N-methyl-D-aspartate receptor encephalitis; SSPE - Subacute sclerosing panencephalitis; OMAS - Opsoclonus-myoclonus-ataxia syndrome; ALERD - Acute leukoencephalopathy with restricted diffusion.

Figure 8: Pie chart representing sub-categorization in children with acquired aetiology (n = 79)



Among the 54.4% of cases with cerebral palsy, 44.3% were due to perinatal asphyxia, followed by hypoglycemia 5.1%, premature rupture of membrane (PROM) 3.8%, and bilirubin-induced neurologic dysfunction (BIND) 1.3%. The infectious/immune causes constitute encephalitis/meningitis in 13.9% of cases followed by NMDAR encephalitis in 6.3% of cases. Where Subacute sclerosing panencephalitis (SSPE), Opsoclonus-myoclonus-ataxia syndrome (OMAS), and Sydenham's chorea were seen in 3.8% cases each, Acute leukoencephalopathy with restricted diffusion

(ALERD) was seen in one (0.9%) cases. Among nutritional causes, neurocutaneous infantile B12 deficiency contributed to 3.8% of cases. Vascular cause includes stroke (3.8%) and Moya Moya disease (1.3%). 3.8% of research participants had a movement disorder as a result of diffuse axonal injuries sustained in collisions with vehicles.

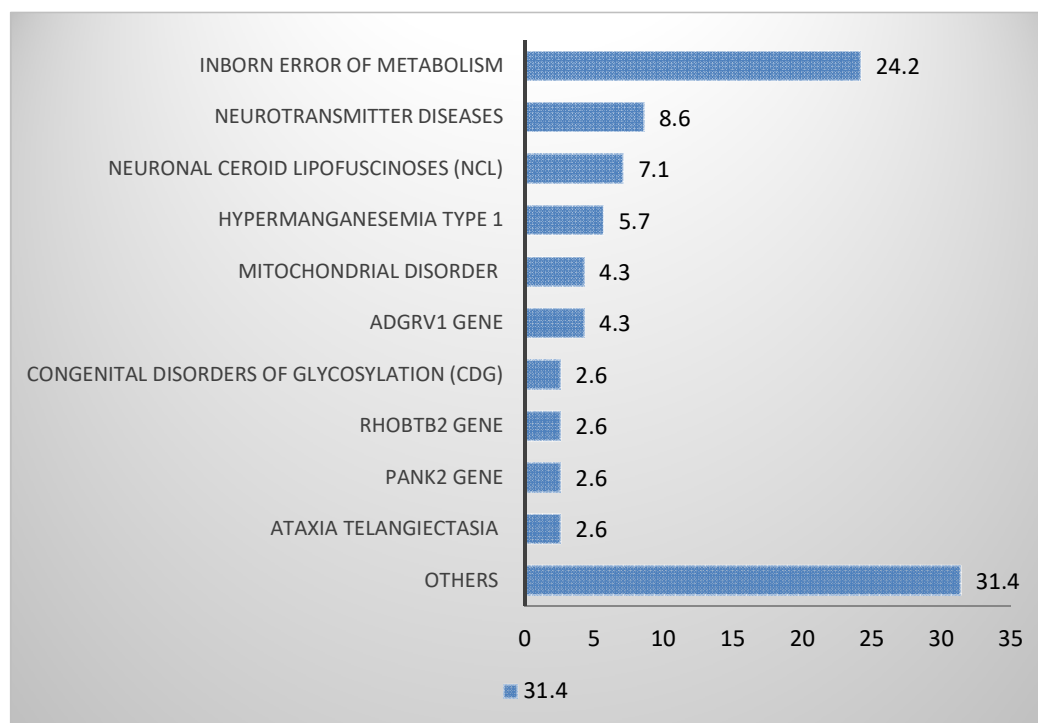
Table 20: Genetic causes of movement disorders in children (n = 69)

Variables		Total (n = 69)
Inborn error of metabolism	Organic acidemias	11 (15.7)
	Hyperphenylalaninemia	2 (2.9)
	Molybdenum cofactor deficiency	1 (1.4)
	Sulfite oxidase deficiency	1 (1.4)
	MSUD	1 (1.4)
	Thiamine Metabolic Dysfunction Syndrome 5	1 (1.4)
Neurotransmitter diseases		6 (8.6)
Neuronal ceroid lipofuscinoses (NCL)		5 (7.1)
Hypermagnesemia Type 1		4 (5.7)
Mitochondrial disorder		3 (4.3)
ADGRV1 gene		3 (4.3)
Congenital Disorders of Glycosylation (CDG)		2 (2.6)
RHOBTB2 gene		2 (2.6)
PANK2 gene		2 (2.6)
Ataxia telangiectasia		2 (2.6)
Others		22 (31.4)
Others (n = 22)		
Rett syndrome		2 (2.8)
LSS		2 (2.8)
PCDH12		2 (2.8)
CNNM2		1 (1.4)
MECR		1 (1.4)
COQ8A		1 (1.4)
PLCB1		1 (1.4)
NKX 2-1		1 (1.4)
EIF2AK2		1 (1.4)
ATP8A2		1 (1.4)
ACOX1		1 (1.4)
TSEN54		1 (1.4)
MAPT		1 (1.4)
KMT2B		1 (1.4)
TTC19		1 (1.4)
RNASEHC		1 (1.4)
CACNA1A		1 (1.4)
Joubert syndrome		1 (1.4)
Krabbe's disease		1 (1.4)
Wilson's disease		1 (1.4)

Values given in brackets were percentage. NCL - Neuronal ceroid lipofuscinoses; CDG - Congenital Disorders of Glycosylation; ADGRV1 - Adhesion G protein-coupled receptor V1; RHOBTB 1 - Rho-related BTB domain-containing

protein; AADC - Aromatic l-amino acid decarboxylase; PANK 2 - Pantothenate kinase 2; CNNM2 - Cyclin M2; MECR - Mitochondrial Enoyl CoA Reductase Protein; COQ8A - Coenzyme Q8A; LSS - Lumbar spinal stenosis; PLC β 1 - Phospholipase C- β 1; NKX2-1 - Homeobox protein; EIF2AK2 - Eukaryotic translation initiation factor 2 alpha kinase 2; ATP8A2 - ATPase phospholipid transporting 8A2; ACOX1 - Acyl-CoA oxidase 1; MAPT - Microtubule-associated protein tau; PCDH12 - Protocadherin 12; KMT2B - Lysine methyl transferase 2B; TTC19 - Tetratricopeptide; RNASEHC - Ribonuclease H subunit C; CACNA1A - Calcium channel subunit alpha 1 A; GCDH - Glutaryl-CoA dehydrogenase.

Figure 9: Diagrammatic representation for the cause of movement disorder on genetic aetiology (n = 69)



The above table shows the various genetic causes and genes identified in this study, along with the frequency and percentages. The most common genetic aetiology in our study were Inborn errors of metabolism n=17 (24.3%), which included Organic acidemias (15.7%), Hyperphenylalaninemia (2.9%), Molybdenum cofactor deficiency (1.4%), Sulfite oxidase deficiency (1.4%), Thiamine metabolic dysfunction syndrome 5 (1.4%). Other genetic causes include Neurotransmitter diseases in 6 patients (8.6%), followed by Neuronal ceroid lipofuscinoses (NCL) in 5 patients (7.1%), Hypermanganeemia Type 1 in 4 patients (5.7 %), mitochondrial disorders in 3 patients (4.3%), ADGRV1 gene mutation was seen in 3 patients (4.3%). Congenital Disorders of Glycosylation (CDG), Ataxia telangiectasia, RHOBTB2 gene and PANK2 gene mutation each had two cases. 22 patients with single gene mutation contributed 1.4% each to the genetic etiology of this study.

Table 21: Prevalence of different movement phenotypes among genetic aetiology:

Genes	Dystonia	Chorea	Tremor	Myoclonus	Athetosis	Stereotypies	Ataxia	Bradykinesia
Neurotransmitter diseases								
Neuronal ceroid lipofuscinoses (NCL)								
Hypermagnesemia Type 1								
Mitochondrial disorder								
ADGRV1 gene								
Congenital Disorders of Glycosylation (CDG)								
RHOBTB2 gene								
PANK 2 gene								
Ataxia telangiectasia								
Rett syndrome								
LSS								
PCDH12								
CNNM2								
MECR								
COQ8A								
PLCB1								
NKX2.1								
EIF2AK2								
ATP8A2								
ACOX1								
TSEN54								
MAPT								
KMT2B								
TTC19								
RNASEHC								
CACNA1A								
Joubert syndrome								
Krabbe's disease								
Wilson's disease								

The phenotypic of movement disorders with a genetic aetiology is shown in the above table. The most prevalent movement condition in this study that is seen in many patients with a genetic aetiology is Dystonia (Neurotransmitter diseases, ADGRV1 gene, RHOBTB2 gene, PANK 2 gene, LSS, CNNM2, MECR, NKX2.1,

EIF2AK2, ATP8A2, ACOX1, KMT2B, TTC19, RNASEHC, CACNA1A). Chorea, myoclonus, athetosis, tremors, and stereotypies were the other movement disorders seen in the patients. There was overlapping of different movements in the same patient (Neuronal ceroid lipofuscinoses (NCL), KMT2B, MAPT, ATP8A2, CNNM2, PCDH12). Hypokinetic cases in this study constitutes only 2%, all of which are due to genetic causes (Wilson's disease, Hypermagnesemia Type 1).

Table 22: Demographic and etiological profile of Dystonia among the study participants

Variable	Dystonia (n = 115)
Age (in years)	
0 – 2	58 (50.4)
> 3	57 (49.6)
Gender	
Male	68 (59.1)
Female	47 (40.9)
Acquired etiology	53 (46.1)
Cerebral palsy	40 (34.8)
Infection/immune	12 (10.4)
Nutritional	1 (0.9)
Genetic etiology	62 (53.9)
Inborn error of metabolism	11 (9.8)
Neurotransmitter diseases	6 (5.2)
Hypermagnesemia with dystonia Type 1	4 (3.5)
Neuronal ceroid lipofuscinoses (NCL)	4 (3.5)
Congenital Disorders of Glycosylation (CDG)	2 (1.7)
ADGRV1 gene	3 (2.6)
RHOBTB2 gene	2 (1.7)
PANK2 gene	2 (1.7)
Ataxia telangiectasia	2 (1.7)
Rett syndrome	2 (1.7)
PCDH12	2 (1.7)
KMT2B	1 (0.9)
TTC19	1 (0.9)
RNASEHC	1 (0.9)
CACNA1A	1 (0.9)
Joubert syndrome	1 (0.9)
CNNM2	1 (0.9)
MECR	1 (0.9)
COQ8A	1 (0.9)
Krabbe's disease	1 (0.9)

The above table summarizes the clinical and demographic characteristics of children with Dystonia. Age distribution shows a significantly higher proportion of young children < 2 years in the Dystonia group (50.4%); male representation was

higher (59.1%), though not statistically significant, suggesting that one gender does not seem to be particularly affected by dystonia.

Among 148 study participants, 115 patients had dystonia.

Children demonstrated generalised dystonia (86.95%) was more commonly than focal/ segmental dystonias (6.6%)

Assessing the aetiology, about 46.1% had an acquired cause, and 53.9% had a genetic cause. Among the acquired causes, dyskinetic CP, infections like Japanese encephalitis, and post-infectious disorders like mumps extrapyramidal syndrome were the predominant causes.

Coming to genetic causes, there were 6 cases of neurotransmitter disorders like L-Aromatic amino acid decarboxylase deficiency (L-AADC) deficiency, one NBIA spectrum disorder, 4 cases each of congenital disorders of glycosylation, and neuronal ceroid lipofuscinosis. Inborn errors of metabolism accounted for 11% of the cases of dystonia in this group.

Table 23: Movement disorders in cerebral palsy among total study participants.

Movement disorders in cerebral palsy	Total (n=52)
Dystonia	46 (88)
Chorea	10 (19.2)
Athetosis	7 (13.4)
Myoclonus	1 (1.9)
Tics	1 (1.9)

The above table highlights the various movement disorders in children with cerebral palsy. The most common movement problem in children with cerebral palsy was dystonia, which was followed by choreo-athetosis. Since many of the patients had multiple movement abnormalities, there was overlap in the disorders.

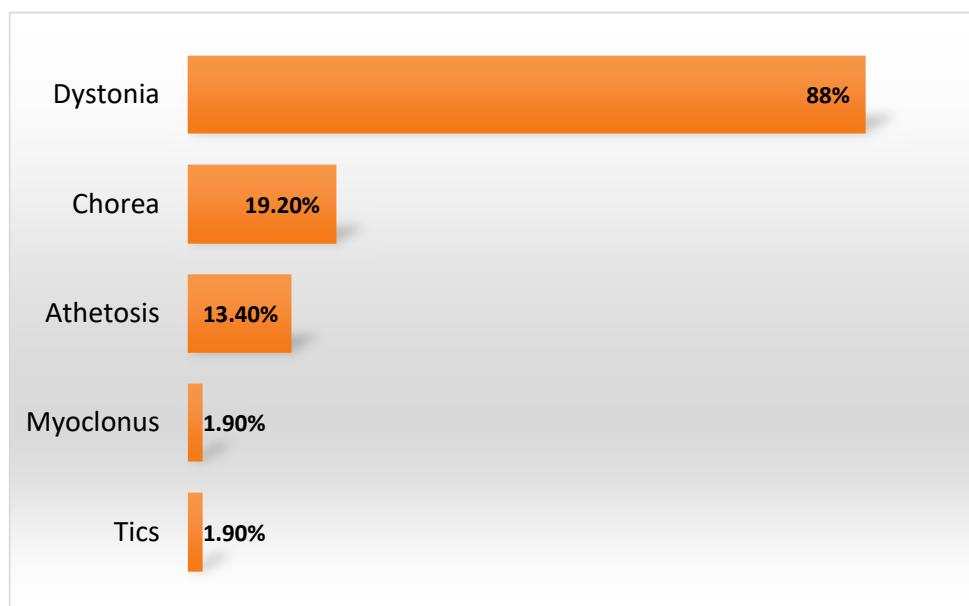
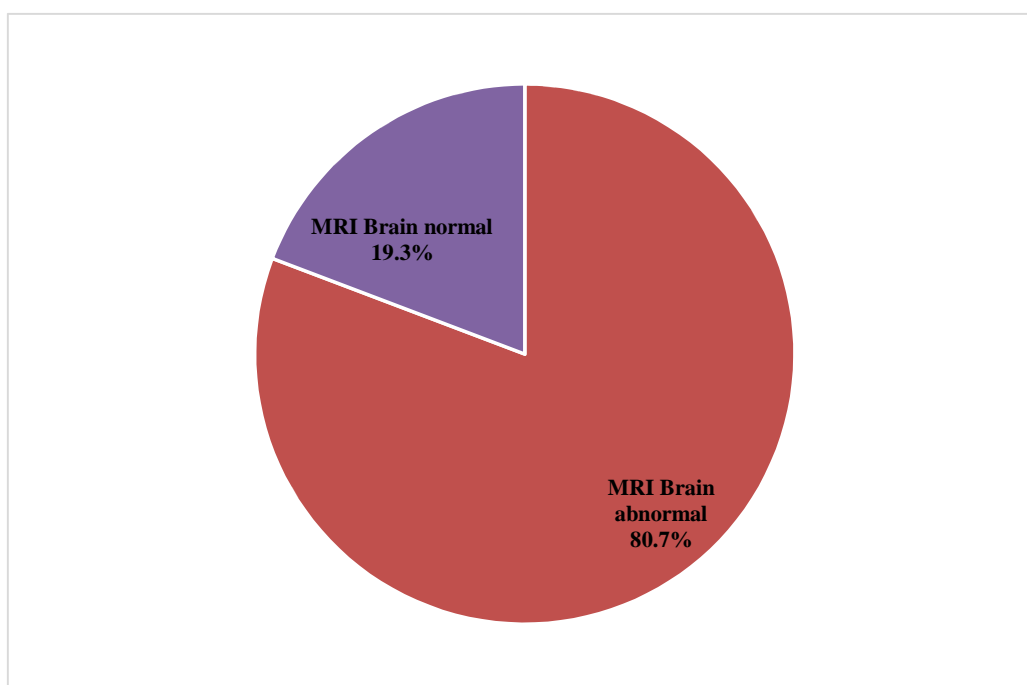
Figure 10: Bar chart showing movement disorders in cerebral palsy patients among total study participants (N = 52)

Table 24: Neuroimaging finding (MRI Brain) among the study participants (N = 140)

Variables	Total (N = 140)	p value
MRI Brain		
Abnormal	113 (80.7)	0.462
Normal	27 (19.3)	

Figure 11: Pie chart showing neuroimaging findings (MRI Brain) among the study participants (N = 140)

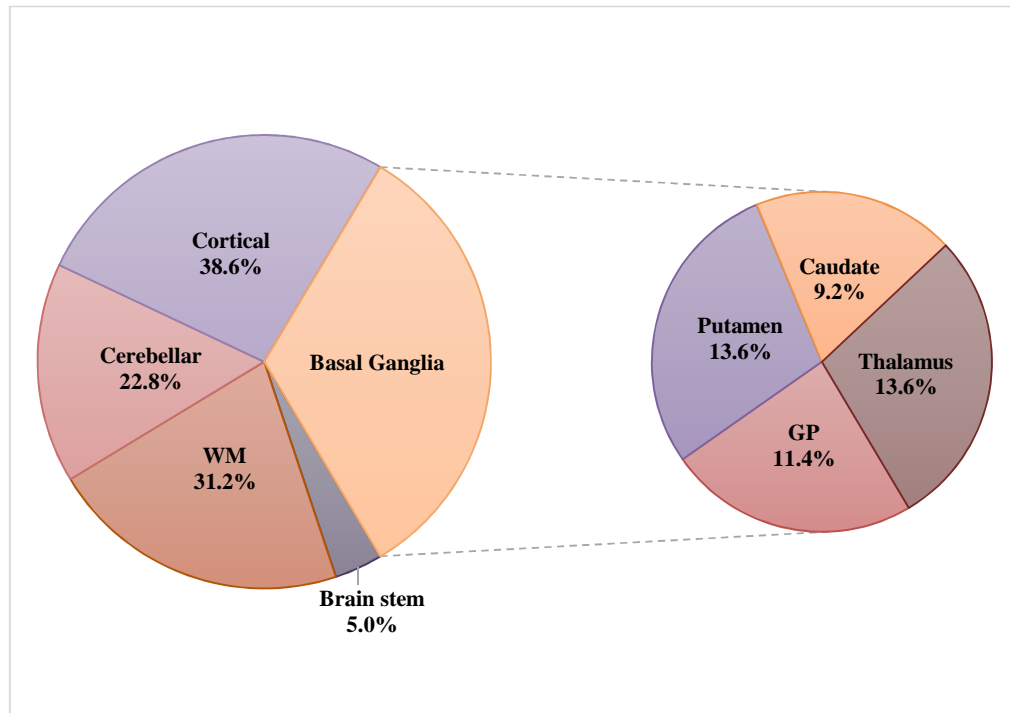


Out of 148 study participants, 140 underwent an MRI brain in which abnormalities were noted in 113 (80.7%) and normal MRI brain is seen in the remaining 27 (19.2%) patients.

Table 25: Neuroimaging findings (MRI Brain) showing lesions in various regions of the brain among the study participants (N = 140)

Variables	Total (N = 140)
Lesions in various regions of the brain	
I. Basal ganglia	67 (47.8)
Globus pallidum	16 (11.5)
Putamen	19 (13.5)
Caudate	13 (9.3)
Thalamus	19 (13.5)
II. Brain stem	7 (5)
III. White matter	44 (31.4)
IV. Cerebellar	32 (22.8)
V. Cortical	54 (38.5)

Figure 12: Pie chart showing lesion site in the MRI Brain findings among the study participants



In our analysis, Basal ganglia lesions were seen in 47.8% of children—putamen (13.6%), caudate (9.2%), thalamus (13.6%), and globus pallidum (11.4%). Lesion in the cortical area was seen in 38.6%, white matter abnormalities were seen in 31.2%, cerebellum in 22.8%, and brain stem lesions were found in 5% of the overall study participants.

Figure 13 - MRI brain of a child with mumps encephalitis showing T2 & FLAIR hyperintensities in B/L caudate and lentiform nucleus

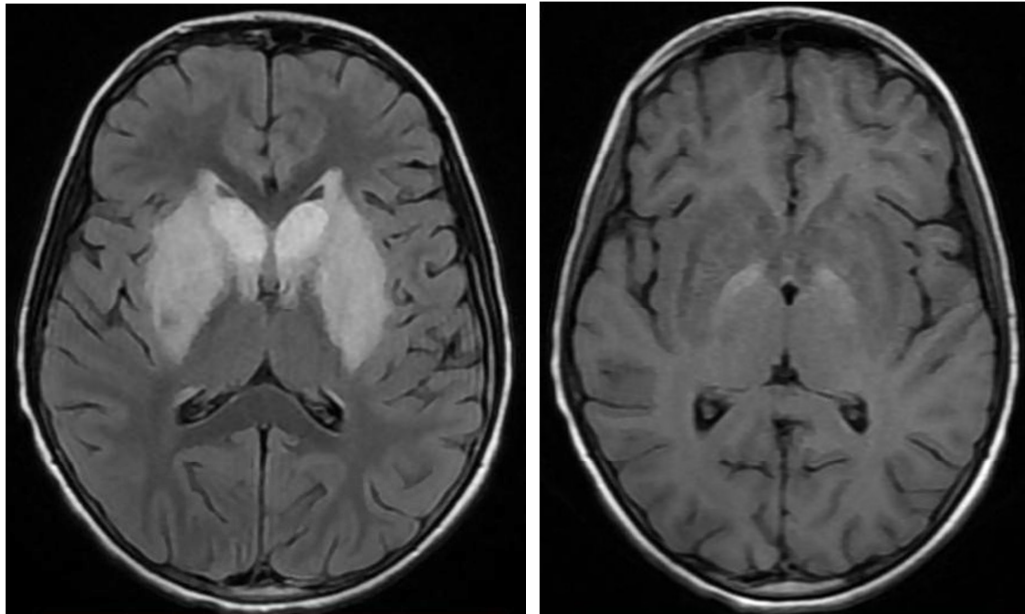


Figure 14 – MRI brain showing eye of tiger sign in a case of neurodegeneration with brain iron accumulation (NBIA)

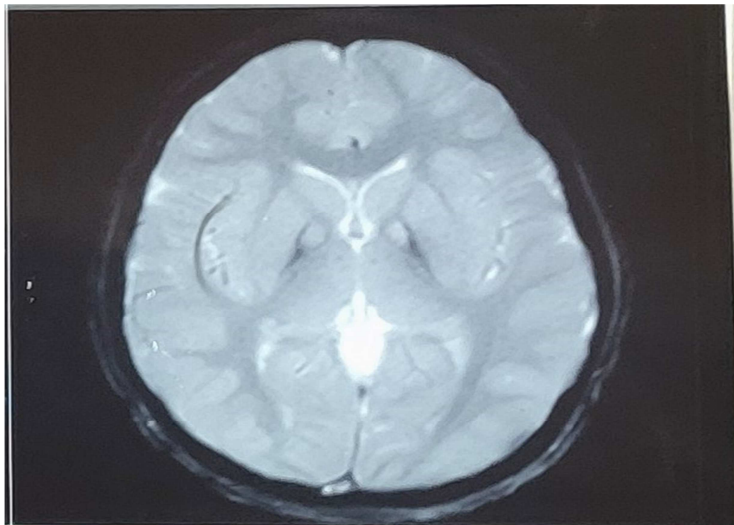


Figure 15 - MRI brain showing periventricular leukomalacia, ex vacuo dilatation of lateral ventricle, cerebral atrophy in a child diagnosed with neonatal hypoglycemic brain injury (NHBI)

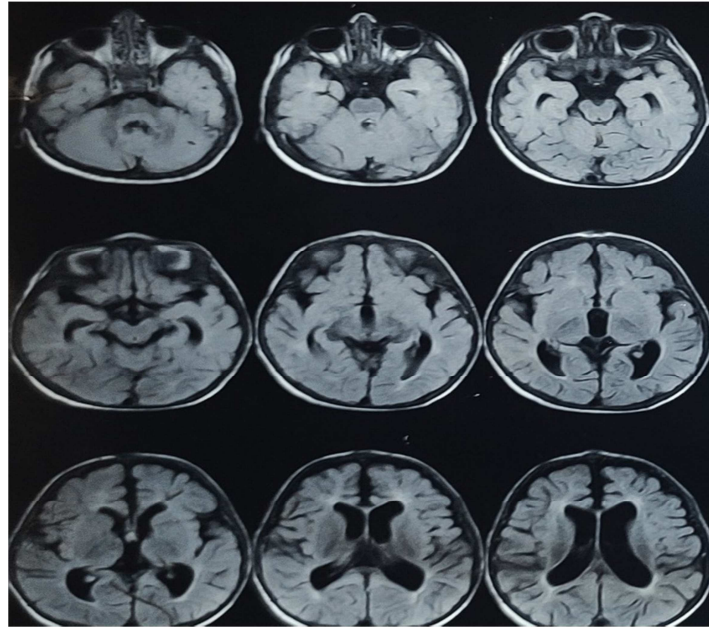


Figure 16 - MRI brain showing B/L Globus pallidus hyperintensities in a child with perinatal asphyxia

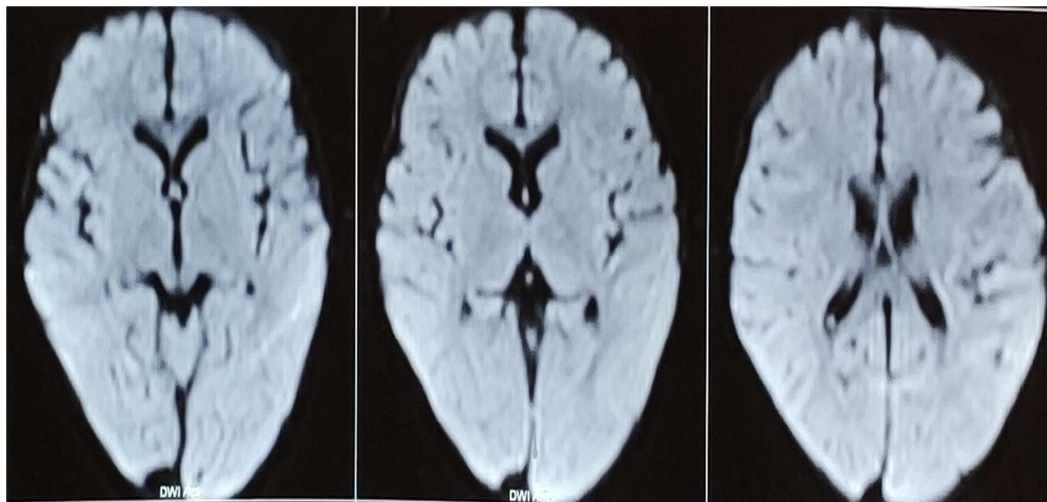


Figure 17 - MRI brain showing multicystic encephalomalacia of B/L cerebral hemispheres

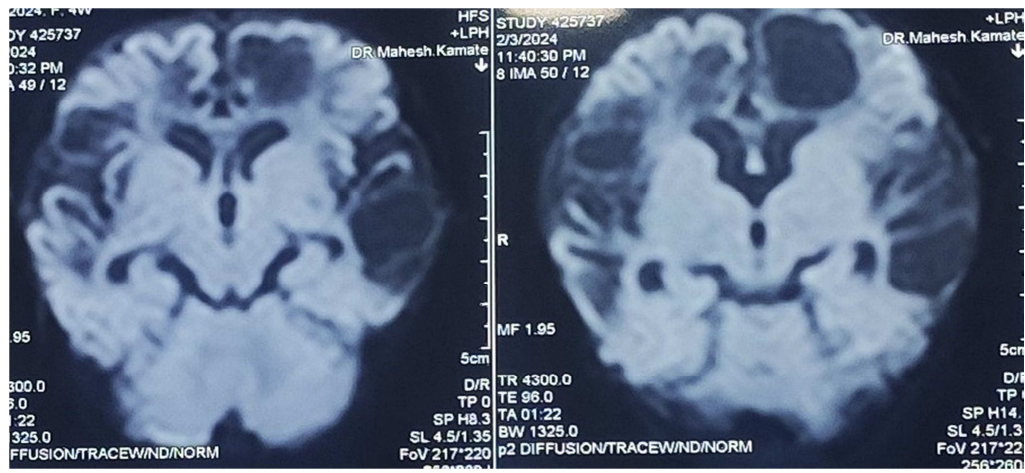
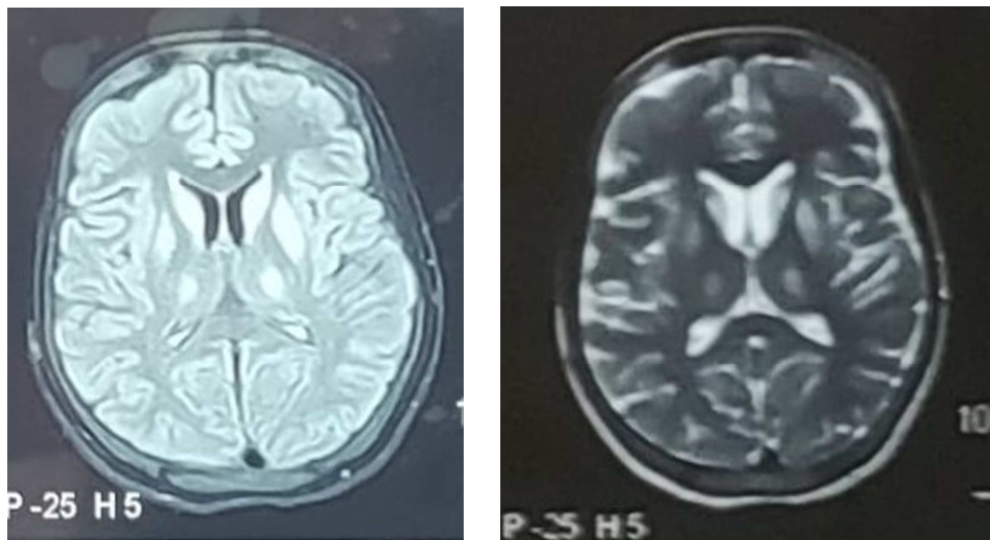


Figure 18 – MRI brain showing T2 and FLAIR heterogeneous hyperintense signal involving head of caudate nucleus, lentiform nucleus and ventrolateral thalamus in a Wilson’s disease patient.



DISCUSSION

This was a prospective study conducted at KLES Prabhakar Kore Hospital and Research centre from July 2022 to July 2023. Over one year, 148 children with movement disorders (age less than 18) attending the Paediatric Neurology OPD or admitted to KLES Prabhakar Kore Hospital were enrolled.

The children with movement disorders were examined, at least a 1-minute video of the abnormal movements was recorded and assessed by two Pediatric neurologists, and the phenomenological classification was assigned. Relevant diagnostic evaluation including MRI brain was performed. The clinical data, including demographics, clinical features, aetiology, and neuroimaging correlations, were recorded. Whenever required, children with movement disorders who were suspected to have a genetic aetiology were subjected to Whole Exome Sequencing (WES) by Next Generation sequencing on a peripheral blood sample. The American College of Medical Genetics' guidelines were followed while reporting the findings of genetic tests. Next-generation sequencing test findings were analysed and correlated clinically.

The mean age of onset of movement disorder observed in our study population is 2.70 ± 3.87 years.

The mean age of presentation for the children in our study was 5.43 years, with a standard deviation of 4.86 years. This is comparable to those from Dale et al., whose mean age at presentation was 6 years and 5 months; Goraya et al., whose mean age was 4 years and 9 months; and Ahirrao et al., who reported a mean age of 5.4

years. Nevertheless, it is less than the mean age of 10.3 years reported by Baummer et al.^{5,21-23}.

Analysing the **gender**, of the 148 enrolled children, 84 (56.8%) were male, while 64 (43.2%) were female with a male-to-female ratio of 1.3:1. Similar to a study by Ahirrao et al. (M:F -1.4:1), Goraya et al. (male to female ratio of 2:1), and Baumer et al. (male to female ratio of 3.3:1), this ratio may be the result of gender bias towards males in our region of the world, where parents or carers tend to provide better care for male than female.²¹⁻²³

A Study done by, Parmeshwarappa et al, in contrast, had higher percentage (52%) of females¹²

The majority of children with movement disorders i.e 65 children (43.9%) were under two years old. This is probably because we have included cases of cerebral palsy in this research and this is the age when the majority of caregivers tend to become more concerned about developmental delay when the child does not walk or speak like other similarly aged children and seek help for developmental delay and abnormal movements. Twenty-five children (16.9%) were in between three to five years, while 31 children (20.9%) fell within the age range of six to ten years. We had 27 children (18.2%) who were older than eleven years. This distribution highlights important age-related trends in the prevalence of movement disorders among children.

There was a high number of children born out of **consanguineous parentage** in our cohort with 90 out of 148 (60.8%) having a history of consanguinity. Data on consanguinity is lacking in most studies probably due to the low prevalence in those communities. It is known that the rate of consanguineous marriages is high in south India where marriages between uncle and niece or between first cousins are common

in Dravidian culture²⁴. In Karnataka state, the rate of consanguinity was reported to be 35%²⁵. This is higher than in most parts of India. Consanguinity was high in both the acquired and genetic aetiology of movement disorders. Increased consanguinity rates can lead to more chances of developing autosomal recessive conditions.

In our cohort, majority of the children 98% (145 children) exhibited hyperkinetic movement disorders, while the remaining three patients (2%) had hypokinetic movement disorders. The distribution observed in this study resembles findings from Ahirrao et al., who reported that hyperkinetic movement disorders accounted for 83.8%, while hypokinetic movement disorders made up only 2.94%. Similarly, Goraya et al. stated that hyperkinetic movement disorders comprised 96.73%, with hypokinetic disorders at 3.3% among their study population^{21,23}. This is consistent with the fact that most of the childhood movement disorders are hyperkinetic while hypokinetic movements are less common and are mainly present in juvenile forms of Parkinson's disease, Wilson's disease, and Huntington's disease²⁶.

Among the children with hyperkinetic cases, 115 (77.7%) had dystonia. Chorea was seen in 35 patients (23.6%), oro-motor dyskinesia in 19 patients (12.8%), athetosis in 17 children (11.5%), and myoclonus in 15 children (10.1%). Additionally, tremors were present in six patients (4.1%), stereotypes were noted in three patients (2%), and two patients (1.4%) had ballism. Two patients (1.4%) presented with catatonia and myorhythmia (1.4%). One had tics (0.7%)

Similar to a study by Parameshwarappa et al.¹², but different from the results of the majority of previous studies, dystonia was found to be the most prevalent movement disorder in our investigation. This disparity might result from the fact that

we included children with cerebral palsy, whereas the majority of research did not. One of the main movement problems in our study was choreoathetosis, which is consistent with Goraya and Dale et al.'s findings^{5,21}

According to a study by Baumer et al.²², which included both adults and children with movement disorders that started in childhood, tics are the most prevalent movement disorder, followed by dystonia. The over-representation of tic disorders and dystonia at their study site, which was specifically interested in Gilles de la Tourette syndrome and dystonia, was attributed by the authors to a referral bias. Other illnesses, especially tremor, were under-represented as a result of this tendency. Since only severe instances were brought to our centre, it's possible that the low prevalence of tics and stereotypes in our study was caused by the under recognition of mild to moderate cases.

Our study had 15 (10%) children with myoclonus which is quite lower than other studies like Goraya et al²¹ who found the most prevalent hyperkinetic movement disorder as myoclonus in their cohort, i.e., 25%, probably because they included cases of benign sleep myoclonus, and ours being a tertiary care center, would see only the most complicated cases. We also encountered two cases of myorhythmia, a very rare movement disorder in children not reported in previous studies. Its phenomenology is important to recognize as it typically provides clues to the underlying aetiology¹⁹.

Our study cohort included only 3 cases of hypokinetic disorder i.e bradykinesia which aligns with most previous studies^{5,12,21} confirming that children's movement abnormalities are typically hyperkinetic in nature.

Assessing the aetiology of movement disorders, about 53.4% of the patients (79 out of 148) had acquired aetiology and 46.6% (69 out of 148) had genetic

aetiology. Our findings differ from previous studies^{12,23} which report lower rates (9.6% and 25%) of genetic aetiology among childhood-onset movement disorders. This could be due to higher rates of consanguinity in our cohort, and ours being a referral center, would cater to complex cases.

Out of 79 patients with acquired conditions, 54.4% of cases were cerebral palsy including 44.3% due to perinatal asphyxia followed by hypoglycemia 5.1%, premature rupture of membrane (PROM) 3.8% and bilirubin-induced neurologic dysfunction (BIND) 1.3%. These results were comparable to a 2023 study.¹² The infectious/ immune causes constituted 39.9% (26 cases), among which encephalitis/meningitis formed 13.9% of cases, followed by NMDAR encephalitis in 6.3% of cases. Where Subacute sclerosing panencephalitis (SSPE), Opsoclonus-myoclonus-ataxia syndrome (OMAS), and Sydenham's chorea were seen in 3.8% cases each, Acute leukoencephalopathy with restricted diffusion (ALERD) was seen in one (0.9%) case. The significance of adequate nutrition in early development is shown by the fact that neurocutaneous infantile B12 insufficiency accounted for 3.8% of cases among nutritional causes. Vascular cause includes stroke (3.8%) and Moya Moya disease (1.3%). 3.8% of research participants had a mobility disorder as a result of diffuse axonal injuries sustained in crashes with vehicles. These findings underscore the diverse range of acquired conditions and the critical need for a comprehensive approach to patient care. Psychogenic movement disorders were uncommon in our study. It is quite likely that some of the children with abnormal movements of psychogenic origin sought treatment from a child psychiatrist rather than a paediatrician or pediatric neurologist.

Among the 69 patients (46.6%) with genetic aetiology, Inborn errors of metabolism constituted 24.3%, neurotransmitter disorders formed 8.6%, followed by

Neuronal ceroid lipofuscinoses (NCL) in 5 patients (7.1%), Hypermagnesemia Type 1 in 4 patients (5.7 %), mitochondrial disorders in 3 patients (4.3%). ADGRV1 gene mutation was seen in 3 patients (4.3%). Congenital Disorders of Glycosylation (CDG), Ataxia telangiectasia, RHOBTB2 gene and PANK2 gene mutation each seen in 2 cases. 22 patients with single gene mutation contributed 1.4% each to the genetic etiology of this study. Our findings were similar to a study²⁷ who identified a genetic cause in 51% of their patients.

The most common movement disorder phenomenology among people with a genetic basis was dystonia, which was followed by chorea and myoclonus. This conclusion is comparable to that of Kim MJ et al.²⁸ who discovered that, in comparison to patients with other movement disorders, patients with dystonia had a noticeably greater rate of genetic diagnosis.

Our findings differed from those of a study in Canada²⁷, they discovered that ataxia was the most prevalent movement condition with a hereditary aetiology, accounting for 56% of cases, followed by dystonia (46%). This could be because we have not classified ataxia as a movement disorder in our study.

Pediatric movement disorders exhibit complex and evolving phenotypic patterns, often appearing alongside various neurological or systemic symptoms. This complexity makes the genetic diagnosis of these disorders quite challenging²⁸. In our study, we took a multidisciplinary approach by collaborating with a pediatric neurologist and a clinical geneticist to better understand the patients' systemic and neurological phenotypes. Additionally, we utilized specific Next-Generation Sequencing (NGS) technology, which may have contributed to achieving a higher diagnostic rate.

Genetic characterization of patients with complex MDs may facilitate selection of appropriate therapies. For the patient ataxia telangiectasia, encoding ATM serine/threonine kinase protein which participates in the DNA repair machinery, antioxidants including vitamin E and alpha-lipoic acid were given to reduce the increased oxidative stress²⁹. The CACNA1A mutation results in reduced calcium current and decreased inhibitory effects of Purkinje cells. Acetazolamide responsiveness is a the disease's characteristic, and about 50–75% of patients show rapid improvement in episode frequency and severity. Many patients with neurotransmitter defects in our series showed significant and sustained improvement with dopaminergic agents.

Among the study participants, 115 patients had dystonia, with half of the children presenting less than 2 years. Children demonstrated generalized dystonia (86.95%) was more commonly than focal/ segmental dystonias (6.6%)

Assessing the aetiology, about 46.1% had an acquired cause, and 53.9% had a genetic cause. Among the acquired causes, dyskinetic CP, infections like Japanese encephalitis, and post-infectious disorders like mumps extrapyramidal syndrome were the predominant causes.

Coming to genetic causes, there were 6 cases of neurotransmitter disorders like L-Aromatic amino acid decarboxylase deficiency (L-AADC) deficiency, one NBIA spectrum disorder, 4 cases each of congenital disorders of glycosylation, and neuronal ceroid lipofuscinosis. Inborn errors of metabolism accounted for 11% of the cases of dystonia in this group. Our findings are similar to studies done by Joshi et al and Kumar V et al^{30,31}

We had a higher rate of children with dystonia having an underlying genetic aetiology probably due to the increased rate of consanguinity in our area²⁵ which further increases the rate of autosomal recessive disorders and also exhaustive workup done at our centre.

Cerebral palsy (CP) accounted for most of the cases, i.e., 35.1%. The most prevalent movement problem among them, affecting 46 patients (88%) was dystonia followed by chorea in 10 patients (19.2%), 7 children with athetosis (13.4%), myoclonus, and tics were present only in one child (1.9%) each. Some of the children in this study had multiple movement abnormalities that overlapped. This is in concordance with other studies^{32,33} and probably the fact is that in a developing country like ours, poor antenatal and perinatal care leading to perinatal asphyxia, hypoglycemia, and BIND still prevail, and the most common physiological type of CP in this part of the world is Dyskinetic CP³³

Accurately diagnosing CP movement disorders is crucial for treatment. Children who have dyskinetic cerebral palsy (CP) may need to take drugs including risperidone, gabapentin, tetrabenazine, and trihexyphenidyl. In contrast, children with spastic CP are typically treated with medications like baclofen, tizanidine, and diazepam. Ankle-foot orthoses, which are often prescribed for children with spastic CP to prevent contractures, may actually worsen muscle tone in children with dyskinetic CP. This is due to the increased sensory stimulation from the tactile contact with the splint.

Magnetic Resonance Imaging (MRI) brain was done in 140 study participants. Eighty percent of our study population exhibited abnormal MRI Brain findings, while normal MRIs were observed in 19.3%.

The most common area in the brain that showed abnormalities was the basal ganglia (47.8%), followed by the cortical regions (38.5%), white matter (31.4%), and cerebellum (22.8%). These findings were similar to Ahirrao M et al²³ and Joshi et al³⁰ who had 85% of children with abnormal neuroimaging with basal ganglia being the most common area affected.

When assessing children's movement problems, neuroimaging is essential. It assists in identifying anatomical abnormalities of the brain, such as vascular lesions and cerebral malformations, that may be causing movement difficulties. Characteristic neuroimaging patterns help identify the aetiology, such as the 'Eye of the Tiger' sign, in the Neurodegeneration with Brain iron accumulation (NBIA) spectrum of disorders. Many movement disorders have a genetic component. Neuroimaging can assist in identifying phenotypic features associated with specific genetic disorders, guiding further genetic testing and counselling. The underlying pathophysiology of movement disorders can be better understood by correlating neuroimaging results with clinical characteristics. This correlation can also help tailor treatment plans more effectively.

STRENGTHS OF OUR STUDY

1. Ours is a prospective study enrolling patients after two pediatric neurologists have assessed the phenomenology of the movement disorder
2. Neuroimaging was either done by us or the records were available for review in all patients.
3. When a suspected genetic aetiology, all of our cases underwent whole exome sequencing which is a much a better testing modality than clinical exome or gene panel testing.
4. We included all the cases of cerebral palsy which were excluded by majority of the studies done previously
5. Early identification of the movement disorder and its aetiology helped prompt management.
6. With a significant number of genetic causes being detected, helped in genetic counselling further reducing the burden of these disorders.

LIMITATIONS OF THIS STUDY

1. Single-centre study with a small sample size.
2. The severity of the movement disorders was not graded.
3. Treatment strategies were not recorded, and Follow-up was not done.

FUTURE IMPLICATIONS

1. Larger cohort studies needs to be done to get a better idea of the movement disorders spectrum in our country
2. Early diagnosis and early intervention/precision therapy is the way forward in Movement disorders.

CONCLUSION

1. Children frequently suffer from movement abnormalities, with hyperkinetic movements being the most common.
2. The most frequent cause of cerebral palsy was determined to be prenatal insult, highlighting the need for better perinatal treatment.
3. It is necessary to seek for several types of movement disorders in the same child and treat them since a considerable number of children had multiple movement abnormalities.
4. Genetic aetiology for childhood movement disorders is increasingly being identified. This can help modify therapy, allow better prognostication, genetic counselling, and prevention at the next pregnancy.
5. Neuroimaging identifies structural brain abnormalities, helps determine the aetiology, and understand the pathophysiology aiding in the management.
6. Accurate diagnosis enhances immediate care and fosters long-term positive outcomes for childhood movement disorders.

SUMMARY

Out of 148 movement disorders cases enrolled, 145 cases (98%) had hyperkinetic movement disorders, and 3 (2%) had hypokinetic disorders. The mean age of onset of movement disorder observed in our study population was 2.70 ± 3.87 years. There was a higher percentage of males (56.8%) compared to females.

The etiological profile showed underlying acquired causes and genetic causes in some cases. In our study, the most frequent acquired cause of mobility problems was cerebral palsy brought on by prenatal insults. Metabolic causes like inborn errors of metabolism and neurotransmitter disorders were the most common causes under genetic aetiology. Single-gene disorders formed 22% of the aetiology in our cohort.

Analysing the phenomenology, the most prevalent movement problem among the participants in our study was dystonia, followed by choreoathetosis and myoclonus.

We also reported movement disorder which are rare i.e in the form of myorhythmia associated with NMDAR encephalitis which is rarely reported in previous studies. Cerebral palsy accounted for 29% of the movement disorders in our cohort. Genetic aetiology for movement disorders was identified in 46.6 % cases. This can help modify therapy, allow better prognostication, genetic counselling, and prevention at the next pregnancy

Movement disorders are difficult to diagnose and have varied presentations. Since a considerable proportion of children suffer from several movement disorders, it is necessary to check for and treat different kinds of movement disorders in the same child..

BIBLIOGRAPHY

1. Fahn S. Classification of movement disorders. *Movement Disorders*. 2011 May;26(6):947-57.
2. Pandey CS, Kumar R, Malhotra HS, Kohli N, Kumar C, Verma SK. Movement disorders in children: an observational study in a tertiary care center in north India. *Journal of Pediatric Neurology*. 2020 Jun;18(03):135-40.
3. Delgado MR, Albright AL. Movement disorders in children: definitions, classifications, and grading systems. *Journal of Child Neurology*. 2003 Jan;18(1_suppl):S1-8.
4. Fernandez TV, State MW, Pittenger C. Tourette disorder and other tic disorders. *Handbook of Clinical Neurology*. 2018 Jan 1;147:343-54.
5. Dale RC, Singh H, Troedson C, Pillai S, Gaikiwari S, Kozłowska K. A prospective study of acute movement disorders in children. *Developmental Medicine & Child Neurology*. 2010 Aug;52(8):739-48.
6. Jain R, Pandey S, Raghav S. Movement disorders in children. *Indian Pediatrics*. 2021 Sep;58:861-70.
7. Kamate M, Detroja M. Which is the Most Common Physiologic Type of Cerebral Palsy?. *Neurology India*. 2022 May 1;70(3):1048-51.
8. Schlaggar BL, Mink JW. Movement disorders in children. *Pediatrics in Review*. 2003 Feb 1;24(2):39-51.
9. Pandey S. Classification of movement disorders: The problem of terminology. *Neurology India*. 2018 Mar 1;66(Suppl 1):S12-4.
10. Sanger TD. Pathophysiology of pediatric movement disorders. *J Child Neurol*. 2003 Sep;18 Suppl 1:S9-24.

11. Swaiman KF, Ashwal S, Ferriero DM, Schor NF, Finkel RS, Gropman AL, Pearl PL. Swaiman's pediatric neurology: principles and practice. Elsevier Health Sciences; 2017 Mar 16.
12. Parameshwarappa NN, Gowda VK, Shivappa SK. Childhood movement disorders: Clinicoetiological pattern and long-term follow-up at tertiary care center from South India. *Journal of Neurosciences in Rural Practice*. 2023 Jan;14(1):21.
13. Singer H, Mink Jonathan, Gilbert Donald, et al. MOVEMENT DISORDERS IN CHILDHOOD. 3rd ed. ELSEVIER; 2022.
14. Brandsma R, van Egmond ME, Tijssen MA, Groningen Movement Disorder Expertise Centre, Eggink H, Gelauff JM, Koens LH, de Koning TJ, Sival DA, van der Stouwe AM, van der Veen S. Diagnostic approach to paediatric movement disorders: a clinical practice guide. *Developmental Medicine & Child Neurology*. 2021 Mar;63(3):252-8.
15. Albanese A, Bhatia K, Bressman SB, DeLong MR, Fahn S, Fung VS, Hallett M, Jankovic J, Jinnah HA, Klein C, Lang AE. Phenomenology and classification of dystonia: a consensus update. *Movement disorders*. 2013 Jun 15;28(7):863-73.
16. Baizabal-Carvallo JF, Cardoso F. Chorea in children: etiology, diagnostic approach and management. *Journal of Neural Transmission*. 2020 Oct;127(10):1323-42.
17. de Gusmao CM, Waugh JL. Inherited and acquired choreas. In *Seminars in Pediatric Neurology* 2018 Apr 1 (Vol. 25, pp. 42-53). WB Saunders.
18. Sanger TD. Pediatric movement disorders. *Current Opinion in Neurology*. 2003 Aug 1;16(4):529-35.

19. Jankovic Joseph, Hallet Mark, Okun Micheal, et al. PRINCIPLES AND PRACTICE OF MOVEMENT DISORDERS. 3rd ed. ELSEVIER: London; 2022.
20. Sanger TD, Chen D, Fehlings DL, Hallett M, Lang AE, Mink JW, Singer HS, Alter K, Ben-Pazi H, Butler EE, Chen R. Definition and classification of hyperkinetic movements in childhood. *Movement Disorders*. 2010 Aug 15;25(11):1538-49.
21. Goraya JS. Acute movement disorders in children: experience from a developing country. *Journal of child neurology*. 2015 Mar;30(4):406-11.
22. Bäumer T, Sajin V, Münchau A. Childhood-onset movement disorders: A clinical series of 606 cases. *Movement disorders clinical practice*. 2017 May;4(3):437-40.
23. Ahirrao M, Bhadane P, Joshi S, Pakhare J, Patil S. Prevalence of Movement Disorders in Pediatric Age Group.
24. Ramegowda S, Ramachandra NB. Parental consanguinity increases congenital heart diseases in South India. *Annals of human biology*. 2006 Jan 1;33(5-6):519-28.
25. Krishnamoorthy S, Audinarayana N. Trends in consanguinity in South India. *Journal of biosocial science*. 2001 Apr;33(2):185-97.
26. Korn-Lubetzki I, Steiner I. Common movement disorders in children: diagnosis, pathogenesis and management. *Neuroscience and medicine*. 2012 Mar 2;3(1):90-100.
27. Cordeiro D, Bullivant G, Siriwardena K, Evans A, Kobayashi J, Cohn RD, Mercimek-Andrews S. Genetic landscape of pediatric movement disorders and management implications. *Neurology: Genetics*. 2018 Sep 26;4(5):e265.

28. Kim MJ, Yum MS, Seo GH, Ko TS, Lee BH. Phenotypic and genetic complexity in pediatric movement disorders. *Frontiers in Genetics*. 2022 Jun 1;13:829558.
29. Blignaut M, Harries S, Lochner A, Huisamen B. Ataxia Telangiectasia Mutated Protein Kinase: A Potential Master Puppeteer of Oxidative Stress-Induced Metabolic Recycling. *Oxidative Medicine and Cellular Longevity*. 2021;2021(1):8850708.
30. Joshi SP, Thomas M, Yoganathan S, Danda S, Chandran M, Jasper A. Clinico-Etiological Spectrum and Functional Outcomes of Children with Pre-Status Dystonicus and Status Dystonicus (SD): A Descriptive Study. *Annals of Indian Academy of Neurology*. 2023 May 1;26(3):268-74.
31. Kumar VN, Garg D, Mukherjee SB, Pandey S, Sharma S. Clinical and Etiological Profile of Dystonia among Children. *Indian Journal of Pediatrics*. 2023 Dec;90(12):1267-.
32. Rice J, Baker F, Russo R. The spectrum of movement disorders in a cerebral palsy population. *Dev Med Child Neurol*. 2016;58(S5):47-.
33. Kamate M, Detroja M. Which is the Most Common Physiologic Type of Cerebral Palsy?. *Neurology India*. 2022 May 1;70(3):1048-51.

ANNEXURES

ANNEXURE I – CONSENT FORM

CONSENT FOR PARTICIPATION

“Prospective study of prevalence and clinico-etiological profile of movement disorders in children”

Principal Investigator: REG NO. BM0121010

Guide: _____

You are hereby requested to involve your child in the above said research to be conducted at KLE’S Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from July 2022 to July 2023 by me.

Purpose of the study:

Movement disorders are characterized by involuntary postures or movements. In children, usually these disorders are transient and complete resolution is possible. The spectrum and etiology of movement disorders are likely to differ in different geographic areas of the world. There are very few studies from India. Because of limited studies, the evidence based therapeutic options are difficult to identify. This study aims to determine the prevalence and study the clinical spectrum of movement disorders in children from this part of Karnataka.

Type of study:

Prospective cross-sectional study for one year at KLE Dr.Prabhakar Kore Hospital And Medical Research Centre, Nehru Nagar, Belagavi.

Voluntary participation:

Your participation in this research is voluntary. It is your choice whether to participate or not. Your decision whether to participate in the study or not will not change the present or future health care services offered to you and will not affect your relationship with Dr. Prabhakar Kore Charitable Hospital and Research Centre, J.N. Medical College, KAHER, Belagavi. If you choose not to participate in this study, you will still be offered good treatment at our hospital and you will continue to receive the routine care at our hospital. If you decide to participate you are free to withdraw at any time and you will not be paid any reimbursement for participation in the research.

Potential risks:

No potential risk in this study.

Benefits:

If the etiology for the movement disorder is found, the treatment will be more accurate and effective.

Confidentiality:

Your confidentiality will be respected. No information that discloses your identity will be released. All the information taken through interviews with you will be kept safely and no person other than authorized local key investigators will be able to trace the information to your name or your address.

Use of photography/ video recording/ identifying details: Any Video recording or Photography details will be disclosed only with your permission.

STATEMENT FOR CONSENT

I have read this consent form or it has been read to me in presence of a witness in my vernacular. I was given opportunity to ask questions and they were answered to my satisfaction. By signing this document I declare that I have consented to participate in this study.

X

Signature or Thumbprint of Person Providing Consent Date:

X

Signature or Thumbprint of Witness/ Parents Date:

X

Signature of Person Obtaining Consent Date:

Person requesting consent, please check applicable boxes:

- Consent obtained (for adult respondent)
- Assent (for minor respondents)
- Consent from authorized person of minor respondent

ANNEXURE II - PROFORMA

Patient Number:

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First name:

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Last name:

--	--	--	--	--	--	--	--	--	--	--	--	--	--

Age (years):

--	--

 Sex:

--	--	--	--	--	--	--	--

Taluka:

--	--	--	--	--	--	--	--	--	--	--

District:

--	--	--	--	--	--	--	--	--	--	--

Phone

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 number:

Video recording of the movement taken: Yes / No

Chief Complaints:

History of Presenting Illness:

Past history:

Family history: Consanguinity:

Similar symptoms in other family members: Yes / No

Pedigree chart:

Birth history:

Antenatal history	Yes	No
Fever with rash		
Drug intake (teratogenic)		
If yes details-		
Radiation exposure		
GDM		
PIH		
Multiple pregnancy		
Antenatal scan abnormality		

Perinatal history		
PROM		
Prolonged labour		
Vaginal delivery/ LSCS (if yes indication)		
Birth weight		
Prematurity		
Perinatal asphyxia		
Mechanical ventilation		
Neonatal meningitis		
Neonatal sepsis		
Hypoglycemia		

Immunization history:

Developmental history:

GROSS MOTOR	FINE MOTOR	LANGUAGE	SOCIAL

Development quotient:

Impression-

ANTHROPOMETRY:

	<u>OBSERVED</u>	<u>EXPECTED</u>	<u>STANDARD DEVIATION</u>
Weight (kg)			
Height(cm)			
Head Circumference (cm)			
Weight for height			
BMI			
Inference			

GENERAL EXAMINATION:

Pulse rate-

Respiratory rate-

Blood pressure-

Neurocutaneous markers (if present specify): Yes / No


SYSTEMIC EXAMINATIONS:

CENTRAL NERVOUS SYSTEM-

GCS-

Higher Mental Function-

pMMSE:

S.No	Functions	Tests	Score I	Score II	Score III
1	Orientation	Sex/name/last name/recognizes relative (one point for each, total score-4) Place/city/state/country (one point for each, total score-4) Day/Date/Month/Year (one point for each, total score 4)			
2	Attention and Concentration	Minimum of 2 and maximum of 5 digits forward (one point for each, total score-4) Minimum of 2 and maximum of 4 digits backward (one point for each, total score- 3)			
3	Registration and Sensory perception	Identify 3 objects by name (One point for each, total score-3)			
4	Recall	Tell 3 objects presented previously (one point for each, total score 3)			
5	Language Name body parts Command(three step) Repeat sentence Reading Writing Copy a design	Points to 5 body parts (one point for each, total score 5) Unwrap the toffee, give the wrapper to the doctor and then eat it (one point for each, total score 3) Billi dhoodh peeti hai (total score 1) Reads his/her name (total score 1) Writes own name (total score 1)  (total score 1)			

Cranial Nerves-

I	
II	
III, V, VI	
IV	
VII	
VIII	
IX	
X	
XI	
XII	

MOTOR SYSTEM-

Muscle Bulk:

	Power	
	Right	Left
Shoulder		
Elbow		
Wrist		
Knee		
Hip		
Ankle		

	Tone	
	Right	Left
Shoulder		
Elbow		
Wrist		
Knee		
Hip		
Ankle		

Reflexes:

	Right	Left
Biceps Jerk		
Supinator Jerk		
Triceps Jerk		
Knee Jerk		
Ankle Jerk		
Plantar Reflex		

Sensory system-

Cerebellar signs-

Signs of meningeal irritation-

RESPIRATORY SYSTEM-

CARDIOVASCULAR SYSTEM-

ABDOMEN-

OTHER RELEVANT CLINICAL FEATURES/ INVESTIGATION-

MOVEMENT DISORDER:

Age of onset:

Types of Movement Disorder:

	Present	Absent
<u>Hyperkinesias:</u>		
Dystonia I. Distribution: a) focal, b) segmental, c) multifocal, d) generalised, e) hemidystonia II. Etiology: a) primary, b) dystonia-plus, c) secondary		
Tremor: I. Normal physiological tremor II. Static tremor III. Postural tremor IV. Intention tremor		
Myoclonous: I. Cortical myoclonus II. Brainstem myoclonus III. Spinal myoclonus		

Tics		
Chorea		
Ballism		
Ataxia		
Athetosis		
Stereotype		
Periodic movement in sleep		
REM sleep behaviour disorder		
<u>Hypokinesias:</u>		
Parkinsonism (Bradykinesia)		
Apraxia		
Hypothyroid slowness		
Rigidity		
Stiff muscles		
Cataplexy and drop attack		

Describe the movement disorder in detail:

Diagnosis -

MRI BRAIN number-

MRI BRAIN findings-

EEG-

CT BRAIN –

Genetic Testing –

Ophthalmology Examination -

Treatment Given-

ANNEXURE III

KEY TO MASTER CHART

Age in months/ years

Sex: M- Male, F- Female

Age of onset when symptoms 1st noticed and concerned is in months

Developmental delay: GDD- global developmental delay; Regression; Normal

Term: Y – term delivery; N- preterm delivery

Cerebral palsy: Y- present; N- not present

Epilepsy: Y- present; N- not present

Movement disorders- 1. Dystonia, 2. Chorea, 3. Stereotypes, 4. Oro-motor dyskinesia (OMD), 5. Myoclonus, 6. Bradykinesia, 7. Athetosis, 8. Ballism, 9. Tremors, 10. Myorhythmia, 11. Catatonia, 12. Tics

Diagnosis: A) perinatal asphyxia; B) HSV/ Mumps encephalitis, HLH; C) NMDAR encephalitis; D) methylmalonic aciduria (MMA) and other organic acidemias; E) Hypoglycemia / BIND; F) Neuronal ceroid lipofuscinosis (NCL); G) congenital disorder of glycosylation (CDG); H) ADGRV1 gene; I) RHOBTB2 gene; J) Hypermanganesemia with dystonia type I; K) AADC; L) Mitochondrial disease; M) Subacute sclerosing panencephalitis (SSPE); N) PANK2 gene; O) Stroke; P) Hyperphenylalaninemia; Q) Sydenham chorea; R) Aminoacidemias; S) Ataxia telangiectasia; T) Preterm/ PROM; U) Neurotransmitter disorders; V) Nutritional; W) Neuroblastoma/ ANEC; X) RTA; Y) Encephalopathy (Molybdenum, leucoencephalopathy); Z) Others (sulfite oxidase deficiency, Niemann pick disease, Krabbe's disease)

MRI brain: Abn- Abnormal; N- Normal; not done

Lesion sites (Glodus pallidus, putamen, thalamus, caudate, cortical, white matter, brain stem, cerebellum): yes- lesion present; no- lesion not present

ANNEXURE III

MASTER CHART

s.no	Name	Age / Sex	age of onset	Developmental delay	term	movement disorder	CP	Epilepsy	Acquired/ Genetic	DIAGNOSIS	MRI BRAIN N/ABN	GP	PUTAMEN	CAUDATE	THALAMUS	BRAIN STEM	WHITE MATTER	CEREBELLAR	CORTICAL	SPINAL CORD
1	pradeep koti	4 yr/ M	3 years	normal	Y	5	N	N	genetic	F	Abn							yes	yes	
2	nitin bhajantri	2 yr / M	2 months	GDD	Y	1	N	N	acquired	V	Abn						yes	yes	yes	
3	sidra kanakyaa	4 yr/ F	20 days	GDD	Y	1	N	Y	genetic	Z	Abn						yes			
4	shourya kotyal	1 yr/ M	6 months	GDD	Y	1,5	N	N	genetic		not done									
5	rayanna terlapur	1yr/ M	2 months	GDD	Y	1	N	Y	genetic	H	N									
6	biresh badal	2 year/ M	3 months	GDD	Y	1	Y	N	acquired	A	Abn						yes	yes	yes	
7	prem tevaratti	16 yr/ M	5 year	GDD	Y	1,2,5	N	N	acquired	Z	Abn									
8	prajwal kamannavar	1 yr 6 month/ M	4 months	GDD	N	1	N	N	acquired	A	Abn	yes								
9	vinamshika valasang	1 yr/ F	1 1/2 months	GDD	Y	1	N	Y	genetic	I	Abn				yes	yes		yes		
10	pavan hadppad	1 month/ M	4 days	GDD	Y	1	N	Y	genetic	Z	Abn						yes	yes	yes	
11	ishan kembavi	2yr/ M	1 1/2 years	normal	Y	1	N	N	genetic	Z	Abn							yes	yes	
12	b/o bharati jambagi	3 yr/ M	2 months	GDD	Y	1,5	N	Y	genetic	Z	Abn								yes	
13	arpita basavaraj	11 yr/F	2 year	GDD	Y	1,2,7,4	N	N	genetic	D	Abn							yes		
14	ashok nayak	1 yr/ M	1 year	normal	Y	5,4	N	N	acquired	W	not done									
15	rohit malakkanavar	9 yr/ M	8 year	normal	Y	11,4	N	N	acquired	C	N									
16	rafiya sanadi	5 yr/ F	2 1/2 years	GDD	Y	1	N	Y	acquired	B	Abn								yes	

17	pranav pagoji	9 yr/ M	8 year	normal	Y	5	N	N	acquired	M	N										
18	kruti harabidi	2 yr/ F	1 1/2 years	regression	Y	8	N	Y	acquired	A	Abn										yes
19	shourya nandihalli	7 months/ M	4 months	normal	Y	1	N	N	genetic	D	Abn	yes									
20	amshika anjanayya	1 month/ F	2 days	GDD	Y	1	Y	N	genetic	N	Abn										yes
21	kushal shirohi	7 yr/ M	2 years	GDD	Y	1	Y	N	acquired	A	Abn			yes							yes
22	sarthak danagouda	1 yr/ M	10 months	GDD	Y	1	N	N	genetic	P	N										
23	ziya brepori	2 yr/ F	2 days	GDD	Y	2,7	N	N	acquired	A	Abn	yes									
24	spoorthi patil	17 yr/ F	2 days	GDD	Y	1,2,7	Y	N	acquired	A	Abn			yes							yes
25	shraddha patil	11 yr/ F	11 years	normal	Y	1	N	N	acquired	B	Abn	yes	yes	yes							
26	aditi babladi	3 yr/ F	1 year	regression	Y	1,4	N	N	genetic	Z	Abn										yes
27	anagha apte	10 yr/ F	6 months	GDD	Y	1	Y	N	acquired	A	Abn										yes
28	druva karaguppi	1 yr 7 month /M	1 1/2 years	regression	Y	1	N	Y	acquired	X	Abn								yes		
29	shivani patil	16 yr/ F	4 years	GDD	Y	1,4	N	N	genetic	S	Abn									yes	
30	ishwari aladakatti	7 yr/ F	6 months	GDD	Y	1	Y	N	acquired	A	Abn										yes
31	ridhi nakadi	7 yr/ F	7 years	GDD	Y	2	N	N	acquired	O	Abn			yes							
32	laxmikant tawar	4 month/ M	2 months	GDD	Y	1	Y	N	genetic	P	N										
33	bhumika bheerappa	4 yr/ F	4 years	normal	Y	2,4	N	N	acquired	X	not done										
34	santosh talwar	12 yr/ M	12 years	normal	Y	2	N	N	acquired	Q	not done										
35	anushree kumbar	1 yr 6 month/ F	3 months	GDD	Y	1,4	Y	Y	acquired	U	Abn										yes
36	tejas kumar basavaraj	1 yr 7 month/ M	1 month	GDD	N	1	Y	N	acquired	T	Abn										yes
37	sanchith walikar	10 month/ M	3 months	GDD	Y	1,4	Y	N	acquired	A	Abn										yes
38	suraj powar	17 yr/ M	2 years	normal	Y	1	N	N	genetic	U	N										
39	kushi rathod	2 yr/ F	4 months	GDD	Y	1	N	N	genetic	D	Abn								yes		yes
40	goutami garoshi	5 yr/ F	3 months	GDD	Y	1	N	N	genetic	D	Abn			yes							yes
41	afiya khanjade	4 yr/ F	6 months	GDD	Y	2,7	Y	N	genetic	Z	Abn				yes						
42	b/o rohini kambar	2 yr/ F	5 months	GDD	Y	1	Y	N	acquired	T	N										
43	abhishek salunke	11 yr/ M	8 years	normal	Y	1,5,9	N	N	genetic	Z	N										
44	ayan jamadar	7 yr/ M	4 years	normal	Y	1,2,7	N	N	acquired	Z	Abn	yes									
45	prutvik tambe	10 months/ M	2 years	GDD	Y	5	N	N	genetic	Z	Abn					yes	yes	yes			
46	durgappa kamashetti	5 year/ M	5 years	normal	Y	1	N	N	acquired	B	Abn	yes	yes	yes	yes					yes	
47	siddarth kesorkor	11 years/ M	10 years	normal	Y	2	N	N	acquired	X	N										
48	harshit prakash	1 year/ M	1 year	regression of attained milestones. not able to sit/ stand	Y	1,2,7	N	N	acquired	V	Abn	yes	yes	yes							
49	vedanth kankanawadi	6 yr/ M	6 months	regression	Y	1	N	N	genetic	J	Abn	yes									yes
50	vikrant kankanawadi	2 yr/ M	1 year	regression	Y	1	N	N	genetic	J	Abn	yes									yes
51	nived patil	8 year/ M	2 1/2 years	regression	Y	1,6	N	N	genetic	J	Abn	yes			yes					yes	yes

52	ayush patil	8 yr/ M	2 1/2 years	normal	Y	1,6	N	N	genetic	J	Abn	yes			yes			yes	yes	
53	advait shyanawadamath	1 year M	5 months	GDD	Y	1,2,4,7	N	N	genetic	Y	Abn	yes						yes		
54	heena shaikh	10 year / F	7 years	GDD	Y	1,2,4	N	N	genetic	N	Abn	yes								
55	spurti neelakant	13 years/ F	13 years	normal	Y	2	N	N	acquired	Q	Abn		yes	yes				yes		
56	siddu dodamani	2 yr/ M	4 months	GDD	Y	1	N	N	genetic	K	N									
57	vikas ijeri	5 yr/ M	5 year	normal	Y	5	N	N	acquired	C	N									
58	rakshita kurabar	18 yr/ F	17 year	normal	Y	1,4	N	Y	acquired	C	N									
59	nakshatra gowda	1 yr 6 month/ F	1 month	regression	Y	1,2,7	N	N	acquired	B	Abn							yes		yes
60	kruthika kumbar	2year/ F	1 year	GDD	Y	1,4	N	N	genetic	K	N									
61	lipika anjaneya	1 yr/ F	1 year	regression	Y	1,4	N	N	acquired	X	Abn							yes		
62	yashwanth chowdki	11 yr / M	1 year	GDD	Y	1,4	N	N	genetic	Z	Abn		yes	yes					yes	
63	bhuvaneshwari nayak	12 yr/ F	10 years	normal	Y	9	N	N	acquired	Y	Abn					yes	yes			
64	b/o vani subbaiah	8 months/ M	6 months	GDD	Y	1,2,7	N	N	genetic	Z	not done									
65	ayush madar		4 months	delay in motor and language milestones	Y	1	Y	N	acquired	A	CT - Abn							yes		
66	b/o nashima nadaf	9 yr/ F	7 years	GDD	N	2	Y	N	acquired	E	Abn		yes		yes					
67	amit kurani	11 yr/ M	8 years	normal	Y	2	N	N	acquired	Q	not done									
68	hurain davangeri	10 month/ F	10 months	normal	Y	1	N	N	acquired	B	Abn				yes					yes
69	jjyoti yadagud	1 yr 6 month/ F	1 year	GDD	Y	1	N	N	acquired	D	Abn							yes		
70	fakkiresh	12 yr/ M	2 years	GDD	Y	1,9	N	N	acquired	Z	Abn	yes	yes					yes		
71	navaraksha mokashi	5 months/ F	5 months	normal	Y	1	N	Y	acquired	B	Abn							yes		yes
72	bheerappa pujari	2 yr/ F	2 years	normal	Y	5	N	Y	acquired	B	Abn							yes		
73	shweta sampur	9 yr/ F	6 years	GDD	Y	1	N	N	genetic	U	N									
74	rama yadage	1 1/2 yr/ M	6 months	GDD	Y	1	N	Y	genetic	Z	Abn		yes	yes				yes		
75	tamim bepari	7 month/ M	7 months	GDD	Y	1	Y	N	acquired	A	Abn							yes		
76	rudresh yallappa malagi	4 year/ M	4 years	no delay	Y	1	N	N	acquired	C	N									
77	aishwarya kundari	5 yr/ F	1 year	GDD	Y	1,2,4,7	Y	N	acquired	A	Abn		yes	yes					yes	yes
78	lakhan kamati	10 yr/ M	6 months	GDD	Y	1,2,4,7	Y	N	acquired	A	Abn		yes		yes					
79	deepa madar	17 year / F	17 years	normal	Y	1,11	N	Y	acquired	C	N									
80	arpita basavaraj	11 year/ F	2 years	GDD	Y	2,7	Y	N	genetic	D	Abn								yes	
81	rayanna tirlapur	11 month/ M	8 months	GDD	Y	1	Y	Y	genetic	H	Abn									yes
82	bhuvan kurani	4 year M	1 1/2 years	GDD	N	1,2	N	N	acquired	A	Abn			yes						
83	shrinika kappatti	8 yr/ F	4 months	regression	Y	1	N	N	genetic	Z	Abn									yes
84	tejashree herakal	4 month/ F	2 months	GDD	Y	1	Y	N	genetic	Z	N									
85	basamma	10 yr/ F	2 years	GDD	Y	1	N	N	genetic	U	N									
86	ariz khan	2 yr/ M	1 year	regression	Y	1	N	N	genetic	G	Abn							yes	yes	yes
87	ayush kale	3 month/ M	3 months	GDD	Y	1	Y	Y	acquired	A	Abn									yes
88	sharavan kumar	10 yr/ M	1 year	regression	Y	1	N	Y	genetic	Z	Abn		yes	yes						
89	aditi raikar	2 yr/ F	1 year	normal	N	1,2,7	N	Y	acquired	B	Abn									yes

129	nandhan adur	7 month/ M	4 months	normal	Y	9	N	N	acquired	V	Abn				yes				
130	aditya bagali	3 yr/ M	6 months	GDD	Y	1,3	N	Y	genetic	H	N								
131	shraraksha	6 month/ F	2 days	GDD	Y	1	Y	N	acquired	A	Abn				yes	yes		yes	
132	rehan majid khan	13 yr/ M	1 year	GDD	N	1	Y	Y	acquired	A	Abn						yes		yes
133	om kokasekar	8 yr/ M	10 months	GDD	Y	1	Y	Y	acquired	W	Abn		yes				yes		yes
134	abhyanth budihal	2 yr/ M	2 days	GDD	N	1	Y	N	acquired	A	Abn							yes	
135	sativkgouda patil	1 yr/ M	2 days	GDD	Y	1	Y	N	acquired	A	Abn								yes
136	prashanthi entettinar	4 yr/ F	1 1/2 years	normal	Y	2	N	Y	acquired	W	Abn				yes	yes			
137	vedanth mallannavar	2 yr/ M	1 day	GDD	Y	1	Y	N	acquired	A	Abn						yes		yes
138	sanidhya kambar	1 yr/ F	10 months	GDD	Y	1	Y	N	acquired	A	Abn						yes		
139	vinayak hongal	7 month/ M	2 months	GDD	Y	1	Y	N	genetic	U	Abn						yes		
140	amrutha belunki	9 yr/ F	7 months	GDD	Y	1,4	Y	Y	acquired	A	Abn							yes	yes
141	anil hanumanth	13 yr/ M	2 years	GDD	Y	1	N	Y	acquired	O						yes	yes		yes
142	indrajith halesh	8 yr/ M	7 years	GDD	Y	3	N	Y	acquired	V	Abn								yes
143	samarth chimani	4 yr/ M	3 years	regression	Y	2	N	Y	genetic	F	Abn				yes		yes	yes	
144	sanvika jhadhav	1 yr/F	8 months	GDD	Y	1	N	N	genetic	F	Abn				yes		yes	yes	yes
145	satvik kubar	2 yr/ M	1 year	regression	Y	1,3	N	Y	genetic	F	Abn				yes		yes		yes
146	tanavi shinde	7 yr/ F	5 years	regression	Y	1	N	Y	genetic	F	Abn						yes	yes	
147	vinayak patil	14 yr/ M	14 year	normal	Y	5	N	N	acquired	M	Abn						yes		
148	malakarisisda konina	9 yr/ M	9 year	normal	Y	1,5	N	N	acquired	M	N								