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Sexual Dysfunction in Women with Neuromyelitis Optica Spectrum Disorders and Multiple Sclerosis

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Abstract

Sexual dysfunction (SD) is a common and significant complication in neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis (MS), though it is often neglected and undertreated. We aimed to compare female sexual dysfunction in patients with NMOSD and MS, and investigate the association between clinical characteristics and SD. In this cross-sectional study, 36 patients with NMOSD and 312 MS patients who visited the MS clinic of Kashani Hospital were recruited. Sexual dysfunction was evaluated using the Iranian version of the Female Sexual Function Index (FSFI) questionnaire. Fatigue, depression, and anxiety were also assessed by fatigue severity score (FSS), Beck depression inventory-II (BDI-II), and Hamilton anxiety rating scale (HAM-A), respectively. Sexual dysfunction was presented in 75% of NMOSD and 63.5% of MS patients ($P=0.127$). The most frequent SD problem in both NMOSD and MS was dysfunctional arousal (50% vs. 48.1%, $P=0.855$). The frequency and mean score of sexual pain dysfunction in NMOSD patients was higher than MS, but it did not remain significant in the adjusted model. No statistically significant differences in the frequency and mean scores of other SD subdomains were detected. In the univariate model, only fatigue was associated with the presence of SD in NMOSD. In MS patients, depression was an independent risk factor of SD in the multivariate model. Our results confirm that SD is a common problem in female NMOSD and MS patients. Further longitudinal studies are needed to evaluate sexual dysfunction and its risk factors in NMOSD. In addition, attention to the management of depression and fatigue could be positively effective on sexual dysfunction in patients with NMOSD and MS.

Keywords Neuromyelitis optica · Multiple sclerosis · Sexual dysfunction · Depression · Anxiety · Fatigue · Islamic Republic of Iran

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Introduction

Neuromyelitis optica spectrum disease (NMOSD) and multiple sclerosis (MS) are chronic inflammatory immune-mediated diseases affecting young adults, aged 20 to 49 [1]. For many years, NMOSD was considered a variant of MS. The discovery of specific NMOSD autoantibodies (AQP4-IgG) against aquaporin-4 (AQP4) proteins -which are water channel proteins and are expressed in the astrocytes foot in the CNS-, declared that NMOSD and MS have two distinct pathophysiological mechanisms [2–4].

MS and other chronic diseases can lead to sexual dysfunction in both men and women. The prevalence of SD among MS was reported from 31 to 92% [5], depending on the study design, population surveyed, and SD definition. Patients with MS are at an increased risk of developing SD than the general population and other chronic diseases [6]. MS affects sexual activity in women and men at different levels. The most frequent SD symptoms in MS men are erectile dysfunction and ejaculatory dysfunction [7]. On the other hand, women have commonly been associated with decreased vaginal lubrication, impair orgasm, and dyspareunia [8].

The exact etiology of SD in MS remains unclear, but it is believed to result from a combination of physical, psychological, and social factors. Sexual dysfunction can be due to lesions involving areas in the brain and spinal cord responsible for sensation or sexual response [9, 10]. Impaired QOL, psychological and emotional problems such as depression and anxiety can adversely affect patient's sexual activity [11, 12]. Physical MS-related symptoms, including bladder/bowel problems, fatigue, neurological impairment, and spasticity, can indirectly impact sexual activity [13].

While several studies have been carried out on MS, there is still very little scientific understanding of SD in NMOSD. The prevalence of SD was reported near 50% in women NMOSD patients and 75% in men [14]. Impaired sexual function has a substantial adverse effect on the emotional well-being of NMOSD patients [15]. Many factors such as reduced QOL, depression, anxiety, fatigue, lower urinary tract dysfunction, and spinal cord lesions can cause SD in patients with NMOSD [14, 16, 17].

Although NMOSD symptoms are similar to the risk factors of SD that have been established in MS, there are differences in the severity of disturbance of psychiatric and physical symptoms exhibited by patients with these diseases [17, 18]. There are also differences in brain and spinal lesion characteristics [19]. Given that, the frequency and pattern of sexual dysfunction may be different in NMSOD compared to MS.

Determining the pattern of SD in NMOSD and MS provides an opportunity to design the best strategy to treat this common problem in NMOSD. Therefore, we carried out the current study to evaluate sexual function in women NMOSD and MS patients.

Methods

Participants

In this cross-sectional study we surveyed NMOSD and MS patients referred to the outpatient MS clinic of Kashani Hospital, affiliated to Isfahan University of Medical Sciences, Isfahan, Iran, from March 2019 to April 2020. The inclusion criteria were at least 18 years old and diagnosis of NMOSD based on the international consensus diagnostic criteria in

2015 [20] or MS according to the McDonald criteria [21–23]. The exclusion criteria were as follows: (a) refusals to participate in the study, (b) current exacerbation, (c) history of psychiatric disorder or severe cognitive impairment, (d) neurological disorder rather than MS or NMOSD, (e) history of diabetes mellitus, heart disease, peripheral artery diseases, and hypo-hyperthyroidism. Demographic and clinical information of participants including age, educational levels, severity and duration of disease were extracted from the database [24]. Education levels were categorized as basic (diploma and lower) or advance (higher than diploma). The severity of NMOSD and MS were measured by a trained neurologist (VS) using the Expanded Disability Status Scale (EDSS) score [25]. The study protocol was approved by the regional bioethics committee of Isfahan University of Medical Sciences and written informed consent was obtained upon participation (IR.MUI.MED.REC.1398.583).

Measures

Female Sexual Function Index

Sexual dysfunction was evaluated by Female Sexual Function Index (FSFI) questionnaire [26]. The FSFI examines women's sexual functioning in six areas: desire, psychological stimulation, moisture, orgasm, satisfaction, and sexual pain. This scale consists of 19 individual items, and answers are given on a five-point Likert scale, with lower scores show lower levels of sexual functioning. The cut-off points used to assess desire was 3.3, arousal was 3.4, lubrication was 3.7, orgasm was 3.4, satisfaction was 3.8, and sexual pain was 3.8. Further, a cut-off of ≤ 28 was employed to identify cases of SD. Adequate construct validity and reliability of the Persian translation of the FSFI was shown previously [27].

Fatigue Severity Scale

The Fatigue Severity Scale (FSS) was used to assess the severity of fatigue [28]. Respondents rated 9 items on a scale ranging from 1 (=strongly disagree) to 7 (=strongly agree); the score range was from 9 to 63, with higher scores showing more severe fatigue. The validity and reliability of this scale were tested in an Iranian investigation [29].

Beck Depression Inventory-II (BDI-II)

The Iranian version of BDI-II was used to assess depression [30]. This scale consists of 21 items, and answers are given on a 4-point rating scale (0–3). The global BDI-II score range was from 0 to 63, with higher scores indicate more severe depression [31].

The Hamilton Anxiety Rating Scale (HAM-A)

The HAM-A was used to assess anxiety symptoms in NMOSD patients [32]. It consists of 14 items; the score range was from 0 to 56; with a higher score, it showed more anxiety. The HAM-A has also demonstrated good test–retest reliability and validated the Iranian population [33].

Statistical Analysis

All data are presented as mean ± standard deviation (SD) or median (interquartile range [IQR]) for continuous variables and frequency (%) for categorical. We used an independent sample t-test to compare the means. Pearson and Spearman's correlations were performed to find correlation between continuous variables. A multivariate generalized linear model (GLM) was conducted to compare the mean of desire, arousal, lubrication, orgasm, pain, satisfaction, and total FSFI score between NMOSD and MS. We adjusted the model for BDI-II, HAM-A, FSS disease duration, and severity of the disease. We used logistic regression analysis to evaluate the risk factors of the presence of SD according to FSFI total score. First, a univariate analysis was conducted to determine the influence of each predictor variable on SD. Then, all predictors that had a significant association in the univariate model were added into the multivariate. The level of significance was set at 0.05 (2-tailed). All statistical analysis procedures were performed using IBM SPSS Statistics (version 20; IBM Corporation, Armonk, NY, USA).

Results

Patients' Characteristics

A total of 348 participants, including 312 women patients with MS patients and 36 NMOSD patients were included in this study. The mean age and disease duration of all participates were 35.56 ± 7.64 and 7 ± 4.6 years, respectively. No significant difference between NMOSD and MS in demographic and clinical characteristics was found. Demographic and clinical characteristics of subjects and scores of FSFI, DBI-II, HAM-A, and FSS were demonstrated in Table 1.

Comparison of the Frequency of Sexual Dysfunction Between NMOSD and MS

The frequency of SD in participants is documented in Table 1. The percentage of NMOSD and MS patients who reported scored less than 28 in the FSFI were 75.0% and 63.5%, respectively. The most prevalent sexual problem in NMOSD patients was arousal and satisfaction dysfunctions reported by half of the patients. In MS patients, dysfunctional arousal was the most frequent sexual problem (48.1%), followed by desire (40.7%) and satisfaction dysfunctions (36.5%). Pain during intercourse was more frequent in patients with NMOSD than MS (n = 14, 38.9% vs. n = 56, 17.9%; P = 0.001). No statistically significant difference between NMOSD and MS in the frequency of other SD domains was observed.

Comparison of the Scores of Sexual Domains Between NMOSD and MS

The results of the GML analysis are shown in Table 2. In the unadjusted model, patients with NMOSD manifested significantly higher pain scores than MS patients (B = −0.586, $P = 0.032$). No significant difference between NMOSD and MS patients in the scores of sexual desire, arousal, lubrication, orgasm, satisfaction, and total FSFI was observed. In

Table 1 Descriptive statistics for patients' clinical characteristics and scores of FSFI, BDI-II, HAM-A, and FSS

Variable		MS (n = 312)	NMO (n = 36)	*P* value
Age; mean (SD)		35.39 (7.43)	37.08 (9.40)	0.317
Education; n (%)	Basic	165 (52.9)	22 (62.9)	0.217
	Advance	146 (46.8)	13 (37.1)	
Disease duration; mean (SD)		7.10 (4.58)	6.40 (3.90)	0.382
EDSS score; mean (SD)		1.64 (1.26)	2.01 (1.246)	0.097
BDI-II score; mean (SD)		25.97 (13.77)	28.54 (12.84)	0.319
HAM-A; mean (SD)		26.69 (8.74)	29.45 (7.79)	0.092
FSS score; mean (SD)		37.59 (13.44)	37.96 (10.17)	0.896
Desire; mean (SD)		3.33 (1.06)	3.00 (1.04)	0.078
Arousal; mean (SD)		3.33 (1.37)	3.01 (1.35)	0.226
Lubrication; mean (SD)		3.83 (1.39)	4.19 (1.33)	0.127
Orgasm; mean (SD)		3.87 (1.60)	4.19 (1.58)	0.241
Pain; mean (SD)		4.28 (1.77)	4.87 (1.51)	**0.030**
Satisfaction; mean (SD)		4.21 (1.61)	3.77 (1.67)	0.144
FSFI total score; mean (SD)		21.97 (7.89)	24.09 (7.50)	0.113
Desire ≤ 3.3; n (%)		17 (47.2)	127 (40.7)	0.452
Arousal ≤ 3.4; n (%)		18 (50)	150 (48.1)	0.855
Lubrication ≤ 3.7; n (%)		11 (30.6)	77 (24.7)	0.423
Orgasm ≤ 3.4; n (%)		11 (30.6)	76 (24.4)	0.426
Pain ≤ 3.8; n (%)		14 (38.9)	56 (17.9)	**0.003**
Satisfaction ≤ 3.8; n (%)		18 (50)	114 (36.5)	0.118
FSFI ≤ 28; n (%)		27 (75.0)	198 (63.5)	0.127
Disease-modifying therapies				
Interferon beta		159 (50.5)	–	
glatiramer acetate		25 (7.9)	–	
Fingolimod		34 (10.8)	–	
Dimethyl fumarate		8 (2.5)	–	
Teriflunomide		19 (6.0)	–	
Rituximab		48 (15.2)	28 (80.0)	
Natalizumab		4 (1.3)	–	
Azathioprine		–	5 (14.3)	
Mycophenolate mofetil		–	2 (5.7)	

Bold font indicates statistical significance

SD standard deviation, *EDSS* Expanded Disability Status Scale, *FSFI* Female Sexual Function Index, *FSS* Fatigue Severity Scale, *BDI-II* Beck Depression Inventory-II, *HAM-A* Hamilton Anxiety Rating Scale

the adjusted model, no significant difference between NMOSD and MS in any type of sexual function was evident.

Table 2 The results of generalized linear model with total FSFI as dependent variable

Variable	Groups		B	SE	95% CI	*p*-value*
	NMOSD B (SE)	MSB (SE)				
Model 1						
Desire	3.331 (0.061)	3.100 (0.177)	−0.231	0.187	−0.599, 0.136	0.216
Arousal	3.306 (0.079)	3.092 (0.230)	−0.214	0.243	−0.692, 0.263	0.378
Lubrication	4.193 (0.077)	3.833 (0.223)	−0.360	0.236	−0.824, 0.105	0.129
Orgasm	4.192 (0.091)	3.867 (0.264)	−0.325	0.279	−0.874, 0.223	0.244
Pain	**4.864 (0.088)**	**4.278 (0.257)**	**−0.586**	**0.272**	**-1.121, −0.051**	**0.032**
Satisfaction	4.199 (0.093)	3.800 (0.271)	−0.399	0.287	−0.963, 0.166	0.166
FSFI total score	24.085 (0.431)	21.969 (1.258)	−2.116	1.330	−4.731, 0.500	0.113
*Model 2**						
Desire	3.091 (0.204)	3.345 (0.067)	−0.254	0.216	−0.679, 0.171	0.241
Arousal	3.156 (0.269)	3.360 (0.088)	−0.204	0.284	−0.763, 0.355	0.473
Lubrication	3.896 (0.274)	4.238 (0.090)	−0.342	0.289	−0.911, 0.228	0.239
Orgasm	3.971 (0.320)	4.258 (0.105)	−0.287	0.338	−0.953, 0.379	0.397
Pain	4.287 (0.320)	4.915 (0.105)	−0.628	0.337	−1.293, 0.037	0.064
Satisfaction	3.938 (0.323)	4.266 (0.105)	−0.327	0.340	−0.998, 0.344	0.338
FSFI total score	22.340 (1.498)	24.381 (0.490)	−2.041	1.581	−5.156, 1.074	0.198

Bold font indicates statistical significance

*Adjusted for age, disease duration, EDSS, BDI-II, HAM-A, and FSS score

SE standard error, *FSFI* Female Sexual Function Index

Correlation Between Sexual Function and Clinical Features, Depression, Anxiety, and Fatigue

Supplementary Tables 1, 2 presents the results of the correlational analysis in NMOSD patients. It can be seen from the data in Supplementary Table 1that higher age was inversely correlated with scores of desire, orgasm, satisfaction, and total FSFI. There was a negative correlation between age at onset and desire, lubrication, orgasm, satisfaction, and total FSFI scores. Higher scores of depression and anxiety correlated with a lower score of desire.

It can be seen from the data in Supplementary Table 2 that age was negatively correlated with all domains of SD and total FSFI scores. Higher scores of EDSS had a significant correlation with lower scores of desire, arousal, orgasm, satisfaction, and total FSFI. Higher scores of depression and fatigue were inversely correlated with all types of sexual function and total FSFI scores. There was an inverse correlation between scores of HAM-A and all domains of sexual dysfunction, except lubrication.

Risk Factors for Developing Sexual Dysfunction in NMOSD and MS Patients

The results obtained from the univariate logistics regression analysis in NMOSD patients are set out in Table 3. Only the BDI-II score was associated with the development of SD

Table 3 Univariate logistic regression analysis with FSFI ≤ 28 as dependent variable, and age, education, EDSS score, disease duration, BD-II, HAM-A, and FSS as risk factors in NMOSD patients

Variables	B	SE	Wald	OR	OR (95% CI)	*P* value
Age	0.099	0.053	3.556	1.104	0.996, 1.224	0.059
Age at onset	0.098	0.060	2.675	1.103	0.981, 1.240	0.102
Education*	-0.531	0.909	0.341	0.588	0.981, 3.491	0.559
EDSS score	0.499	0.482	1.070	1.647	0.640, 4.235	0.301
Disease duration	0.518	0.900	0.332	1.679	0.874, 1.654	0.258
BDI-II score	**0.106**	**0.053**	**4.050**	**1.112**	**1.003, 1.323**	**0.044**
FSS score	0.104	0.073	2.030	1.109	0.962, 1.280	0.154
HAM-A score	0.121	0.087	1.939	1.128	0.952, 1.337	0.164

Bold font indicates statistical significance

*Reference group for education status = basic

SD standard deviation, *EDSS* Expanded Disability Status Scale, *FSFI* Female Sexual Function Index, *FSS* Fatigue Severity Scale, *BDI-II* Beck Depression Inventory-II, *HAM-A* Hamilton Anxiety Rating Scale

Table 4 Univariate and multivariate logistic regression analysis with FSFI ≤ 28 as dependent variable, and age, education, EDSS score, disease duration, BD-II, HAM-A, and FSS as risk factors in MS patients

Variables	Univariate Model			Multivariate model		
	OR	OR (95% CI)	*P* value	OR	OR (95% CI)	*P* value
Age	**1.044**	**1.008, 1.083**	**0.018**	0.985	0.938, 1.034	0.532
Age at onset	0.016	0.981, 1.051	0.378	–	–	–
Education*	**0.460**	**0.276, 0.766**	**0.003**	0.736	0.385, 1.408	0.354
EDSS score	**1.360**	**1.082, 1.709**	**0.008**	0.917	0.684, 1.230	0.562
Disease duration	**1.065**	**1.004, 1.129**	**0.038**	1.053	0.971, 1.143	0.212
Course of disease*	2.140	0.611, 7.790	0.230	–	–	–
BDI-II score	**1.045**	**1.024, 1.067**	**0.000**	1.019	0.993, 1.046	0.146
FSS score	**1.065**	**1.039, 1.092**	**0.000**	**1.0161**	**1.031, 1.091**	**0.000**
HAM-A score	1.174	0.995, 1.056	0.106	–	–	–

Bold font indicates statistical significance

*Reference group for education status = basic

*Reference group for course of disease = RRMS

SD standard deviation, *EDSS* Expanded Disability Status Scale, *FSFI* Female Sexual Function Index, *FSS*, Fatigue Severity Scale, *BDI-II* Beck Depression Inventory-II, *HAM-A* Hamilton Anxiety Rating Scale

in the univariate model. For one unit increase in BDI-II score, the likelihood of developing SD increase by 11.2% (95%CI: 1.003, 1.323; $P = 0.044$).

On univariate analysis, age, education levels, EDSS, disease duration, BDI-II, and FSS scores were risk factors for the presence of sexual dysfunction in MS patients. Nevertheless, only FSS score remained significant in the multivariate model (Table 4). One point increase in FSS score was associated with higher odds of SD (OR = 1.061, CI: 1.031, 1.091; $P = 0.000$).

Discussion

Sexual dysfunction is a substantial burden for people with neurological diseases, particularly MS patients [8, 34]. The prevalence and severity of sexual dysfunction in NMOSD are comparable to MS, though it has not been investigated as much as done in MS [14]. Both NMOSD and MS usually affect young women aged 20 to 49, when sexually active. Sexual dysfunction as a common symptom in young women with MS can negatively affect intimacy and sexuality resulting in reduced quality of life, serious problems in the relationship with their partner, and various emotional and psychological problems [35]. Despite the crucial importance of SD in women with NMOSD and MS, it is commonly underdiagnosed and undertreated in general clinical practice [36].

It is substantiated that fatigue is present in sexual dysfunction and is associated with neurological symptoms, fibromyalgia, Sjögren's syndrome, or myofascial pain.The prevalence of depression varies in patients with SD [37]. Also, effects of depression on sexual dysfunction and the quality of life can even result in suicide [38]. Moreover, anxiety is able to inhibit the processes of sexual arousal [39]. Investigates shows that dysfunctional arousal was the most frequent sexual problem in NMOSD and MS, reported by nearly half of patients. The rate of arousal dysfunction in NMOSD and MS patients is higher than the general Iranian population, estimated at 34% [40]. Sexual arousal dysfunction in women is characterized by the lack or reduction in the feeling of sexual excitement, vulval swelling, or vaginal lubrication [41]. Because arousal problems can be diminished by using lubricants, people with this dysfunction rarely seek medical attention [42]. Without suitable and professional treatments, arousal dysfunction can lead to painful intercourse, avoiding sexual activity, and relationship distress.

A more significant proportion of our NMOSD sample suffered from pain during intercourse in comparison with MS. In unadjusted regression model, the mean score of pain was significantly higher than MS, but it doesn't remain significant in adjusted model. The frequency of pain problems in 38% of our NMOSD patients is higher than the reported prevalence of 20% reported in the general population [40]. A high rate of pain dysfunction might be related to the high prevalence of neuropathic and musculoskeletal pain in NMOSD patients [43], overlapping and associating with painful intercourse [44].

No significant difference between NMOSD and MS in frequency and scores of desire, satisfaction, lubrication, and orgasm were observed. Desire and satisfaction dysfunctions were the following common sexual problems in both NMOSD and MS patients. The prevalence of dysfunctional desire in our NMOSD and MS samples was 47% and 40%, according to M. Lew-Starowicz study [14, 45] and slightly higher than the prevalence of 35% [40] reported in Iranian women in the general population.

This study showed a statistically significant correlation between age and SD in both NMOSD and MS patients. In accordance with the present results, previous studies have demonstrated the negative impact of age on sexual activity in the general women population and women patients with NMOSD and MS [14, 46, 47]. Consistent with Zhang et al. [14], this research found correlation between age at NMOSD onset and scores of desire, arousal, orgasm, satisfaction, and total FSFI. However, we found no statistically significant relationship between sexual symptoms and age at MS onset.

NMOSD relationship of diminished desire with anxiety and depression was observed. Surprisingly, no significant correlation between SD and disease duration symptoms, EDSS, depression, and fatigue in NMOSD was detected. In contrast to NMOSD, the correlation of depression, anxiety, and fatigue with FSFI scores in MS patients was statistically

significant with a negative correlation in all subscales, except anxiety with lubrication and pain.

Identifying risk factors of SD could help health care providers to design an appropriate prevention and management approach. We found an association between an increase in BDI-II score and higher odds of SD in NMOSD patients. In the multivariate model, fatigue severity was the only factor that independently affected the development of SD in MS patients. Depression is a significant predictor for the deterioration of sexual activity in MS patients [48]. The relation of depression with SD is bi-directional, is that depression symptoms could be expected to produce dysfunctions in sexual activity and people with SD are more likely to develop these psychological problems [49]. Fatigue as an essential risk factor for secondary SD, can indirectly affect sexual activity. MS patients have less energy than the general population, and working during the day drains patients; consequently, they feel exhausted at night and probably avoid sexual activity.

Our study has some limitations. The major limitation of this study is the small number of patients with NMOSD. The absence of healthy control is another limitation. However, the scope of the current study was the comparison of sexual activity between NMOSD and MS patients, not with a control group. The study population was recruited from a single tertiary care medical center. We included only women patients; therefore, the findings might not be generalized to all NMOSD and MS patients. Because of the cross-sectional design of the present study, we were unable to draw a causal relationship. Moreover, we were unable to assess changes in sexual activity at different time points.

In conclusion, our study showed that sexual dysfunction is a common problem in both NMOSD and MS patients. Sexual dysfunction in our NMOSD patients follows a similar pattern as in women patients with MS. Women who suffer from sexual dysfunction find it difficult to consult with health professionals and seek treatment or support. Therefore, active screening for the diagnosis of sexual dysfunction in both NMOSD and MS is recommended. Accordint to the effects of fatigue, anxiety, and depression on SD, we suggest that these patients resolve the symptoms of fatigue, depression, and anxiety to improve sexual dysfunction. Also, attention to the management of depression and fatigue might have a positive impact on sexual dysfunction in both patients with NMOSD and MS. Despite the obtained results, we require to conduct an interventional study to investigate the effects of symptom management on the remission of sexual dysfunction.

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Authors' Contributions Conceptualization: OM, MB, AN, VS; Methodology: OM, MB, AM, SB, VS; Formal analysis and investigation: OM, MB, AN, AMH, AM, MG; Writing—original draft preparation: MB, AN; Writing—review and editing: OM, MB; Funding acquisition: VS; Resources: VS; Supervision: VS.

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Availability of Data and Material Anonymized data of this study will be available from the corresponding author on reasonable request from any qualified investigator, following the General Data Protection Regulation.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethics Approval Regional bioethics committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1398.583) approved this study.

Consent for Publication Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient/parent/guardian/ relative of the patient.

Consent to Participate All participants received an written consent form and were assured of data confdentiality. Participants who consented to participate were then forwarded to the survey.

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