SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY

THIRUVANANTHAPURAM, KERALA

"THE CLINICAL PROFILE AND PREDICTORS OF OUTCOME IN FUNCTIONAL MOVEMENT DISORDERS"

Dissertation submitted in partial fulfillment of the rules and regulations for

Post-Doctoral Fellowship in Movement Disorders

By

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DECLARATION BY THE STUDENT

I, Dr. Sayooja Sachithanandan, hereby certify that I have personally carried out the work depicted in the thesis titled, “The Clinical Profile and Predictors of Outcome in Functional Movement Disorders”. No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.



Date: 30.12.2024 Dr. Sayooja Sachithanandan

CERTIFICATE BY THE RESEARCH GUIDE

Name of the Guide: Dr. Syam K

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This is to certify that Dr. Sayooja Sachithanandan, Department of Neurology of this institute has fulfilled the requirements prescribed for the Post-doctoral fellow in Movement disorders of the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum. The thesis entitled, “The Clinical Profile and Predictors of Outcome in Functional Movement Disorders” was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date. Clearance was obtained from the Institutional Ethics Committee for carrying out the study.



Date: 30-12-24 Dr. Syam K

Forwarded:

This is to certify that the dissertation entitled “The Clinical Profile and Predictors of Outcome in Functional Movement Disorders” is a bonafide research work done by Dr Sayooja Sachithanandan, Post-doctoral fellow in the Department of Neurology, in partial fulfillment of the requirement of the Post-doctoral fellowship in Movement disorders.



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LIST OF ABBREVIATIONS

S.No.	Abbreviation	Full form
1.	FMD	Functional movement disorders
2.	DSM 5	Diagnostic and Statistical Manual of Mental Disorders 5
3.	S-FMDRS	Simplified functional movement disorders rating scale
4.	PNEE	paroxysmal non-epileptic events
5.	mRS	modified Rankin scale
6.	MRI	Magnetic resonance imaging

INTRODUCTION

Functional (psychogenic) movement disorders (FMD) are conditions where the subject experiences the occurrence of various movement disorders as involuntary, despite clinically demonstrating preserved neurological function and a volitional component to the movements or paucity of movements. FMDs form 2-20% of new patients attending movement disorder clinics worldwide, women are found to be more frequently affected than men, with a mean age of onset of 37 to 50 years, although FMD may present at any age(1). Diagnosing FMD involves a careful history and examination for positive signs; the diagnosis is not one of exclusion (1). Although several diagnostic criteria are proposed, they are not used routinely and the most practically identified positive signs include distractibility, entrainability, and variability (2,3).

The term “functional” has replaced “psychogenic” in the Diagnostic and Statistical Manual of Mental Disorders (DSM5) (4) as this is a complex neuropsychiatric disorder best conceptualized using a biopsychosocial framework where predisposing factors render the nervous system vulnerable to the development of FMDs, which then emerge in the context of precipitating events, with perpetuating factors reinforcing these symptoms over time (1).

Given the level of disability and impairment in quality of life reported by patients, there are probably substantial associated health and social care costs. While there is no definitive treatment for this disorder, important factors indicative of a better prognosis include acceptance of diagnosis by the patient, management of concurrent

psychiatric disorders and psychological stressors, and maintenance of a supportive social network (5). FMD patients may need follow-up to establish the diagnosis in some cases. We conducted this systematic study including long-term follow-up data to understand the characteristics of patients diagnosed with FMDs attending the Movement Disorder Clinic services of a tertiary care centre and to find out the long-term outcome, clinical evolution, and predictors of outcome in FMD.

LITERATURE REVIEW

Symptoms of FMD are subjectively experienced as involuntary, despite historical and examination findings demonstrating preserved neurologic function and a volitional component. Common phenomenological manifestations of FMD include tremor, dystonia, myoclonus, tics, gait disorder and parkinsonism (7).

Predisposing factors: Female gender, poor socioeconomic status; financial strain, comorbid neurologic conditions, comorbid psychiatric disorders, Health anxiety and somatic vigilance, physical, sexual or emotional trauma; neglect, major losses such as bereavement or divorce, maladaptive personality traits

Precipitating factors: Physical injury or surgery, preceding illness, accidents, autonomic hyperarousal event (eg panic attack), dissociation event, interpersonal conflict, job loss or employment-related stressors, significant acute loss event

Perpetuating factors: Chronic pain and fatigue, chronic medical conditions, physical deconditioning, entrenched abnormal motor programs, invalidation by the healthcare system; stigma, maladaptive illness beliefs; lack of diagnostic agreement, anxiety and hypervigilance around symptoms, avoidance pattern, interpersonal or work-related stressors, pending litigation, unconscious secondary gains

Operationalised diagnostic criteria for FMDs put forward by Fahn-Williams(2), provides gradation in certainty of diagnosis as follows:

- Documented: Persistent relief by psychotherapy, suggestions, or placebo demonstrated, which may be helped by physiotherapy; or the patient was seen

without the movement disorder when believing himself or herself unobserved.

- Clinically established: The movement disorder is incongruent with a classical movement disorder or there are inconsistencies in the examination, plus at least one of the following three: other psychogenic signs, multiple somatisations, or an obvious psychiatric disturbance.
- Probable: The movement disorder is incongruent or inconsistent with typical movement disorders or there are psychogenic signs or multiple somatisations.
- Possible: Evidence of an emotional disturbance.

The co-occurrence of functional and organic movement disorders also needs to be expected, given the common co-occurrence of other functional disorders with organic disorders.

Simplified functional neurological rating scale(8) is a useful scale for scaling the disability due to FMD. It takes into account the body parts affected by a particular movement as well as the functional disability in mainly speech and gait caused due to the movement

AIMS AND OBJECTIVES

1. Primary objective: To study the phenomenology and clinical characteristics of patients diagnosed to have FMDs attending the Movement Disorder Clinic services of a tertiary care centre
2. Secondary objective: To find out the long-term outcome, clinical evolution, level of disability, and predictors of outcome in FMD

METHODOLOGY

This was a hospital-based observational study. All consecutive patients with a clinical diagnosis of FMD made by a Movement disorder specialist, with at least 3-month follow-up data, during twenty-five years (1999- 2024) were recruited to the study. The most consistent characteristics that led to the clinical diagnosis were variability, distractibility, and entrainability of the involuntary movements (5). Other clinical features were reviewed from medical records and video documentation (for available cases) to identify the proportion of patients who meet two of the popular proposed diagnostic criteria for functional movement disorders; using the 10-point clinical criteria (satisfying >7 out of 10 points) (3) and those satisfying documented or clinically established level of diagnostic certainty according to the diagnostic criteria by Fahn and William(2)

Those with obvious organic etiology in initial investigations or on follow-up (though phenomenology may suggest functional), diagnosis of malingering, paroxysmal non-epileptic events (PNEE), purely non-movement neuraxis of functional neurological disorders (such as sensory, visual, and hearing impairment) were excluded.

Follow-up data of the subjects were collected from case files and the current status as of 2024 was evaluated through telephonic interviews. Remissions, worsening symptoms, changes in phenomenology, and functional status were assessed. Outcomes of the patients at the last follow-up were dichotomised into complete remission and failure to achieve complete remission of symptoms. Complete remission was defined as remission of symptoms for the past 3 months at the last

follow-up. Those who failed to have complete remission were the ones who either had persistent or worsening symptoms or relapsed within the previous 3 months of follow-up.

Statistical analysis:

The data was entered using MS Excel and analysed with the help of the SPSS 26 trial version for Windows (IBM Corp). The variables are represented as percentages or mean +/- standard deviation as defined appropriately for qualitative and quantitative variables. Baseline demographic and clinical features, various predisposing/ precipitating and perpetuating factors, and other neurological, psychiatric, or medical comorbidities, were compared among the two groups to identify the factors associated with complete remission (favourable outcome) or absence of full remission. Regression analysis was performed on statistically significant variables to find out predictors of outcome in FMD

RESULTS

Demographics:

One hundred and ninety-eight subjects diagnosed with functional movement disorders were recruited to the study after applying the inclusion and exclusion criteria (Figure 1). The mean age at presentation was 35.2 ± 15.4 years. Almost one-fifth was represented by the paediatric or adolescent population (less than 18 years), the youngest was 6 years and the eldest subject was 79 years of age. Females predominated (Male: female ratio of 1: 1.15). They presented after an average duration of 22.21 ± 48.2 months of initial symptom onset. Other baseline characteristics are listed in Table 1.

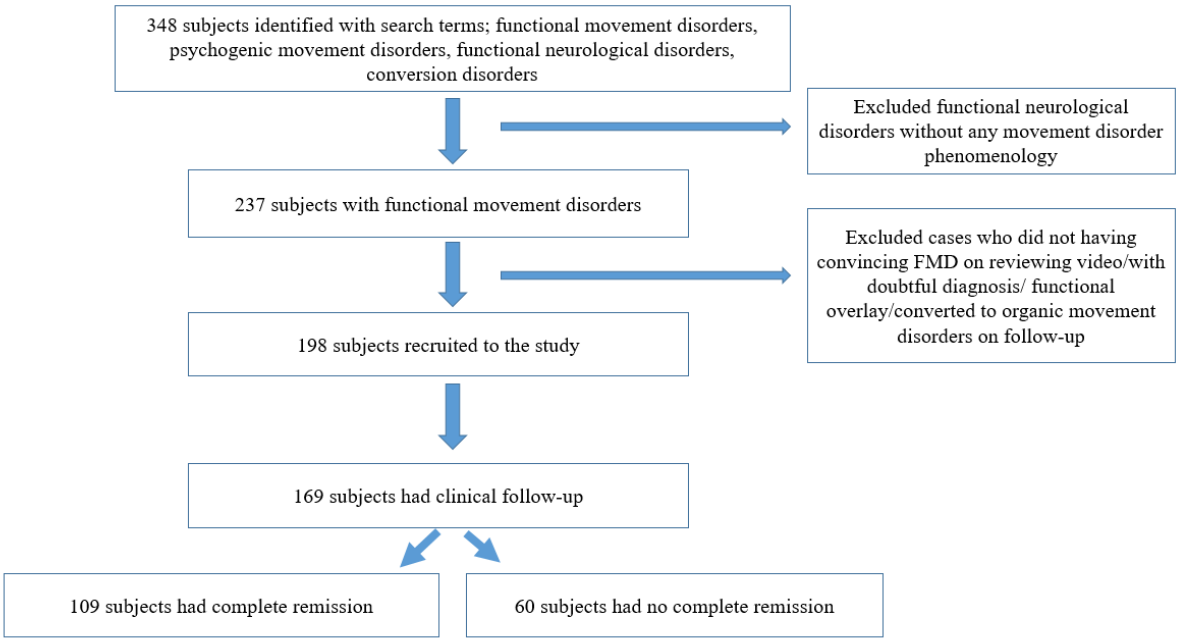


Figure 1: Flow-chart depicting patient recruitmen

Table 1: Baseline characteristics of patients with clinically diagnosed Functional movement disorders

Variables	Mean ±SD (Minimum- Maximum)	Frequency (Percent)
Age at presentation, in years: Age < 18 years Age≥ 18 years	35.17 ± 15.4 (6-79)	- 39 (19.7) 159 (80.3)
Gender: Male Female	-	78 (39.4) 120 (60.6)
Age at onset, in years	33.41 ± 15.4 (6-77)	-
Duration of symptom at initial visit, in months	22.21 ± 48.2 (0-360)	-
Number of years of education, in years	11.24 ± 3.6 (0-17)	-
Occupational class: Student Unemployed Employed	-	46 (23.2) 60 (30.3) 92 (46.5)
Marital status: Single Married Divorced Widowed Underage Missing data	-	35 (17.7) 107 (54) 5 (2.5) 4 (2) 42 (21.2) 5 (2.5)

Residence: Rural Urban	-	111 (56.1) 87 (43.9)
Family history or neighbours with similar illness	-	21 (10.6)
Any neuroimaging abnormalities	-	31 (15.7)
	Mean ±SD (Minimum- Maximum)	Frequency (Percent)
Mode of onset: Hyper-acute (within 24 hours) Acute (1 day- 4 weeks) Subacute (4-8 weeks) Gradual (>8 weeks)	-	61 (30.8) 93 (47) 28 (14.1) 16 (8.1)
Clinical course: Static Steadily progressive Step-wise progressive Improving Fluctuating	-	29 (14.6) 22 (11.1) 24 (12.1) 6 (3) 117 (59.1)
Phenomenology: Tremor Dystonia Tic	-	61 (30.8) 65 (32.8) 16 (8.1)

Chorea		4 (2)
Myoclonus		28 (14.1)
Bizarre hyperkinetic		61 (30.8)
Parkinsonism		10 (5.1)
Mixed movements		87 (43.9)
Falls		28 (14.1)
Weakness (Hemi/para/monoplegia)		40 (20.2)
Gait disturbances		94 (47.5)
Body distribution: Focal	-	40 (20.2)
Segmental		45 (22.7)
Multifocal		7 (3.5)
Hemi-body		5 (2.5)
Generalized		28 (14.1)
Gait		94 (47.5)
Mean S-FMDRS score	9.31 ± 6.9 (1-36)	-
Mean mRS score	2.66 ± 0.827 (1-4)	-
Abbreviations: FMD, functional movement disorders; mRS, modified Rankin scale; S-FMDRS, Simplified functional movement disorder rating scale		

The various predisposing, precipitating, and perpetuating factors were identified (Table 2). Eighty-five percent were predisposed to the development of FMD with the female gender (60.6%), being the most frequent one. Preceding physical injury surgery/ illness/accidents (36.9%) were identified as the most common precipitating factor. Anxiety, hypervigilance, and avoidance patterns (47.5%) were the most commonly reported perpetuating factors. Coexisting functional neurological axes other than movement disorder were noted in 64% of subjects with sensory disturbance (31%) being the most commonly reported symptom. Non-neurological somatization disorders were observed in 25%.

Table 2: Predisposing, precipitating, perpetuating factors in patients with Functional movement disorders at baseline

Variables	Frequency	Percent
Any predisposing factors	170	85.9
• Female	120	60.6
• Financial strain/low socioeconomic status	36	18.2
• Chronic neurological or psychiatric comorbidities	102	51.5
• Maladaptive traits	106	53.5
• Physical, sexual, or emotional trauma	32	16.2
• Health anxiety and somatic vigilance	19	9.6
• Neglect	14	7.1

• Major losses such as bereavement or divorce	19	9.6
Any precipitating factors	128	64.6
• Physical injury/surgery/Preceding illness/Accidents	73	36.9
• Autonomic hyperarousal event	27	13.6
• Dissociation event, Interpersonal conflict	72	36.4
• Job loss or employment-related stressors	64	32.3
• Significant acute loss event	11	5.6
Any perpetuating factors	130	65.7
• Chronic pain, fatigue, Chronic medical conditions	55	27.8
• Anxiety and hypervigilance, avoidance pattern	94	47.5
• Interpersonal or work-related stressors, unconscious secondary gains	90	45.5
• Invalidation by the healthcare system; stigma, lack of diagnostic agreement, maladaptive illness beliefs	56	28.3
Comorbidities	Frequency	Percent
Any coexisting other functional neuraxis:	127	64.1
• Speech	17	8.6
• Weakness/ataxia	40	20.2
• Sensory/pain	62	31.3
• Visual defects	11	5.6
• Hearing defects	4	2

• Bladder issues	11	5.6
• Ptosis	6	3
Any other somatisation disorders:	49	24.7
• Chest pain	11	5.6
• Respiratory difficulty	19	9.6
• Abdominal discomfort	11	5.6
• Loss of consciousness	23	11.6
• Palpitation	3	1.5
Any coexisting Psychiatric disorders	131	66.2
• Anxiety	83	41.9
• Depression	45	22.7
• Schizophrenia	6	3
• BPAD	16	8.1
• Personality disorders	25	12.6
Any coexisting organic movement disorders	12	6.1
• Parkinsonism	4	2
• Hyperkinetic	11	5.6
Any coexistent organic neurological disorders	93	47
• Epilepsy	11	5.6
• Neuromuscular	12	6.1
• Immune-mediated	4	2

• Stroke	12	6.1
• Migraine	45	22.7
• Peripheral vertigo	5	2.5
• Low backache	13	6.6
• Miscellaneous	12	6.1
Any medical comorbidities	68	34.3
• Diabetes mellitus	29	14.6
• Systemic Hypertension	25	12.6
• Dyslipidemia	13	6.6
• Hypothyroidism	10	5.1
• Coronary artery disease	5	2.5
• Chronic kidney disease	1	0.5
• Obesity	2	1
• Miscellaneous	19	9.6
Appetite issues	19	9.6
Sleep disturbances	99	50
Substance abuse	13	6.6

Around two-thirds had either a history or currently active psychiatric disorder at the time of diagnosis of FMD, of which anxiety was the most common. Eleven subjects

had an additional genuine hyperkinetic movement disorder and 4 subjects had Parkinsonism, which was distinct from the FMD phenomenology and distribution.

A 47-year-old gentleman had abrupt onset of non-rhythmic slow pelvic rotatory movements lasting 1-2 minutes, at frequency of 4-5 per day. He was admitted and revealed work-related stressors and had stopped going to job after the onset of these movements. There was complete remission of these movements at discharge. He developed right hemifacial spasm 8 years later which responds to botulinum toxin injection.

A 37-year-old gentleman with schizophrenia on antipsychotics, developed tardive dyskinesia, later on bizarre gait with odd gyrations

A 32-year-old-lady (P) with bipolar affective disorder in remission with valproate, was admitted for evaluation of paroxysmal perioral and neck movements of multiple semiologies and varying duration, and was found to be consistent with functional movement disorder. She was also found to have drug induced parkinsonism.

A 20-year-old girl who had beta-blocker induced fine postural tremors, and she presented with abrupt clustering of violent episodic shaking of all four limbs which was judged to be functional in origin.

A 63-year-old lady with a history suggestive of parkinsonism of less than 6 months duration, on 450mg of levodopa per day, had, in addition, paroxysmal events characterised by trembling of the whole body lasting 1-2 minutes with spontaneous improvement. She has scanty extrapyramidal signs (hypomimia and right upper limb rigidity) on examination. The phenomenology of paroxysmal event were highly suggestive of FMD and Levodopa was tapered and stopped on follow-up as

extrapyramidal signs were scanty and non-disabling. There was no progression of extrapyramidal signs or non-motor symptoms of PD even after 6 months of stopping Levodopa.

A 53 year old gentleman, on psychiatric medications for mood disorder, with drug induced parkinsonism also had bizarre neck and upper limb movements of varying phenomenology not compatible with any known organic neurological disorder

Clinical features:

The mode of onset of symptoms according to the duration at presentation was arbitrarily defined in the study as “hyper-acute” (within 24 hours), “acute” (more than 24 hours, less than 4 weeks), “subacute” (4- 8 weeks), and “chronic” (more than 8 weeks). The clinical course of symptoms before presentation was grouped into “static”, “steadily progressive”, “step-wise progressive”, “improving”, and “fluctuating types”. Most presented with acute (47%) or hyperacute (30.8%) onset and 59.1% had fluctuating course. The most common FMD phenomenology was gait dysfunction (47.5%) followed by mixed movement disorders (43.9%). Dystonia was the most common (34%) individual movement disorder phenomenology (Video).

Two scales were used to quantify the disability; the Simplified functional movement disorder rating scale (S-FMDRS) (which is a composite score of 0-54, lowest score depicting lowest disability and the highest score depicting highest disability) and the modified Rankin scale (mRS) (which is an ordinal score of 0-6, lowest score depicting, lowest level disability and the highest score depicting the highest level of disability). The categorisation of body parts affected adapted from the S-FMDRS scores is shown in Figure 2.

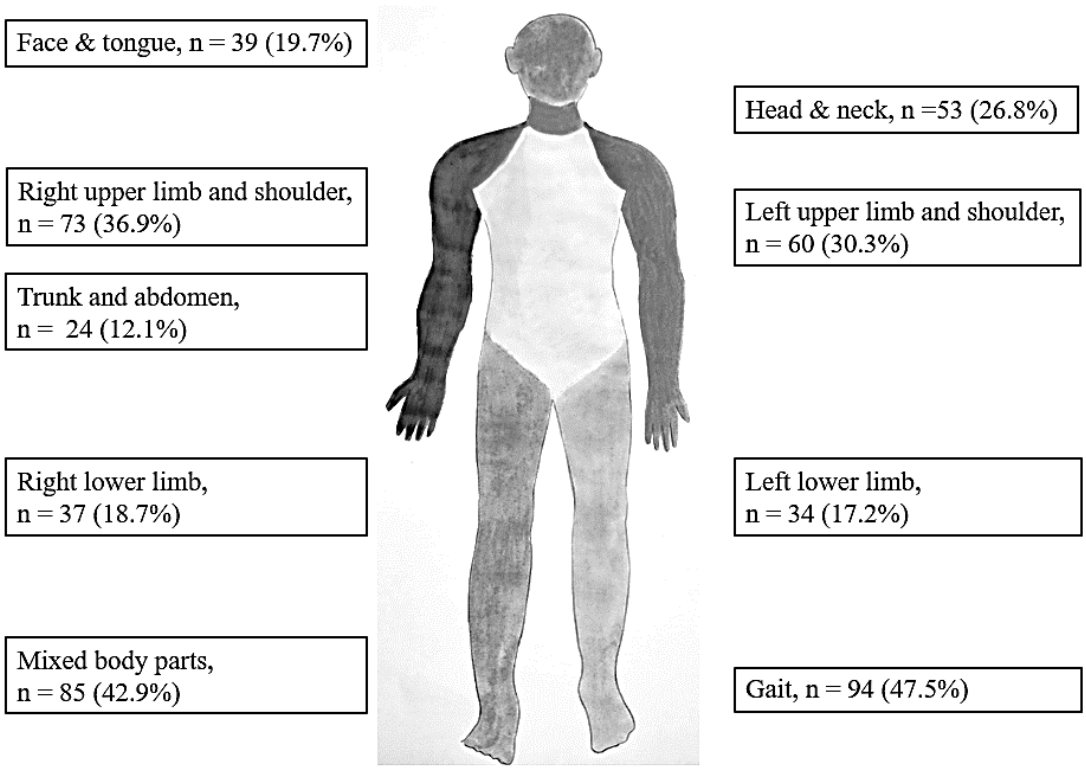


Figure 2: Body parts affected by various functional movement disorders

All the subjects had a minimum follow-up of 3 months before they were clinically diagnosed as FMD by a Movement disorder specialist. The subjects who initially had a possible FMD-like presentation and later developed organic movement disorder were excluded from the final analysis. The clinical diagnostic pointers collected retrospectively from medical records (and video documentation whenever available) were compared against two popular diagnostic criteria for FMD; Fahn and William's diagnostic levels of certainty and the 10-point inclusion criteria (Table 3)

Table 3: Clinical features satisfied according to various diagnostic criteria

Variables	Frequency	Percent
10-point inclusion criteria		
Inconsistency	172	86.9
Incongruency	182	91.9
Paroxysmal	140	70.7
Static	101	51
Rapid onset	163	82.3
Distractibility	124	62.6
Suggestibility	115	58.1
Lack of sensory tricks	88	44.4
Spread to multiple sites	73	36.9
Spontaneous remission	130	65.7
A. 10-point inclusion criteria >=7/ 10 satisfied by: 124/198 (62.6%)		
Diagnostic levels of certainty (Fahn & William)		
Documented	116	58.6
Clinically established	27	13.6
Probable,	36	18.2
Possible	19	9.6
B. Documented or Clinically established levels satisfied by 143/198 (72.2%)		

Twelve subjects received botulinum toxin injections, of which nine of them had complete remission of symptoms, two of them had further relapse and one was lost to follow-up. Abrupt and drastic improvement soon after administration of botulinum toxin injections was observed in two subjects.

A 40-year-old lady, presented with abnormal multidirectional neck movements of 10 years duration. The incongruity, varying phenomenology, distractibility and coexistent hyperventilation suggested a FMD. She received Botulinum toxin injection to neck muscles following which she had immediate disappearance all the neck movement (video).

A 17-year-old boy, developed painful posturing of left foot of 6 months duration. He was tried on various medications including alternative medicines, pain management with Physiotherapy, Orthopedic casts/splints, lumbar sympathetic plexus and intravenous ketamine and lignocaine infusions, underwent left ankle explorative surgery with curettage and tendon lengthening from elsewhere. He was anxious with indifference to his disability, with pain restricting ankle joints. After a detailed counselling session to both the boy and parents, he was given botulinum toxin injection to left TP following which he dramatically improved immediately and started walking normally and even ran in the wards which suggested functional etiology

Follow-up:

Follow-up status in 2024 (after a mean duration of 5.34 ± 5.2 years), was available in 169 subjects. Among them, 64.5% had complete remission. Various demographic, clinical, and coexistent factors were compared among subjects who had complete

remission (improved outcome) and not complete remission (no improvement outcome) (Table 4). Those with complete remission had a younger age, shorter duration at presentation, hyper-acute onset, weakness as presenting phenomenology, some identifiable precipitating event particularly dissociation event or interpersonal conflict, received formal psychologist counseling, and more often associated with resuming work/ routine activities. Those who failed to have complete remission had a higher frequency of unemployed status, coexistent organic neurological disorders, medical comorbidities, segmental distribution, and predisposing health anxiety behavior.

Table 4: Comparison of various parameters among subjects with FMD who had and did not have complete remission on long-term follow-up

Variables	Complete remission, n=109 (64.5%)	No complete remission, n=60 (35.5%)	p-value
Age of onset	31.25±13.77	39.12±16.68	**0.001**
Age at presentation	32.22±13.92	42.43±15.68	**<0.001**
Female gender	66 (60.6)	40 (67.7)	0.431
Number of years of education	11.48±3.65	10.87±3.45	0.315
Occupational class: Student Unemployed Employed	 30 (27.5) 28 (25.7) 51 (46.8)	 7 (11.7) 24 (40) 29 (48.3)	**0.03**

Marital status: Single Married Divorced Widowed Underage Missing data	 18 (16.5) 55 (50.5) 3 (2.8) 3 (2.8) 27 (24.8) 3 (2.8)	 13 (21.7) 39 (65) 1 (1.7) 1 (1.7) 5 (8.3) 1 (1.7)	0.149
Coexistent other functional neuraxis	75 (60)	36 (68.8)	0.249
Coexistent non-neurological somatisation	26 (23.9)	20 (33.3)	0.185
Coexistent psychiatric disorders	79 (72.5)	39 (65)	0.311
Coexistent organic movement disorders	6 (5.5)	5 (8.3)	0.476
Coexistent organic neurological disorders	44 (40.4)	38 (63.3)	**0.004**
Medical comorbidities	23 (21.1)	34 (56.7)	**<0.001**
Family history or neighbours with similar illness	11 (10.1)	8 (13.3)	0.452
Resumed work/ education	92 (85.2)	30 (50)	**<0.001**
Duration of symptoms, in months	12.89±23.37	40.90±77.11	**<0.001**
Mode of onset: Hyper-acute Acute	 46 (42.2) 44 (40.4)	 7 (11.7) 34 (56.7)	**<0.001**

Subacute	10 (9.2)	14 (23.3)	
Gradual	9 (8.3)	5 (8.3)	
Clinical course:			0.219
Static	18 (16.5)	8 (13.3)	
Steadily progressive	11 (10.1)	10 (16.7)	
Step-wise progressive	11 (10.1)	9 (15)	
Improving	6 (5.5)	0 (0)	
Fluctuating	63 (57.8)	33 (55)	
Phenomenology:			
Hyperkinetic	63 (57.8)	37 (61.7)	0.624
Hypokinetic	49 (45)	34 (56.7)	0.145
Weakness	31 (28.4)	4 (6.7)	**0.001**
Falls	18 (16.5)	9 (15)	0.797
Gait	49 (45)	34 (56.7)	0.145
Mixed	48 (44)	23 (38.3)	0.472
Body distribution:			
Focal	22 (20.2)	10 (16.7)	0.577
Segmental	19 (17.4)	21 (35)	**0.010**
Multifocal	6 (5.5)	0 (0)	**0.064**

Hemi	1 (0.9)	2 (3.3)	0.255
Generalized	15 (13.8)	5 (8.3)	0.296
10-point inclusion criteria:			
Inconsistency	98 (89.9)	48 (80)	**0.072**
Incongruency	102 (93.6)	54 (90)	0.404
Paroxysmal	74 (67.9)	41 (68.3)	0.953
Static	61 (56)	32 (53.3)	0.742
Rapid onset	93 (85.3)	45 (75)	**0.097**
Distractibility	63 (57.8)	41 (68.3)	0.178
Suggestibility	61 (56)	36 (60)	0.612
Lack of sensory tricks	48 (44)	23 (38.3)	0.472
Spread to multiple sites	39 (35.8)	21 (35)	0.919
Spontaneous remission	75 (68.8)	35 (58.3)	0.172
Mean 10-point	6.53±1.76	6.27±1.83	0.357
Mean S-FMDRS score	8.62±6.47	9.99±7.88	0.253
Mean mRS score	2.70±0.94	2.65±0.68	0.734
Treatment modality:			
Received formal neuro-psychological	99 (90.8)	48 (80)	**0.014**
counselling	7 (6.4)	4 (6.7)	0.951
Botulinum toxin injection			

Predisposing factors			
Any	95 (87.2)	54 (90)	0.430
Female	66 (60.6)	40 (67.7)	0.431
Financial strain/low socioeconomic status	20 (18.3)	13 (21.7)	0.603
Chronic neurological or psychiatric comorbidities	55 (50.5)	36 (60)	0.234
Maladaptive traits	61 (56)	34 (56.7)	0.930
Physical, sexual, or emotional trauma	16 (14.7)	11 (18.3)	0.535
Health anxiety and somatic vigilance	6 (5.5)	11 (18.3)	**0.008**
Neglect	6 (5.5)	6 (10)	0.276
Major losses such as bereavement or divorce	12 (11)	6 (10)	0.839
Precipitating factors			
Any	75 (68.8)	33 (55)	**0.088**
Physical injury/surgery/Preceding illness/Accidents	41 (37.6)	20 (33.3)	0.579
Autonomic hyperarousal event	15 (13.8)	9 (15)	0.825
Dissociation event, Interpersonal conflict	47 (43)	18 (30)	**0.093**
Job loss or employment-related stressors	41 (37.6)	17 (28.3)	0.224
Significant acute loss event	7 (6.4)	4 (6.7)	0.951
Perpetuating factors			
Any	72 (66.1)	43 (71.7)	0.755

Chronic pain, fatigue, Chronic medical conditions	26 (23.9)	21 (35)	0.122
Anxiety and hypervigilance, avoidance pattern	52 (53.3)	32 (47.7)	0.484
Interpersonal or work-related stressors, unconscious secondary gains	53 (48.6)	27 (45)	0.652
Invalidation by the healthcare system; stigma, lack of diagnostic agreement, maladaptive illness beliefs	31 (28.4)	19 (31.7)	0.660

Multivariate logistic regression analysis was performed on the statistically significant variables, to find out the Odd's ratio and predictors of complete remission in FMD. Shorter duration at presentation, hyper-acute mode of onset, and absence of any medical comorbidities were identified as independent predictors for complete remission (Table 5).

Table 5: Multivariate regression analysis to find out predictors of a favourable outcome in Functional movement disorders on Follow-up

Variables	Odd's ratio (OR)	95% Confidence Interval		p-value
Younger age at onset	1.45	0.092	22.911	0.792
Younger age at presentation	0.598	0.073	4.89	0.632
Shorter duration at the initial visit	3.476	1.315	9.191	**0.012**
Unemployed	0.632	0.24	1.666	0.353
Hyper-acute mode of onset	4.842	1.341	17.491	**0.011**
Weakness as FMD phenomenology	3.609	0.743	17.533	0.111
Segmental body distribution	0.563	0.212	1.494	0.249
Inconsistency	2.184	0.564	8.452	0.258
Rapid onset	0.385	0.121	1.229	0.107
Health anxiety and somatic vigilance	0.331	0.081	1.345	0.122
Any precipitating factor	0.713	0.262	1.938	0.507
Dissociation event, Interpersonal conflict	0.819	0.318	2.109	0.679
Presence of coexistent neurological disorders	2.076	0.806	5.348	0.130
Presence of medical comorbidities	4.654	1.818	11.913	**0.001**
Psychological counselling received	1.825	0.412	8.085	0.428
Resumed work/ education	2.911	1.131	7.494	**0.027**

DISCUSSION

We conducted a long-term follow-up to study the clinical profile and predictors favouring complete remission of FMD. The duration of follow-up ranged from 3 months to 20 years, which is the longest to date. The wide range noted in age of onset in our study is an awareness that FMD can occur in any age group, manifesting based on the various cultural and psychosocial influences at different phases of life. The proportion of the paediatric population in our cohort was less compared to other Indian studies which have reported up to 30-43%, which may be partly due to the referral bias to our centre (9–11). Around 10% of them reported having an acquaintance (family member or neighbour) with a similar movement disorder before the onset, which favours a volitional component in the genesis of FMD. Unemployed status was noted at a higher frequency among those with a poor outcome.

The onset of symptoms was abrupt in most of the previous studies as in ours (5). Around 30% of our subjects had a hyperacute presentation, which often presented as a stroke mimic and resulted in a full-fledged protocol-driven evaluation including magnetic resonance imaging (MRI). This could represent a subpopulation of FMD where clinical impression with positive signs alone may not suffice in ruling in the diagnosis. The most common phenomenology in our cohort was gait dysfunction followed by mixed movement disorders, and dystonia was the most common individual movement disorder. This was contrary to other studies where tremor and myoclonus were at the forefront(5).

The shorter symptom duration is an already established good prognostic factor in FMD (5). Apart from this, our study revealed that the subgroup of subjects who improved on follow-up were younger, with hyper-acute onset, and had weakness as the presenting phenomenology. Whether the prompt seeking of medical attention and a more convincing delivery of diagnosis to the patient in case of hyper-acute presentation and functional weakness has influenced the outcome needs to be considered. The acceptance of diagnosis is a factor well established as a good prognosis in FMD.

The right upper limb and shoulder were noted to be the most commonly affected body parts in the study. Being a right-handed dominant population, and assuming our study population was predominantly right-handed, involvement of the same could again point towards a subconscious volitional component of the disorder (12). The chances for a pronounced functional and social disability due to the dominant limb involvement is another implication derived by noting the body part affected. The

physical disability due to FMD as assessed with S-FMDRS and mRS was of mild-moderate levels, which represents only the tip of the iceberg. A comprehensive assessment of the psychological, functional, and social disability would have been appropriate, however, limited by the retrospective design of the study.

Segmental distribution was noted at a higher frequency among those with poor outcomes.

Although psychiatric comorbidities are not currently considered a pre-requisite to diagnose FMDs, a significant number of subjects were noted to have coexisting psychiatric illnesses similar to previous reports (5). We attempted to delineate the presence of any predisposing, precipitating, or perpetuating factors from the available data. Park et al identified a history of significant trauma in life and recent interpersonal conflicts as the most notable predisposing and precipitating factors for FMD (5). In our data, apart from the female gender, the most commonly identified predisposing factor was maladaptive traits, (53%) particularly in children and young ladies reported by their parents or spouse. For example, fear of a particular subject or teacher and its association with worsening symptoms, and the tendency for throwing difficult-to-manage temper tantrums were the commonest reported maladaptive traits in children. In young adults, most of them had a history of worsening symptoms when they had to cope with a responsible situation or quarrel at house or workplace. The identifiable precipitating event particularly interpersonal conflict or dissociative events was observed at a higher frequency among those with complete remission in our study. Whereas predisposing health anxiety behaviour, and coexistent neurological or other medical comorbidities were more frequently associated with a

poor outcome. Physicians should be aware of the various ego-defense mechanisms prevalent in general which may give an insight into the etiology of FMDs (13). As this was retrospective data and a standardized neuropsychiatric evaluation might not have been complete, there could be a potential underestimation too. Active surveillance of mental health should be an integral strategy in the management and counseling of patients with FMDs.

Shorter duration at presentation, hyper-acute mode of onset, and absence of any medical comorbidities were identified as independent predictors for complete remission

SUMMARY AND CONCLUSION

In this hospital-based study, overall, FMD showed a favourable outcome, and baseline clinical features predicted long-term outcome.

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ANNEXURES

1. CV of Principal Investigator- Dr Sayooja Sachithanandan

Last Name SACHITHANANDAN	First Name SAYOOJA	Middle Name
Date of Birth (dd/mm/yy) 04/12/1989		Sex FEMALE
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) PRINCIPAL INVESTIGATOR, SCTIMST		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
dmneuro@sctimst.ac.in		PDF MOVEMENT DISORDERS DEPARTMENT OF NEUROLOGY, SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY THIRUVANANTHAPURAM KERALA 695011
Telephone (Office):		Mobile Number: 9496369238
Telephone (Residence): 0474 2433551		Email: sayooja.04@gmail.com
Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
DM NEUROLOGY	2023	SREE CHITRA TIRUNAL INSTITUTE FOR MEDI SCIENCES AND TECHNOLOGY, THIRUVANANTHAPURAM, KERALA, INDIA
MD GENERAL MEDICINE	2019	GOVERNMENT MEDICAL COLLEGE, THIRUVANANTHAPURAM, KERALA, INDIA
MBBS	2014	GOVERNMENT MEDICAL COLLEGE, THIRUVANANTHAPURAM, KERALA, INDIA
Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration TRAVANCORE COCHIN MEDICAL COUNCIL		

REGISTRATION NUMBER: 52138
YEAR OF REGISTRATION: 2014

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
January 2024	PDF MOVEMENT DISORDERS	SCTIMST, INDIA
2021-2023	SENIOR RESIDENT, NEUROLOGY	SCTIMST, INDIA

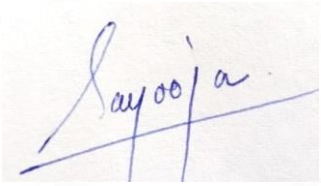
Brief summary of relevant research experience:

PUBLICATIONS

1. Sachithanandan S, Ramachandran H, Jayadevan ER, Kannath SK, Sreedharan SE, Syl PN. CT angiographic patterns predict carotid pseudo-occlusion in acute ischemic stroke. Indian Acad Neurol. 2024 Jan-Feb;27(1):72-76. doi: 10.4103/aian.aian_750_23. Epub 2024 22. PMID: 38495242; PMCID: PMC10941882.
2. Vijayaraghavan, A., Sundaram, S., Sachithanandan, S. et al. Gyratory Seizures: An Earl Clue to Anti NMDAR Encephalitis. Indian J Pediatr (2023). https://doi.org/10.1007/s12098 04566-0

FINISHED PROJECTS AS PRINCIPAL INVESTIGATOR

1. Utility of Clock Drawing test and Cube construction test in diagnosing early cognitive impairment (submitted as Thesis for DM Neurology Degree)
2. Clinical and radiological profile of Pseudo PSP phenotypes
3. Autism spectrum disorder with and without epilepsy- a comparative study on clinical, developmental, electrophysiological, and radiological profile
4. Frozen gaze in ALS- a Dubious paradox (Case report)
5. Parenchymal hemorrhages and hydrocephalus—unusual life-threatening complicatio Listeria rhombencephalitis (Case report)

Signature: 

Date:
25/06/2024

Place:
Trivandrum

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

CDSCO Registration No: ECR/189/Inst/KL/2013/RR-21
DHR Registration No:EC/NEW/INST/2022/2775

SCT/IEC/2210/MARCH/2024

12.04.2024

Dr. Sayooja Sachithanandan
Post Doctoral Fellow
Department of Neurology
SCTIMST, Thiruvananthapuram

Dear Dr. Sayooja Sachithanandan,

The Institutional Ethics Committee held on 16th March, 2024, reviewed and discussed your application to conduct the study titled **"CLINICAL PROFILE AND PREDICTORS OF OUTCOME IN FUNCTIONAL MOVEMENT DISORDERS (IEC /2210) "**

Principal Investigator	Dr Sayooja Sachithanandan, PDF in Movement disorders, Department of Neurology, SCTIMST
Co-Principal Investigator(s)	Dr Syam K (Guide) , Professor and In Charge, Comprehensive Care Centre for Movement disorders, Department of Neurology, SCTIMST Dr Divya K P, Associate Professor, Department of Neurology, SCTIMST Dr Asish Vijayaraghavan, Assistant Professor, Department of Neurology, SCTIMST
Duration of the study	1 year

The following members of the Ethics Committee were present at the meeting held on 16th March, 2024

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Prof. C.C. Kartha	MBBS,MD	Male	Basic Medical Scientist (Chairman)	No
2.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Adv. N Anand	BAL, L.LB	Male	Legal Expert	No
5.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
6.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
7.	Dr. Harikrishna Varma PR	Ph.D (Materials Science)	Male	Medical Technology	Yes
8.	Dr. Manikandan.S	MBBS,MD,PDCC	Male	Clinician	Yes
9.	Dr. Narayanan Namboodiri. K K	MBBS,MD,DM	Male	Clinician	Yes
10.	Dr. Biju Soman	MBBS,MD, DPH, MSc, DLSHTM	Male	Basic Medical Scientist	Yes
11.	Dr. Syam K	MBBS, MD, DM	Male	Clinician	Yes
12.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

The following documents were reviewed:

Original submission

1. *Responses/Amendments made based on the Reviewer's comments*
2. *Checklist Form*
3. *Covering letter addressed to the Chairperson, IEC, SCTIMST dated 15.01.2024*
4. *IEC Application Form*
5. *Study Proposal*
6. *Declaration Form*
7. *CV of PI and Co-PIs*
8. *Proforma*
9. *SRC Recommendation* Letter

Revised submission

1. *Covering letter addressed to the Member Secretary, IEC, SCTIMST dated 09.04.2024*
2. *Responses/Amendments made based on the Reviewer's comments*
3. *Checklist Form*
4. *IEC Application Form*
5. *Study Proposal*
6. *Declaration Form*
7. *CV of PI and Co-PIs*
8. *Proforma*

IEC Decision
The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Dr. G. Srinivas
Member Secretary, IEC

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST, THIRUVANANTHAPURAM

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST
THIRUVANANTHAPURAM

PROFORMA

INITIAL PRESENTATION:

Demographics

- Age:
- Age group: < 18 years, 18-60 years, > 60 years
- Sex: M/F
- Education:
- Occupation:
- Financial status:
- Residence: Rural / Urban
- Marital status: Married/ single/ divorced/ unmarried partner/ widowed

Clinical features

- Age of onset of movement disorder
- Year of onset-
- Mode of onset-
- Time taken to evolve:
- Duration of symptom at initial visit
- Phenomenology of movement disorder- Tremor/ Dystonia/ Tic/ Chorea/ HFS/ Multiple movement/ Parkinsonism/ gait abnormality/
- Body part affected- Head, stomatognathic system, neck, arm, trunk, leg
- Other neuraxis involvement- Speech/ weakness/ sensory/ ataxia/ vision/ hearing
- 10 point inclusion for diagnosing FMD: rapid onset, static course, paroxysmal symptoms, spreading to multiple sites, spontaneous remission, inconsistent symptoms, distractibility, incongruous symptoms, lack of sensory tricks, and suggestibility
- Level of diagnostic certainty: documented, clinically established, probable, and possible
- Psychiatric symptoms- Anxiety/ Depression/ Delusion/ hallucinations/ Personality disorders
- Predisposing/ precipitating/ perpetuating- Physical trauma/ illness/ mental stressors/ unknown
- Appetite- normal/ reduced/ increased
- Sleep- Normal/ abnormal
- Substance abuse- Alcoholism/ smoking/ others
- Family history of similar movement disorder
- EEG (if available) for BP: Present/ absent
- Neuroimaging (if available): Normal/ abnormal

Disability

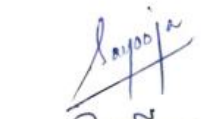
- Number of days of leave from job/ education
- Financial expenditure during diagnosis and treatment
- Physical disability (mRS score)

Outcome

- Disclosure of diagnosis of psychogenicity/ functional nature to patient
- Acceptance of diagnosis- positive/ denial
- Treatment modality: Formal Psychiatry assessment/ Psychologist counselling/ Self-motivation exercises/ Family support
- Treatment outcome at Last follow up- improved/ not improved
- Follow up duration

Declaration by Investigators

We hereby certify that we are fully involved in the conception & design of this study (Title: CLINICAL PROFILE AND PREDICTORS OF OUTCOME IN FUNCTIONAL MOVEMENT DISORDERS) and assume full responsibility for the ethical and scientific conduct of this study.

Designation	Name	Signature	Date
P I	Dr. Sayooja Sachithanandan		15.01.24
Co-PI	Dr. Syam K		15.01.24
Co-PI	Dr. Divya KP		15.01.24
Co-PI	Dr. Asish Vijayaraghavan		15.01.24

PLAGARISM CERTIFICATE



grammarly Report: Sayooja thesis Plagarism certificate

Sayooja thesis Plagarism certificate

by krishna mohan

General metrics

63,022	9,613	1019	38 min 27 sec	1 hr 13 min
characters	words	sentences	reading time	speaking time

Score

57

This text scores better than 57% of all texts checked by Grammarly

Writing Issues

728	369	359
Issues left	Critical	Advanced

Plagiarism

13 %

78 sources

13% of your text matches 78 sources on the web or in archives of academic publications

SYNOPSIS

Background:

In functional movement disorders (FMD) the subject perceives various movement disorders as involuntary, despite clinical findings demonstrating intact neurological function and a volitional component. Understanding the factors associated with a favourable outcome has important treatment implications

Aims:

To delineate clinical profile of Functional Movement Disorders and predictors of long-term outcome

Methodology:

We retrospectively reviewed the baseline demographic and clinical profile of all patients with FMD diagnosed in our hospital from 1999-2024. Their current status was evaluated through systematic telephonic interviews. The patients were retrospectively categorized based on published diagnostic criteria and the outcome and functional status were noted[1,2]. The baseline factors influencing outcome were determined

Results:

Data from 198 subjects with a mean age of 35.2 ± 15.4 years were available for analysis; 60.6% were women. Most presented with acute (47%) or hyperacute (30.8%) onset and 59.1% had fluctuating course. The most common FMD phenomenology was gait dysfunction (47.5%) followed by mixed movement disorders (43.9%). Dystonia was the most common

(34%) individual movement disorder phenomenology. The most frequent body distribution was segmental (22.7%). Female gender (60.6%), and preceding physical injury (36.9%) were the most common predisposing and precipitating factors. Anxiety, hypervigilance, and avoidance patterns (47.5%) were the most common perpetuating factors.

Follow-up data after a mean duration of 5.34 ± 5.2 years, was available in 169 subjects and 109 (64.5%) had complete remission. Those with complete remission had a younger age and shorter duration at presentation, hyperacute onset, weakness as presenting phenomenology, some identifiable precipitating event particularly dissociation event or interpersonal conflict, received psychiatric counseling, and more often associated with resuming work/ routine activities. Those who failed to have complete remission (persistent or worsening symptoms or relapsed within the last 3 months of follow-up) had a higher frequency of unemployed status, coexistent organic neurological disorders, medical comorbidities, segmental distribution, predisposing health anxiety behaviour.

Among them, shorter duration at presentation, hyper-acute mode of onset, and absence of any medical comorbidities were the independent predictors for complete remission

Conclusion:

Overall, FMD in this hospital-based study showed a favourable outcome, and baseline clinical features predicted long-term outcome

References:

1. Fahn S, Williams DT. Psychogenic dystonia. Adv Neurol. 1988;50:431–55.

2. Yoshida K. Clinical Characteristics of Functional Movement Disorders in the Stomatognathic System. Front Neurol. 2020;11:123.

3. Lidstone SC, MacGillivray L. The Biopsychosocial Formulation for Functional Movement Disorder. Functional Movement Disorder: An Interdisciplinary Case-Based Approach. Humana Press; 2022