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Challenges faced by pediatric patients with multiple sclerosis during disease progression and treatment: A multicenter cross-sectional study in Türkiye

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Abstract

Background & Objective: Multiple sclerosis is a chronic and progressive disease characterized by inflammation, demyelination and degeneration of the central nervous system. This study aimed to describe the sociodemographic and clinical characteristics of children with multiple sclerosis. *Methods:* The cross-sectional study was collected data from 120 children who met the research criteria and were under follow-up at 7 hospitals in Türkiye between August 2021 and February 2022. Ethical approval was obtained from the Medical Research Ethics Committee of Ege University. The researchers developed the "The Sociodemographic Form "used in the study by based on a comprehensive literature review and previous research experiences. The form was used according to expert opinion. *Results:* The study included 120 eligible patients, of whom 71.2% were girls. The mean age (±SD) at disease onset was 13.6±2.2 years, while the mean age at the time of the study was 15.7±1.5 years. Most of the participants were high school students (84.2%), and 53.3% resided in metropolitan areas. All participants were receiving disease-modifying therapy. The study found that 67.5% of the children had school absenteeism due to the disease. Furthermore, 75% of the children experienced supratentorial symptoms, with 50% presented with optic symptoms, and 37.5% exhibiting brainstem symptoms prior to diagnosis. Drug-related side effects were reported in 58.3% of children. Additionally,99.2% of the children received information about the disease. Furthermore, 75% of the children experienced challenges during the disease and treatment process. Among these children who encountered difficulties, 52.5% reported psychological problems, 42.5% experienced side effects due to medication, 42.5% had difficulty accessing accurate and sufficient information about disease and treatment management, 32.5% encountered social and school-related issues, and 5.8% had concerns related to the clinical environment.
Conclusion: Childhood multiple sclerosis is more prevalent among girls, particularly in the relapsing-remitting form. The most commonly used treatments for pediatric multiple sclerosis include interferon beta-1a and glatiramer acetate. The findings of this study indicate that a significant proportion of participating children encountered challenges during the disease and treatment process, with more than half experiencing drug-related side effects. These challenges underscore the potential negative impact on treatment adherence in this population.

Keywords: Multiple sclerosis, children, nursing, treatment, adherence

INTRODUCTION

Looking at scientific studies, many theories attempt to explain pediatric multiple sclerosis (pMS).[1-4] In light of current knowledge, it is stated that numerous factors play a role in the etiology of pMS.[5,6] pMS often arises as a result of the interaction of genetic and environmental factors.[5] The goal of treatment in pMS patients is to prevent the occurrence of attacks, facilitate recovery after an attack, and slow down neurodegeneration.[1,7,8] The European Medicines Agency approves most immunomodulatory drugs that alter the disease course in pMS patients over 12 years of age.[9] Other treatments, such as interferons, glatiramer acetate, dimethyl fumarate, teriflunomide,

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natalizumab, rituximab, and cyclophosphamide, are also currently used for pMS patients.[10-15] Having a progressive chronic disease in childhood, including adolescence, is challenging for a child. Living with a progressive chronic illness during childhood and adolescence presents significant challenges for both the child and their family. The prolonged and demanding treatment process often results in frequent hospital visits, treatment-related side effects, school disruptions, and disease progression.[16,17] Furthermore, families may experience financial difficulties, parental feelings of inadequacy and self-blame, and restrictions in daily activities, all of which can contribute to emotional and psychological distress.[18-20]

In this multicenter cross-sectional study, the challenges encountered by children diagnosed with pMS during their disease and treatment processes were described and analyzed in comparison with the current literature. This study is expected to provide valuable insights for future pediatric cohort studies and contribute to the improved management of the disease.

METHODS

Study design and participants

Between August 2021 and February 2022, a descriptive cross-sectional study was conducted involving 120 children who met the research criteria and were under follow-up at six university hospitals and one training and research hospital. Due to the coronavirus pandemic and the subsequent lockdowns, the data collection method of our research has encountered some limitations. As a result, the face-to-face interviews of the study were conducted via online video conferencing using the Zoom platform. As part of this change, given the young age group of patients to be included in the study and their tendency to use online technology in this age group. The inclusion criteria were as follows: 1. Diagnosis of multiple sclerosis (MS) at least six months prior, 2. Age between 12 and 18 years, 3. Receiving any form of immunomodulatory treatment, 4. No psychological or behavioral medical diagnosis, and 5. Willingness of both the child and the family to participate in the research. All children included in the study met the McDonald Criteria for MS, and differential diagnoses, such as myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) were excluded. Interviews were conducted in a private, comfortable, and safe home environment to ensure participant well-being. Detailed information about the study's purpose and methodology was provided, and informed consent was obtained from the families before participation. Participation was entirely voluntary. In addition to patient interviews, clinical data related to MS diagnosis, symptoms, and treatments were reviewed for each participant. These records ensured that MS diagnostic criteria were met and differential diagnoses, such as MOGAD syndrome, were excluded. Both patient interviews and case note reviews were utilized to enhance data reliability.

Data collection tools

The questionnaire form was designed to be completed in approximately 10 minutes. The researchers developed the "Participant Information Form" based on relevant literature reviews [15,21,22] and previous research experiences. The first author, who had worked as a MS education nurse in the MS unit at the university hospital for seven years and participated in clinical research, contributed to the development of this form. The form consisted on 26 questions covering sociodemographic characteristics such as age, gender, education level, number of siblings, initial complaints, clinical findings, received treatments, and disease-related information. In this form, responses regarding the disease status, treatment, academic achievement status, and overall health levels were categorized as "very poor, poor, good, and very good. "These responses rely on patients' self-assessments and reports, without additional objective measurement tools to evaluate these responses. The three experts who have been engaged in pMS studies and have published works on this topic within the department of pediatric neurology provided their expert opinions. To ensure content validity, three experts specializing in pediatric multiple sclerosis (pMS) and with published work in pediatric neurology provided their expert opinions on the questionnaire. The final version of the questionnaire form was formulated revised on their recommendations. After this expert review, a pilot test was conducted with a draft 26-item form,which was administered to 20 children for pilot testing.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 26 software. Descriptive statistics were used to summarize the data, including, absolute numbers, frequencies, percentages, mean and standard deviation, median, and range.

RESULTS

The pediatric patients (n=120) were diagnosed with MS, 71.7% were girls, the mean age of the patients was 15.784±1.55 (±SD), 84.2% of the patients were high school students and 53.3% lived in metropolitan areas. The mean age at diagnosis was 13.63 ± 2.28 years (min=4, max=17). Additionally, 75% of the children had supratentorial symptoms, 50% of the children had been on medication for more than 12 months. 58.3% of the children experienced treatment side effects, and 75% of the children encountered difficulties during the disease and treatment process.

The sociodemographic characteristics of the participants are presented in Table 1, their school achievements in Table 2, and their disease and treatment-related characteristics in Table 3. and Table 4 provides an overview of the participants' illness and overall health status.

Upon analyzing the findings, it was found that 71.7% of the participating children were girls, with a mean age of 15.78 ± 1.55 years (min=12, max=18). Additionally, 84.2% of the children were high school students, and 53.3% lived in metropolitan areas. No significant differences were found between children residing in metropolitan/urban areas and those in rural/village areas regarding these demographic characteristics. Most of the children (93.3%) had social security coverage (Table 1). The study revealed that 67.5% of the children experienced school absenteeism, with the mean number of absent days being 22.26 ± 33.50 (min=1, max=155). Participants' school absenteeism, academic achievement, MS duration, social participation, annual attack numbers, and EDSS scores showed no statistically significant differences. However, 49.2% of the children reported having good academic success, while 27.5% reported moderate success. Additionally, it was determined that 90.8% of the children had siblings, and 71.6% were not involved in sports or social activities (Table 2).

When examining the disease and treatment-related characteristics of the participants (as shown in Table 3), it was found that 77.5% of the children received their diagnosis at a university hospital, with a mean age at diagnosis of 13.63 ± 2.28 years (min=4, max=17). The analysis revealed that before diagnosis, 75% of the children exhibited supratentorial symptoms, 50% experienced optic symptoms, and 37.5% presented with brainstem symptoms before diagnosis. Regarding treatment modalities, it was determined that 42.5% of the children received immunomodulatory subcutaneous injections, 37.5% used oral tablets, and 14.2% were administered immunomodulatory intramuscular drugs. Additionally, 50% of the children had been on medication for more than 12 months. Among the participants, 58.3% reported experiencing side effects from the treatment. Of those, 34.2% primarily encountered flu-like symptoms and similar effects, while 10.8% experienced hair loss (Table 3).

Table 1: Children's sociodemographic characteristics (n=120)

Variables	Category	n (%)
Gender	Girl	86 (71,7)
	Boy	34 (28,3)
Age	Mean age= 15.78 ± 1.55	
Education level	Illiterate	1 (0,8)
	Primary School	2 (1,7)
	Secondary Education	16 (13,3)
	High School	101 (84,2)
Place of residence	Village	7 (5,8)
	District	17 (14,2)
	City	32 (26,7)
	Metropolitan	64 (53,3)
Social security	Yes	112 (93,3)
	No	8 (6,7)
Number of siblings	Yes	109 (90,8)
	No	11(9,2)
	Mean number of siblings=1.89 ± 1.44	

Table 2: Children's school achievement status and social activities (n=120)

Variables	Category	n (%)
School absenteeism	Yes	81 (67,5)
	No	39 (32,5)
	Number of days absent=22.26±33.50	
School achievement Status	Very bad	2 (1,7)
	Bad	5 (4,2)
	Middle	33 (27,5)
	Good	59 (49,2)
	Very good	21 (17,5)
Participation in sports or social activities	No	34 (28,3)
	Yes	86 (71,6)

As indicated by the findings presented in Table 4, 99.2% of the children received information about the disease. Among these, 89.2% obtained information from doctors, 40.8% from the internet, 25% from family members and relatives, and 23.3% from nurses. It was discovered that 75% of the children encountered difficulties during the disease and treatment process. Among those

Table 3: ***Characteristics of children in relation to disease and treatment*** **(n=120)**

Variables	Category	n (%)
Hospital diagnosis	University Hospital	93 (77.5)
	State Hospital	23 (19.2)
	Private Hospital	4 (3.3)
Average age at diagnosis	13,63±2,28	
Initial symptoms	Supratentorial symptom	90 (75.0)
	Optical symptom	60 (50.0)
	Brain stem symptom	45 (37.5)
	Spinal symptom	13 (10,8)
Medication used	Immunomodulator SC	51 (42.5)
	Immunomodulator IM	17 (14.2)
	Oral Tablet	45 (37.5)
	IV Injection	7 (5.8)
Medication duration	Less than one month	3 (2.5)
	1-3 months	15 (12.5)
	3-6 months	17 (14.2)
	6-12 months	25 (20.8)
	12-18 months	12 (10.0)
	18-24 months	10 (8.3)
	More than 24 months	38 (31.7)
Experiencing side effects	Yes	70 (58.3)
	No	50 (41.7)
Types of side effects	Flu-like symptoms	41 (58.5)
	Injection site reactions	4 (3.3)
	Hair loss	14 (11.6)
	Elevated liver enzymes	1 (0.8)
	Stress, depression	3 (2.5)
	Facial rash-allergic reactions	6 (5.0)
	Cardiac symptoms	2 (1.7)

Table 4: Characteristics of children in relation to disease and general health status (n=120)

Variables	Category	n (%)
Receiving information about the disease	Yes	119 (99.2)
	No	1 (.8)
Source of information	Doctor	107 (89.2)
	Nurse	28 (23.3)
	Internet	49 (40.8)
	Family members and relatives	30 (25.0)
	Friends	4 (3.3)
Experiencing any challenges	Yes	90 (75.0)
	No	30 (25.0)
Lack of accurate and adequate information about disease and treatment management	Yes	51 (42.59
	No	69 (57.5)
Problems with the clinical environment	Yes	7 (5.8)
	No	113 (94.2)
Problems with social and school life	Yes	39 (32.5)
	No	81 (67.5)
Experiencing side effects due to medication	Yes	51 (42.5)
	No	69 (57.5)
Psychological distress	Yes	63 (52,5)
	No	57 (47.5)
Family history of multiple sclerosis	Yes	21 (17.5)
	No	99 (82.5)
Attacks in the last six months	Yes	30 (25.0)
	No	90 (75.0)
General state of health now	Very bad	1 (.8)
	Bad	3 (2.5)
	Middle	30 (25.0)
	Good	59 (49.2)
	Very good	27 (22.5)

who experienced challenges, 52.5% exhibited psychological issues, including social withdrawal, depression, anxiety regarding the future, and anger management problems.

Moreover, 42.5% experienced side effects due to medication, while an equal proportion (42.5%) encountered difficulties in accessing accurate and sufficient information regarding disease and treatment management, 32.5% encountered problems in their social and school lives (including stigma, peer bullying, inability to participate in social activities, and attention deficit), and 5.8% had issues with the clinical environment (such as ineffective communication with healthcare professionals and lack of access to adequate and accurate information). Furthermore, it was observed that 17.5% of the children had a family history of MS, 25% had experienced an attack within the last six months, and 71.7% of the participating children assessed their general health status as good or very good. In addition, the mean Expanded Disability Status Scale (EDSS) score among children undergoing treatment was calculated as 0.26 (range: 0–3.5), while the annual mean number of attacks was reported as 1.6 ± 0.7.

DISCUSSION

Sociodemographic characteristics of the children

The study revealed that the majority (71.7%) of the participating children were girls, with a mean age of 15 years. Moreover, 84.2% were high school student, and 80% lived in urban or metropolitan areas. A retrospective study examining the clinical and demographic features of children diagnosed with MS in Türkiye reported a higher prevalence among girls, with a mean age of 16

years at diagnosis.[15] Similar findings have been observed in other studies in the literature, which indicate a predominance of female patients among pediatric MS cases, with mean ages ranging from 13 to 16 years.[13,23] During the diagnosis and treatment process, prolonged episodes and frequent hospitalizations may negatively impact both children and their families. The concentration of participants in urban areas or large cities may provide advantages, such as easier access to healthcare services and medical information, as well as improved continuity of care.

The study found that 81% of the participating children had experienced school absenteeism, with an average of 22 missed school days (min=1-max=155). Moreover, 63.7% of the children rated their school performance as good or very good, while 27.5% rated it as average. To date, no other study, either globally or in our country, has been conducted to assess the academic achievement of children with MS. However, studies have been carried out involving children with chronic conditions such as chronic kidney disease, juvenile idiopathic arthritis, and type 1 diabetes.[24-28] Children with chronic diseases may experience school absenteeism due to physical limitations, psychosocial impacts, the treatment process, and parental attitudes toward the disease.[24-26]

Additionally, research indicates that children with chronic conditions are more likely to experience school absenteeismcompared to their peers without such conditions.[22,25,26] Numerous studies have highlighted that the extent of school absenteeism is associated with disease progression, treatment regimens, physical and psychosocial needs, and the missing school days is one of the most common consequences of chronic illness.[25,29-31] Richardson *et al*. (2018) investigated the relationship between children's academic performance and school attendance, identifying a significantcorrelation.[25] In our study, we found that the average number of school days missed was 22. Further analysis revealed that 24.8% of the participating children had been absent for more than 22 days. Althoughthe majority (81%) of the children experienced school absenteeism, almost two-thirds (63.7%) assessed their academic performance as good or very good, while 27.5% rated it as average. These findings suggest that families and educators provided the necessary academic support and encouragement, effectively addressing the potential negative impact of absenteeism on educational outcomes.

The study revealed that 90.8% of the participating children had siblings, and 71.6% were not engaged in sports or social activities. The presence of chronic disease affects not only the diagnosed children but also the entire family. When a child is diagnosed with a chronic disease, family members often must adapt to their lifestyles due to factors such as frequent hospitalization, side effects, disruptions to school and social life, and overall uncertainty. This necessary adaptation can negatively affect the biopsychosocial well-being of healthy siblings. Interestingly, there is a lack of studies specifically focusing on the siblings of children with MS in existing literature. However, studies involving the healthy siblings of children with other chronic conditions, such as cancer, epilepsy, cerebral palsy, and Type 1 diabetes, have indicated that chronic illnesses and disabilities can influence the well-being of healthy siblings.[32] These studies have suggested possible declines in cognitive functions, weakening of psychosocial skills, and the persistence of these effects into adulthood.[33] The research findings are believed to highlight the need for further studies focused on the well-being of healthy siblings of children with MS.

Characteristics of children in relation to disease and treatment

An analysis of the disease and treatment characteristics of the children revealed that 77.5% of the children were diagnosed at a university hospital, and with a mean age at diagnosis of was 13.63 ± 2.28 (min=4, max=17). In a descriptive study conducted by Yılmaz *et al*. (2017), the age of the first attack was reported as 14 years (min=4, max=17).[13] Additionally, a study by by Langille *et al*. (2016), determined the age of disease onset among pediatric multiple sclerosis (MS) patients to be 14.7 years (min=4, max=17).[34]

In pediatric MS patients, variations in symptoms and clinical manifestations may occur depending on the age at disease onset. When the disease begins before the age of 10, its progression differs from that observed in adults. In such cases, cognitive and emotional disturbances, including confusion, seizures, increased irritability, and movement coordination disorders such as gait imbalances may become apparent.[3] While children under the age of ten commonly with multifocal symptoms, adolescents tend to exhibit symptoms more similar to those seen in adults.[3] Among pediatric MS patients, sensory symptoms (15-30%), motor impairments (30%), and brainstem dysfunction (25-41%) have been most frequently reported.[21] Multicenter

studies in the literature indicate thatpediatric MS patients most frequently experience involvement of the supratentorial, brainstem, and orbital regions, respectively.[1,23,34,35] In the present study, the most prevalent symptoms observed among children aged 12 to 18 diagnosed with MS were as follow : supratentorial involvement (75%), orbital involvement (50%), and brainstem involvement.

In the study conducted by Langille *et al.* (2016), the majority (42.5%) of the participating children received immunomodulatory intramuscular (IM)/subcutaneous (SC) treatment. Similarly, a retrospective study examining the clinical and demographic characteristics of children diagnosed with MS in Türkiye reported that80% of the patients received immunomodulatory IM/SC treatment, with a mean duration of drug use was 18 months.[15] In another study by Yılmaz *et al.* (2017), 66.6% of the children diagnosed with MS were found to have received immunomodulatory IM/SC treatment. Over the past 15 years, international collaborative studies in the field of pMS have contributed to a better understanding of the disease's pathophysiology.[9,36] In this study, it was observed that approximately half of the patients (56.7%) received immunomodulators via SC or IM administration, 37.5% were treated with oral tablets, and 5.7% received intravenous IV injections. This finding suggests that the centers where the study was conducted predominantly adhere to globally accepted treatment approaches for pMS patients. Additionally, in this study, 58.3% of the children experienced side effects. Among them, 34.2% reported from flu-like symptoms, and 10.8% experienced hair loss. Similar findings have also been documented in the literature.[15]

Characteristics of children in relation to disease and general health status

Following the study, nearly all the children (99.2%) received information about the disease. Most of them (89.2%) obtained this information from their physicians, followed by the Internet (40.8%), family members and relatives (25%), and nurses (23.3%). However, no existing research findings were available concerning pMS patients. Similar studies conducted on parents and children with other chronic or acute conditions have indicated that parents often have limited information provided by nurses.[37-39] The findings of this study align with research on children with chronic illnesses. As with other diseases, it is believed that informing children and their families about the diagnosis, treatment, and care of MS by pediatric nurses could help reduce the stress and anxiety, facilitate effective treatment and care, and improve the overall quality of healthcare service.

It was determined that 75% of the children experienced distress during the disease and treatment process. Among those reported distress, 52.5% experienced psychological distress, 42.5% reported side effects related to medications, 42.5% faced challenges in accessing accurate and sufficient information about disease and treatment management, 32.5% encountered difficulties in their social and academic lives, and 5.8% experienced problems related to the clinical environment. When children with chronic diseases are diagnosed, various factors negatively can negatively impact their physical, social, psychological, and developmental health.[40,41] In a phenomenological qualitative study conducted in Türkiye with individuals diagnosed with MS during childhood, key themes such as "difficulty in school and social life", "frequent attacks and side effects," "intense stress," and "lack of access to adequate information" as reported by young adults who participated in the study.[42,43]

Adolescence is a period already characterized by numerous psychological challenges, and the presence of a chronic disease (CD) further complicates the developmental tasks associated with this transition to adulthood.[42,43] Managing a CD can impose significant limitations on adolescents' daily lives due to the lifestyle adjustments required—such as changes in diet, exercise, and medical treatment—as well as the continuous need for healthcare monitoring.[44] CD can affect adolescents' emotional well-being, social and family relationships, as well as their academic performance, often as a result of school absences due to medical appointments.[45] Research indicates a higher prevalence of emotional and relational difficulties among adolescents with chronic illnesses.[43,46] This study found similar results, aligning with existing literature.

Additionally, it was observed that 17.5% of the children had a family history of MS, 25% had experienced an attack in the last six months, and 71.7% evaluated their general health status as good or very good. The genetic predisposition to MS has long been recognized, and epidemiological studies have been conducted on this topic.[3] In another study, 9.4% of pediatric patients were reported to have familial of MS[23], a finding consistent with similar studies in the literature. In this study, more than half (58.3%) of the treated patients experienced side effects, suggesting a potential

impact on treatment adherence. Several studies have documented that pMS patients frequently encounter medication-related side effects, and with treatment non-compliance often attributed to factors such as the frequency of medication administration.[5,9,41,47-49]

In conclusion, the study revealed that the majority of the participating children reported experiencing distress during the disease and treatment process, and more than half of them experienced drug-related side effects, which may impact treatment adherence . The frequency and severity of medication side effects are well-recognized factors influencing adherence in pMS patients. To ensure effective treatment and support recovery, it is recommended to regularly assess treatment adherence in pediatric patients, provide education for those with low adherence, adjust treatment doses as needed based on disease progression , improve patient-doctor and patient-nurse relationships, and implement psychological interventions that promote adherence. A proactive approach incorporating these strategies may help prevent treatment interruptions and delays in recovery.

Although this study makes a significant contribution to the literature, certain limitations are inherent in the chosen research methodology. Despite a few technical issues and internet interruptions during the online video conference, all interviews were completed without interruption. In addition, the assessment of children's academic performance and the challenges they faced during the illness and treatment process is based on their personal self-evaluation.

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DISCLOSURE

Ethics: This study was conducted in accordance with the Declaration of Helsinki on Human Rights and decision 21-2.1T/1 of the Medical Research Ethics Committee of University (date: 18.02.2021).

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