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Original Article

Symptom Duration and Treatment Timing as Prognostic Factors in Pediatric Functional Motor Disorders

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ABSTRACT

Background: Functional Motor Disorders (FMDs) are increasingly recognized in pediatrics, yet prognostic indicators remain poorly characterized. We examined clinical and health-care variables associated with one-year clinical outcomes.
Methods: This retrospective study included 72 patients aged 9-18 years diagnosed with FMD at two tertiary pediatric hospitals in Italy and the Czech Republic between 2019 and 2023, with at least 6 months of follow-up and two valid Simplified Functional Movement Disorders Rating Scale assessments. Demographic and clinical features, referral history, therapy type and timing, and Simplified Functional Movement Disorders Rating Scale scores were analyzed at baseline, 6, and 12 months.
Results: Overall, 69.4% were female, and mean symptom-onset age was 13.5 ± 1.99 years. Motor severity improved from baseline (10.25) to 12 months (3.55; $P < 0.001$), with 43.1% achieving remission. Longer symptom duration was independently associated with higher severity at baseline ($\beta = 1.19$, $P = 0.021$), 6 months ($\beta = 2.07$, $P < 0.001$), and 12 months ($\beta = 1.79$, $P < 0.001$). More prior referrals independently predicted higher 12-month severity ($\beta = 1.00$, $P = 0.047$). Longer time to FMD-directed treatment was associated with higher follow-up severity and a different symptom trajectory (Time × treatment timing: $P = 0.007$). Trajectories did not consistently differ by sex or symptom phenotype.
Conclusions: Longer symptom duration, more previous referrals, and delayed treatment were associated with greater one-year motor severity. These findings underscore the prognostic relevance of symptom duration and the potential importance of timely access to care, although prospective studies are needed to establish causality.
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Introduction

Functional Motor Disorders (FMDs) are a subgroup of Functional Neurological Disorders (FNDs), an increasingly recognized neurological condition, common to both adults and children. Estimated prevalence in the pediatric population varies between 2.8% and 23%.[1,2] FND is also associated with a considerable financial burden due to extensive use of medical services.[3] While the precise nature of FND remains incompletely understood, it is

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believed to arise from an intricate interplay of biological, psychological, and social factors.[4]

A growing body of imaging and neurophysiological evidence supports the view of FND as a multinetwork brain disorder involving dysfunctional motor, prefrontal, and limbic circuits, with alterations in neurotransmission, neuroplasticity, and predictive processing.[4,5] Diffusion-tensor imaging has also identified reduced microstructural integrity in corticolimbic white-matter pathways in adults with FND.[6] Psychological factors such as stress or maladaptive coping may contribute in some cases, together with disturbances in emotion processing and interoception.[7-9] In pediatric populations, additional stressors such as academic pressures and family dynamics further complicate the clinical picture.[10] Clinically, FMD can present with a hypokinetic or, most often, a hyperkinetic movement disorder, either isolated or combined.[11] Hypokinetic FMD can include weakness and paresis, while hyperkinetic disorders are mainly represented by tremor, dystonia, jerks, myoclonus, and gait disorders but also tic-like disorders.[11] These symptoms are genuine and not intentionally produced,[12] yet they can still lead to significant disability, impairing daily activities and reducing quality of life.[10] In children and adolescents, the presentation is often further complicated by a mix of motor and nonmotor symptoms, including cognitive disturbances that may overlap with what is now conceptualized as functional cognitive disorder,[8] emphasizing the need for early, multidisciplinary intervention.[10]

Despite increasing attention, clinical predictors of outcome in pediatric FMD remain poorly established. In a large prospective cohort of children and young people with FND, including motor subtypes, no specific clinical or demographic characteristic — such as age, sex, socioeconomic status, psychiatric comorbidity, or precipitating events — reliably predicted symptom improvement or resolution at follow-up.[10]

This uncertain prognostic landscape contrasts with adult research, where shorter symptom duration, earlier diagnosis, and greater satisfaction with care have been associated with better outcomes, while delayed diagnosis and personality disorder predict poorer prognosis.[4,13]

However, recent adult evidence from a specialist physiotherapy cohort found that greater perceived control over recovery and lower perceived symptom permanence were weak predictors of improvement, whereas illness duration, pain, and fatigue were not associated with the outcomes measured.[14]

In pediatric samples, predisposing and precipitating factors — including family dysfunction, bullying, peer pressure, and psychiatric symptoms — are frequently reported, yet their prognostic value remains inconsistent.[10,15]

Overall, although approximately half of pediatric cases show symptom improvement or resolution at medium-term follow-up, robust and clinically applicable predictors of outcome are still lacking,[10,15] underscoring the need for further multicenter investigations.

Given the limited evidence on prognostic factors in pediatric FMD, key questions remain regarding which clinical and health-care pathway variables influence recovery. We therefore conducted a retrospective multicenter study involving two European tertiary pediatric centers to characterize pediatric FMD and identify factors associated with symptom evolution over 12 months. Because FMD presentation and care pathways are shaped by health-care system organization, comparing different countries may help distinguish generalizable predictors from context-specific features.

The primary outcome was the change in motor symptom severity over 12 months, measured using standardized assessment tools. Based on adult literature and clinical experience, we hypothesized that (a) longer symptom duration at initial evaluation, (b) a greater number of prior referrals, and (c) delayed initiation of therapy would predict worse outcomes. Secondary, exploratory aims included examining whether symptom phenotype, psychiatric comorbidity, and other clinical or demographic variables were associated with baseline severity or recovery trajectories.

Materials and Methods

Study design and setting

This retrospective study analyzed clinical data from children and adolescents diagnosed with FMDs between 2019 and 2023 at two European tertiary pediatric centers, one specializing in child and adolescent neuropsychiatry in Central Italy and the other in pediatric neurology in the Czech Republic. Data were extracted from medical records and retrospectively analyzed. The study was conducted in accordance with the Declaration of Helsinki and approved by the local institutional review boards of participating centers (nr. 8098/2025).

Participants

Patients were eligible if they met the following inclusion criteria: (1) age 9-18 years at onset; (2) a clinically established diagnosis of FMD, confirmed by pediatric neurologists specialized in movement disorders; (3) at least 6 months of follow-up; and (4) $\geq$2 valid Simplified Functional Movement Disorders Rating Scale (S-FMDRS)[16] assessments. Diagnosis was established according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) criteria,[17] corroborated by previously proposed phenotype-specific diagnostic criteria,[18] which emphasize unequivocal clinical features (inconsistency and incongruence) in the neurological examination, independent of historical or psychiatric variables. Both inpatient and outpatient cases were included. “Possible” or “probable” FMD were excluded, i.e., those patients lacking unequivocal neurological examination findings consistent with positive diagnostic signs of FMD.

Data collection

At the Czech center, data were extracted by a pediatric neurologist, and at the Italian center by a child and adolescent neuropsychiatrist; both investigators had specific training in pediatric FND and were directly involved in the local care pathways. Before formal extraction, pilot extraction and harmonization meetings were conducted to align extraction criteria across centers. Both electronic and paper medical records were reviewed, including complete clinical notes. The clinical supervisors of both programs subsequently reviewed the extracted data and performed random accuracy checks. Baseline (T0) corresponded to the first specialist assessment at the participating center, when the clinically established diagnosis was confirmed. Collected information comprised demographic variables, clinical history and manifestations, therapeutic interventions, and follow-up data. Symptom onset was categorized from source records as acute/subacute or chronic; this onset-pattern variable was analyzed separately from symptom duration. All patients had been routinely assessed with the S-FMDRS, used to monitor FMD characteristics and severity.[16] According to this clinician-rated scale, higher scores indicate greater motor symptom severity; the S-FMDRS has demonstrated good inter-rater reliability and sensitivity to change.[16] Treatment timing was defined as the interval between symptom onset and initiation of the first FMD-directed treatment.

Because this interval included the prebaseline clinical history, it could exceed 12 months even though outcomes were assessed over the subsequent 12 months. Information regarding symptom severity and evolution was analyzed and correlated with clinical and demographic characteristics, as well as with the type and timing of therapeutic interventions. ACEs were systematically assessed as part of standard-of-care history taking. Psychiatric comorbidities were diagnoses established through standardized clinical interviews during the initial assessment, whereas neurological and other medical comorbidities were collected from the clinical history and family report. The primary outcome was the change in S-FMDRS scores from baseline to 12 months. Secondary outcomes focused on determining which clinical variables predicted initial symptom severity and their evolution over time.

Statistical analysis

All statistical analyses were performed using R within the RStudio environment. Data management, transformation, and visualization were carried out using the tidyverse package.[19] Descriptive statistics were calculated to summarize demographic and clinical variables. Group differences were assessed using independent-sample *t* tests or one-way analysis of variance (ANOVA) for continuous variables, and Chi-square or Fisher exact tests for categorical variables. Longitudinal variation in motor symptom severity (S-FMDRS) was examined through paired-sample tests and repeated-measures ANOVA. Primary repeated-measures models tested Time × clinical predictor interactions for symptom duration, number of prior referrals, and treatment timing. Separate unadjusted exploratory repeated-measures models examined each additional demographic, clinical, and treatment variable listed in Table 1; variables with fewer than five participants in either binary comparison group were tabulated but not modeled, and no multiplicity correction was applied. The recruiting center was included in sensitivity models for symptom duration and referral count. Mauchly test was used to assess sphericity, and Greenhouse–Geisser correction was applied when required. Repeated-measures models report partial eta-squared (ηp^2); cross-sectional one-way ANOVAs report eta-squared (η^2). To assess independent predictors of symptom severity at each time point, multivariable linear regression analyses included symptom duration, number of prior referrals, age at diagnosis, symptom type (isolated/combined), psychiatric comorbidity, and recruiting center. Model performance was evaluated using adjusted R^2 and Akaike Information Criterion; multicollinearity and residual independence were assessed using the Variance Inflation Factor and Durbin–Watson statistic, respectively. All tests were two-tailed with $P < 0.05$. Missing data were handled by complete-case analysis for the relevant model. Full coefficients, model diagnostics, treatment-timing analyses, and nonsignificant exploratory results are reported in the Supplementary Materials.

Results

Sample characteristics

A total of 72 children and adolescents with FMD were included (mean age at last follow-up: 14.73 ± 2.18 years; 69.4% female). The average age at symptom onset was 13.5 ± 1.99 years, with a mean symptom duration of 1.02 ± 1.23 years at first evaluation. Most patients showed an acute onset of symptoms (77.8%) and nearly half presented with a combined phenotype (51.4%), frequently involving gait disorders (62.5%). Nonmotor functional symptoms were common, particularly pain (66.7%) and sensory disturbances (48.6%), while neurological comorbidities were present in 15.3% and psychiatric comorbidities in 44.4% of cases. Neurological comorbidities included migraine (n = 4), epilepsy/seizures (n = 2), hyperkinetic movement disorder (n = 1), neuropathy (n = 1), and other conditions (n = 3). Psychiatric comorbidities comprised anxiety disorders (n = 19), major depressive disorder (n = 5), neurodevelopmental disorders (n = 5), somatic symptom disorders (n = 4), eating disorders (n = 2), and one case each of schizophrenia spectrum disorder, impulse-control disorder, dissociative/fugue state, unspecified mood disorder, and personality disorder; categories were not mutually exclusive.

The role of precipitating factors was also investigated: the most frequently reported ones were psychological precipitating factors (n = 27) and physical/medical illness (n = 22), while 18 patients reported no precipitating factor.

At baseline, 77.8% of patients had an acute/subacute symptom onset and 22.2% had a chronic onset; baseline S-FMDRS scores were similar between the two onset-pattern groups.

Nearly all patients received treatment (97.2%), most commonly combined physiotherapy and psychotherapy (56.9%), followed by psychotherapy alone (25.0%) and physiotherapy alone (9.7%). Pharmacological treatments were prescribed in 45.8% of cases, including benzodiazepines, selective serotonin reuptake inhibitors, anti-seizure medications, and antipsychotics. One-year outcomes were available for 70 patients, with remission observed in 43.1% of the cohort.

Table 1 reports the main demographic and clinical variables and comparisons between centers.

Longitudinal changes in motor symptom severity

S-FMDRS scores significantly improved over time. Longitudinal analyses were conducted on 72 patients at baseline and 71 at the 12-month follow-up, due to one missing S-FMDRS value at 12 months. Paired-sample *t* tests showed a reduction from baseline to 6 months (mean difference = 5.08, standard error [SE] = 0.52; t (71) = 9.81, $P < 0.001$, Cohen d = 1.16, 95% confidence interval [CI; 0.86, 1.45]) and from 6 to 12 months (mean difference = 1.63, SE = 0.28; t (70) = 5.84, $P < 0.001$, Cohen d = 0.69, 95% CI [0.43, 0.95]). A significant overall reduction from baseline to 12 months was also observed (mean difference = 6.79, SE = 0.54; t (70) = 12.52, $P < 0.001$, Cohen d = 1.49, 95% CI [1.15, 1.82]). Nonparametric Wilcoxon tests confirmed these findings.

Repeated-measures ANOVA demonstrated a significant within-subject effect of time on S-FMDRS scores (F (1.42, 99.46) = 117.0, $P < 0.001$, partial $\eta^2 = 0.626$), with Greenhouse–Geisser correction applied due to violation of sphericity (Mauchly W = 0.592, $P < 0.001$).

Estimated marginal means showed progressive improvement from baseline (M = 10.25, S.D. = 4.54) to 6 months (M = 5.17, S.D. = 5.42) and 12 months (M = 3.55, S.D. = 5.22).

Predictors of recovery over time

We ran separate repeated-measures analyses of covariances with Time (baseline, 6 months, 12 months) as a within-subject factor and each clinical variable (symptom duration, number of prior referrals, and treatment timing) entered as a between-subject predictor, testing the Time × Predictor interaction. This analysis showed that patients with longer symptom duration exhibited a less favorable recovery trajectory (Time × Symptom Duration: F (1.43, 98.59) = 7.15, $P = 0.004$, partial $\eta^2 = 0.094$). When additionally controlling for the recruiting center, the Time × Symptom Duration interaction remained significant (F (1.35, 91.58) = 7.60, $P = 0.003$, partial $\eta^2 = 0.101$). The Time × Center interaction did not reach

TABLE 1.
Main Demographic and Clinical Variables of the Total FMD Sample and Differences Between the Italian and Czech Centers

Variable	Total Sample n = 72	ITA n = 44	CZE N = 28	*P* Value IT vs. CZ
Female gender, n (%)	50 (69.4)	28 (63.6)	22 (78.6)	0.180[C]
Age at the onset, mean (S.D.)	13.5 (1.99)	13.3 (1.96)	13.9 (2.01)	0.239[M]
N of previous referrals, mean (S.D.)	**1.78 (1.46)**	**1.11 (1.04)**	**2.82 (1.42)**	**<0.01**[M]
Symptom duration (years), mean (S.D.)	1.02 (1.23)	0.95 (1.31)	1.14 (1.11)	0.701[M]
Previous misdiagnosis, n (%)	41 (56.9)	26 (59.1)	15 (53.6)	0.645[C]
Acute onset of symptoms, n (%)	56 (77.8)	31 (70.5)	25 (89.3)	0.061[C]
Spontaneous remissions, n (%)	3 (4.2)	2 (4.5)	1 (3.6)	1.000[F]
Precipitating factors, n (%)	54 (75)	35 (79.5)	19 (67.9)	0.264[C]
Physical/medical precipitating factor	22 (30.6)	11 (25)	11 (39.3)	0.200[C]
Psychological precipitating factor	**27 (37.5)**	**25 (56.8)**	**2 (7.1)**	**<0.001**[F]
Previous surgery	1 (1.4)	0	1 (3.6)	0.389[F]
Previous general anesthesia	0	0	0	/
Adverse drug reactions	1 (1.4)	1 (2.3)	0	1.000[F]
Infection	9 (12.5)	3 (6.8)	6 (21.4)	0.140[F]
Isolated n (%)	35 (48.6)	18 (40.9)	17 (60.7)	0.101[C]
Combined n (%)	37 (51.4)	26 (59.1)	11 (39.3)	0.101[C]
FMD phenotype, n (%)				
Weakness	48 (66.7)	26 (59.1)	22 (78.6)	0.087[C]
Dystonia	6 (8.3)	3 (6.8)	3 (10.7)	0.672[F]
Jerks/myoclonus	11 (15.3)	7 (15.9)	4 (14.3)	1.000[F]
Tremor	15 (20.8)	11 (25)	4 (14.3)	0.376[F]
Tic	5 (6.9)	4 (9.1)	1 (3.6)	0.642[F]
Parkinsonism	1 (1.4)	1 (2.3)	0	1.000[F]
Gait disorders	**45 (62.5)**	**32 (72.7)**	**13 (46.4)**	**0.025**[C]
Nonmotor associated symptoms, n (%)				
Sensory symptoms	35 (48.6)	20 (45.5)	15 (53.6)	0.502[C]
Visual disorders	15 (20.8)	7 (15.9)	8 (28.6)	0.197[C]
Pain (including headache)	48 (66.7)	27 (61.4)	21 (75)	0.231[C]
Functional seizures	14 (19.4)	10 (22.7)	4 (14.3)	0.543[F]
Neurological comorbidities, n (%)	11 (15.3)	8 (18.2)	3 (10.7)	0.511[F]
Migraine	4 (5.6)	2 (4.5)	2 (7.1)	0.640[F]
Epilepsy	2 (2.8)	2 (4.5)	0	0.518[F]
Hyperkinetic movement disorder	1 (1.4)	1 (2.3)	0	1.000[F]
Neuropathy	1 (1.4)	1 (2.3)	0	1.000[F]
Stroke	0	0	0	/
Other	3 (4.2)	2 (4.5)	1 (3.6)	1.000[F]
Psychiatric comorbidities, n (%)	32 (44.4)	20 (45.5)	12 (42.9)	0.829[C]
Non-neurological and nonpsychiatric comorbidities, n (%)	28 (38.9)	17 (38.6)	11 (39.3)	0.956[C]
Family history of neurological disease, n (%)	13 (18.1)	10 (22.7)	3 (10.7)	0.228[F]
Predisposing ACEs, n (%)	**15 (20.8)**	**13 (29.5)**	**2 (7.1)**	**0.035** [F]
Physical ACEs	1 (1.4)	0	1 (3.6)	0.389[F]
Psychological ACEs	**14 (19.4)**	**13 (29.5)**	**1 (3.6)**	**0.006**[F]
Treated	70 (97.2)	42 (95.5)	28 (100)	0.253[C]
Treatment timing				
<3 months	36 (50)	25 (56.8)	11 (39.3)	0.147[C]
3-6 months	10 (13.9)	4 (9.1)	6 (21.4)	0.172[F]
6 months-one year	15 (20.8)	9 (20.5)	6 (21.4)	0.921[C]
>one year	9 (12.5)	4 (9.1)	5 (17.9)	0.297[F]
Physiotherapy only	**7 (9.7)**	**7 (15.9)**	**0**	**0.038**[F]
Psychotherapy only	**18 (25)**	**18 (40.9)**	**0**	**<0.001**[F]
Physiotherapy + psychotherapy	**41 (56.9)**	**13 (29.5)**	**28 (100)**	**<0.001**[C]
Occupational therapy	2 (2.8)	2 (4.5)	0	0.518 F
Drug therapy	33 (45.8)	22 (50)	11 (39.3)	0.374[C]
Outcome available at one year	70/72	44/44	26/28	/
Remission, n (% of full cohort)	31 (43.1)	18 (40.9)	13 (46.4)	0.645[C]

Abbreviations:
ACEs = Adverse childhood experiences
C = Chi-square test
CZE = Czech center
F = Fisher test
FMDs = Functional motor disorders
ITA = Italian center
M = Mann-Whitney *U test*
n = Number
T = Independent sample *t test*
Statistically significant values are in bold.
Psychiatric comorbidities include schizophrenia spectrum disorders (n = 1), major depressive disorder (n = 5), anxiety disorders (n = 19), impulse control disorders (n = 1), dissociative/fugue state (n = 1), somatic symptom disorders (n = 4), eating disorders (n = 2), unspecified mood disorder (n = 1), personality disorder (n = 1), neurodevelopmental disorders (n = 5). Non-neurological and nonpsychiatric comorbidities category includes heart diseases (n = 2), diabetes (n = 2), high blood pressure (n = 1), dyslipidemia (n = 1), dysthyroidism (n = 2), rheumatic diseases (n = 3), gastrointestinal diseases (n = 5), other diseases (n = 16).

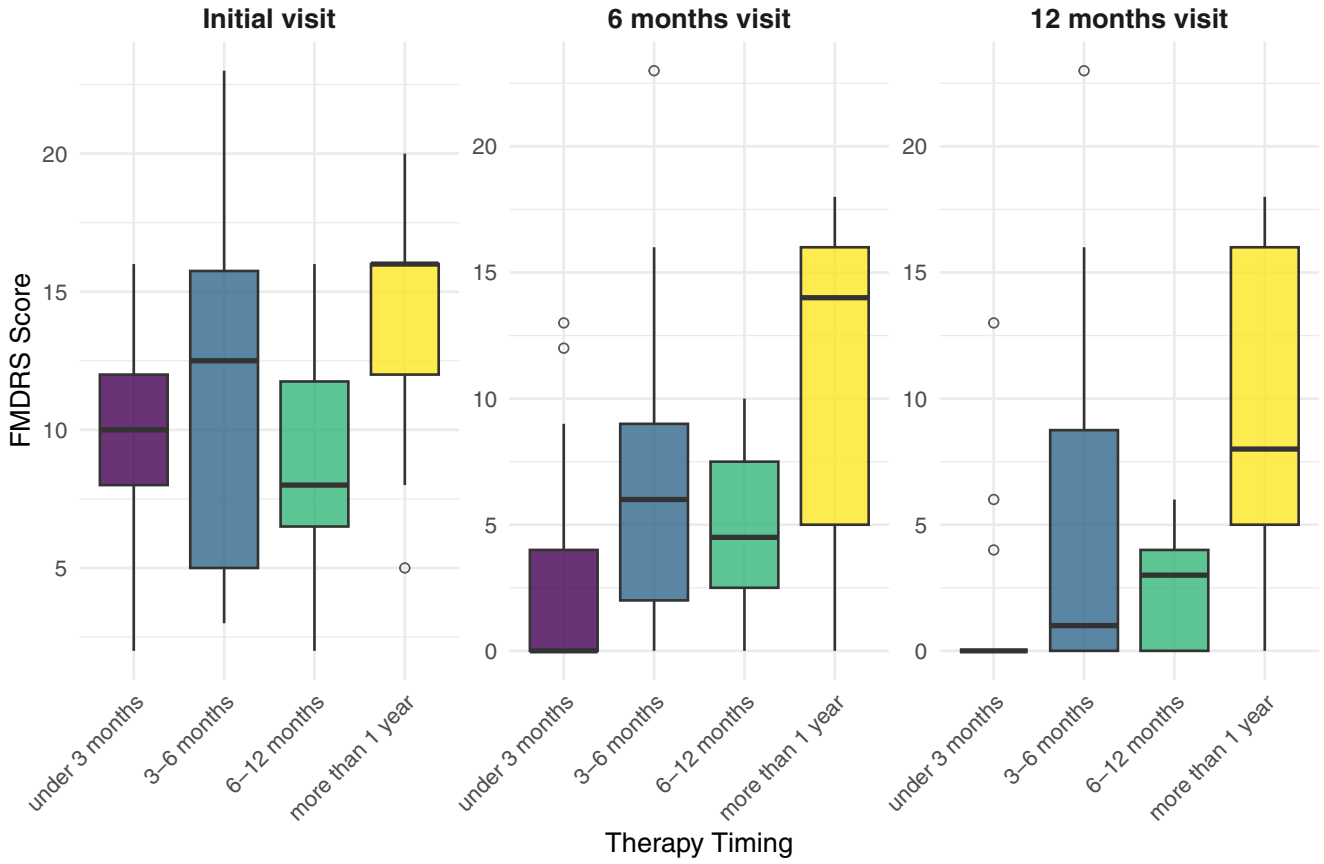


FIGURE. Simplified Functional Movement Disorders Rating Scale (S-FMDRS) scores over time according to treatment timing, defined as the interval between symptom onset and initiation of treatment (categorized as: <3 months, n = 36; 3–6 months, n = 10; 6–12 months, n = 15; >12 months, n = 9). Of the 72 patients included in the study, two did not receive treatment and were therefore not assigned to a treatment-timing category. Among the 70 treated patients, one participant in the 6–12-month group lacked a 12-month S-FMDRS score; complete-case analyses therefore included 69 participants. Error bars represent standard errors. Higher scores indicate more severe motor symptoms. The color version of this figure is available in the online edition.

significance (F (1.35, 91.58) = 2.82, $P = 0.085$), indicating comparable improvement trajectories across sites.

Similarly, a higher number of prior referrals before diagnosis predicted a slower reduction in motor symptom severity over time (Time × Number of Referrals: F (1.48, 101.88) = 8.91, $P = 0.001$, partial $\eta^2 = 0.114$). Treatment timing was also associated with symptom evolution (Time × Treatment Timing: F (4.41, 95.60) = 3.64, $P = 0.007$, partial $\eta^2 = 0.144$). In complete-case cross-sectional comparisons, treatment-timing groups differed at 6 months (F (3,65) = 9.14, $P < 0.001$, $\eta^2 = 0.297$) and 12 months (F (3,65) = 11.70, $P < 0.001$, $\eta^2 = 0.351$), but not at baseline (F (3,65) = 2.55, $P = 0.063$), as shown in Figure. Full results of the primary repeated-measures models are reported in Supplementary Table S3. Complementary descriptive visualizations of prior referrals and symptom duration are provided in Supplementary Figures S1 and S2, while descriptive treatment-timing means and

TABLE 2.
Comparison of Multiple Linear Regression Models Predicting Motor Symptom Severity (Simplified Functional Movement Disorders Rating Scale) Across Clinical Visits

Predictor/Model Fit Indices	Baseline S-FMDRS β (*P*)	6 months S-FMDRS β (*P*)	12 months S-FMDRS β (*P*)
Symptom duration	**1.19 (0.021)**	**2.07 (<0.001)**	**1.79 (<0.001)**
Number of prior referrals	−0.81 (0.100)	0.95 (0.069)	**1.00 (0.047)**
Age at diagnosis	−0.20 (0.456)	−0.23 (0.419)	−0.37 (0.185)
Center (ITA vs. CZE)	**−3.63 (0.010)**	1.04 (0.479)	−1.18 (0.399)
Symptom type (combined)	**2.36 (0.032)**	0.86 (0.459)	0.58 (0.602)
Psychiatric comorbidity	0.19 (0.859)	−0.81 (0.471)	−1.43 (0.186)
Adjusted R^2	0.117	0.292	0.305
AIC	422	431	419
Durbin–Watson	1.71	1.98	2.17
VIF range	1.06-1.93	1.06-1.93	1.06-1.93

β = Unstandardized Regression Coefficient
AIC = Akaike Information Criterion
CZE = Czech Center
ITA = Italian Center
S-FMDRS = Simplified Functional Movement Disorders Rating Scale
VIF = Variance Inflation Factor
In bold, statistically significant associations ($P < 0.05$).

complete cross-sectional ANOVA results are reported in Supplementary Tables S4 and S5.

These findings indicate that longer and more fragmented care pathways were associated with less favorable functional improvement.

Regression models predicting motor symptom severity

To further examine independent predictors of symptom severity at each time point, we ran multiple linear regression models (Table 2). At baseline, higher S-FMDRS scores were independently associated with longer symptom duration ($\beta = 1.19$, $P = 0.021$), combined symptom presentation ($\beta = 2.36$, $P = 0.032$), and recruiting center ($\beta = -3.63$, $P = 0.010$). Longitudinally, symptom duration remained associated with higher motor severity at 6 months ($\beta = 2.07$, $P < 0.001$) and 12 months ($\beta = 1.79$, $P < 0.001$), while the number of prior referrals independently predicted higher severity at 12 months ($\beta = 1.00$, $P = 0.047$). Adjusted R^2 ranged from 0.117 to 0.305, and Variance Inflation Factor values ranged from 1.06 to 1.93. Full model coefficients and diagnostic statistics are reported in Supplementary Tables S1A–C and S2, respectively.

Group differences in motor symptom severity

We examined whether S-FMDRS scores differed according to clinical and demographic subgroups at each time point.

In unadjusted cross-sectional analysis, baseline S-FMDRS scores did not differ significantly between combined and isolated presentations ($F(1,70) = 3.79$, $P = 0.056$). In the multivariable baseline model, however, combined presentation was independently associated with higher severity ($\beta = 2.36$, $P = 0.032$). In the unadjusted exploratory repeated-measures models, no additional Time × predictor interaction reached $P < 0.05$ for sex, symptom phenotype, precipitating factors, comorbidities, adverse childhood experiences, or treatment categories (Supplementary Tables S6A and B).

Treatment approaches

No treatment-category interaction reached statistical significance in the exploratory repeated-measures models. Reductions in S-FMDRS were observed across treatment groups, but these observational comparisons were unadjusted and may be affected by confounding by indication; descriptive trajectories according to drug-therapy status are shown in Supplementary Figure S3, and complete exploratory model results are reported in Supplementary Tables S6A and B.

Discussion

The present study offers several insights into factors influencing severity and outcome of FMD in children and adolescents. Consistent with previous pediatric cohorts, we observed a marked reduction in motor symptom severity over 12 months, with complete remission in 43% of patients.[10,15] However, this overall favorable course was not uniform: longer symptom duration at baseline was consistently associated with higher S-FMDRS scores at all time points, in line with adult findings linking prolonged symptom persistence to worse prognosis.[20] In addition, a greater number of prior referrals emerged as an independent correlate of poorer clinical status at the 12-month follow-up, suggesting that a fragmented diagnostic pathway may be related to symptom persistence, a concept that resonates with literature on prolonged symptom duration and chronification in FND.[21,22] Nevertheless, given the retrospective design, no causal relationship can be inferred, and referral history may also reflect baseline clinical complexity or structural barriers to accessing specialized care.

Treatment timing was associated with symptom evolution: patients who began FMD-directed treatment later had higher follow-up S-FMDRS scores and a different longitudinal trajectory. Because treatment allocation was not randomized, this association should not be interpreted as evidence that earlier treatment caused better outcomes; baseline severity, service availability, and other unmeasured factors may have influenced both timing and outcome.

At baseline, combined presentation was associated with greater severity in the multivariable model, although the unadjusted group comparison did not reach statistical significance. The association was not evident at follow-up, suggesting that initial motor complexity did not independently predict later severity in these models.

Adjusted baseline scores were higher in the Czech center, while center differences were not significant at follow-up and the Time × Center interaction was not significant. Other between-center differences in referral history, psychiatric comorbidity, adverse childhood experiences, and clinical presentation may reflect differences in referral pathways and service organization.[23] These contextual differences warrant cautious interpretation and do not establish a causal effect of health-care setting.

In our study, several factors often regarded as clinically relevant — including gender, previous misdiagnosis, symptom phenotype, and the presence of precipitating events — did not show a consistent, statistically significant impact on S-FMDRS trajectories. This pattern mirrors recent pediatric data, where demographic and psychiatric variables rarely emerge as robust predictors of outcome,[10,15] and is also broadly consistent with adult prognostic modeling indicating only modest predictive value of baseline clinical features.[4,14,20] Taken together, these findings suggest that system-level and care-related variables, such as referral pathway and treatment timing, may be at least as relevant for prognosis as individual clinical characteristics, even though neither set of factors currently allows precise prediction at the single-patient level.

No specific treatment category was associated with a statistically different S-FMDRS trajectory in the exploratory analyses. These nonrandomized comparisons were not designed to estimate comparative treatment effectiveness and remain vulnerable to confounding by indication, so they should be interpreted descriptively.

From a biopsychosocial perspective, prolonged symptom duration and fragmented referral pathways may contribute to the consolidation of maladaptive illness beliefs, heightened symptom-focused attention, and school or social withdrawal, thereby interacting with the cognitive-affective mechanisms implicated in FND.[5,7,24]

This study has several limitations that warrant consideration. Its retrospective design limits causal inference, and unmeasured confounders (e.g., psychological characteristics, family dynamics) may have influenced outcomes. Furthermore, eligibility required at least 6 months of follow-up and two valid S-FMDRS assessments; therefore, patients not retained in specialist follow-up or lacking serial standardized assessments were excluded. This may have selected families with greater diagnostic acceptance, treatment engagement, or access to follow-up care, and our findings should be generalized primarily to patients retained in specialist follow-up. Although the sample size is among the largest cohorts of pediatric FMDs with standardized follow-up, statistical power remains limited for subgroup analyses. Treatment strategies were not standardized, and choices regarding modality and timing likely reflected clinical severity or local service organization. Longitudinal models examined treatment timing and recruiting center, but

residual confounding by indication and service availability cannot be excluded. Additionally, structural differences between health-care systems may introduce further heterogeneity in referral pathways and case complexity. Finally, qualitative aspects of patient and family experience were not captured, and future prospective work integrating standardized treatment protocols and mixed-methods approaches will be essential to strengthen the robustness and interpretability of prognostic findings.

Despite these limitations, the study also presents notable strengths. It is one of the few multicenter investigations in pediatric FMD with standardized longitudinal assessment using a validated severity scale.[16] The inclusion of two distinct health-care environments also enhances external validity and highlights modifiable, system-level correlates of outcome.

Conclusion

In pediatric FMDs, longer symptom duration, multiple prior referrals, and delayed initiation of FMD-directed treatment were associated with greater motor severity over time. These observational findings identify potentially modifiable features of the diagnostic and care pathway, but do not establish causality. Earlier specialist assessment and FMD-directed treatment merit prospective evaluation in multicenter cohorts with harmonized treatment protocols, predefined referral pathways, and qualitative assessment of the diagnostic journey and service organization.

CRediT authorship contribution statement

Patrícia Všianská: Writing – original draft, Methodology, Data curation, Conceptualization. **Dario Esposito:** Writing – original draft, Methodology, Data curation, Conceptualization. **Alice Innocenti:** Writing – original draft, Data curation. **Vít Všianský:** Writing – original draft, Visualization, Methodology, Formal analysis. **Zuzana Špilárová:** Writing – review & editing, Data curation. **Christian Geroin:** Writing – review & editing, Supervision. **Michele Tinazzi:** Writing – review & editing, Supervision. **Pavlina Danhofer:** Writing – review & editing, Project administration, Conceptualization. **Valentina Baglioni:** Writing – review & editing, Supervision, Project administration, Conceptualization.

Ethics declaration

Written informed consent to take part in the study and to publish the article has been obtained from all participants or their legal representatives. The privacy rights of participants have been observed.

This study was performed in compliance with relevant laws, regulatory frameworks and guidelines where the research took place. This study was conducted in accordance with RECORD and STROBE. This study was approved by the CET Lazio Area 1. (Approval No. 8098/2025)

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT (OpenAI) to assist with language editing and stylistic refinement. After using this tool, the authors reviewed and edited all content as needed and take full responsibility for the content of the publication.

Declaration of competing interest

The authors declare no conflict of interest or financial disclosures concerning the materials or methods used in this study or the findings specified in this article.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.pediatrneurol.2026.09.022.

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