An Assessment of the Knowledge, Attitudes, and Practices of Pediatricians and Pediatric Residents in Duchenne Muscular Dystrophy

Duchenne Musküler Distrofide Pediatri Uzmanları ve Pediatri Uzmanlık Öğrencilerinin Bilgi, Tutum ve Uygulamalarının Değerlendirilmesi

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ABSTRACT

Objective: Pediatric residents and pediatricians play an important role in the management of Duchenne Muscular Dystrophinopathy (DMD) which is the most frequent hereditary muscle disease of childhood. Our study aims to evaluate the knowledge levels and approaches of pediatric residents and pediatricians on DMD.

Material and Methods: In this study, pediatric residents and pediatricians were asked to answer questions on the genetic, pathophysiological, clinical, and laboratory features, in addition, to follow-up and management of DMD. Data acquisition was carried out using an online questionnaire consisting of 17 questions prepared by the authors via Google forms (Google LLC, Mountain View, Ca, USA).

Results: The distribution of 197 responders was as follows: 53.8% were pediatricians, 13.7% were pediatric subspecialty fellows and 32.5% were pediatric residents with a total of 197 responders. 74.6% of the responders gave correct answers on the X-linked inheritance of DMD, 42.6% on the fact that it affected both genders, 93.3% on the fact that the disease is caused by the primary deficiency of dystrophin protein. 91.9% of the responders reported that the patients lost the ability to walk around 9-11 years of age. More than 50% of the responders did not have adequate information on the departments that could participate in the management of DMD patients.

Conclusion: This study has evaluated a wide range of physicians playing important roles in the follow-up and management of pediatric patients and has revealed a necessity for improvement in knowledge about genetic and clinical features of DMD and its management via learning.

Key Words: Attitude, Duchenne muscular dystrophy, Knowledge, Neuromuscular diseases, Rare disease

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ÖZ

Amaç: Kronik ve ilerleyici bir seyir gösteren Duchenne Musküler Distrofinopati (DMD), çocukluk çağının en sık karşılaşılan herediter kas hastalığı olup, yönetiminde pediatri uzmanlık öğrencileri ve pediatristler önemli rol oynamaktadır. Bu çalışmada; pediatri uzmanlık öğrencileri ve pediatristlerin DMD hakkındaki bilgi düzeyleri ve tutum özelliklerinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışmamızda pediatri uzmanlık öğrencisi hekimler ve pediatri hekimlerinin DMD'nin genetik, patofizyolojik, klinik ve laboratuvar özellikleri yanısıra izlem ve yönetim özelliklerini kapsayan soruları cevaplamaları istenmiştir. Bu çalışma için veriler Google forms (Google LLC, Mountain View, CA, ABD isimli online tool yolu ile; makale yazarları tarafından hazırlanan 17 soruluk araştırmacılar tarafından tasarlanan bir anket aracılığıyla online ortamda toplanmıştır.

Bulgular: Çalışmaya %53.8'i pediatrist, %13.7'si pediatri yandal uzmanlık öğrencisi, %32.5'i pediatri uzmanlık öğrencisi olmak üzere toplam 197 katılımcı alındı. DMD'nin X-linked geçiş gösterdiği katılımcıların %74.6'sı, her iki cinsiyette de görülebileceği %42.6'sı, distrofin proteinin primer eksikliği sonucu geliştiği bilgisi katılımcıların %93.3'ü tarafından doğru yanıtlandı. Katılımcıların %91.9'u DMD'li hastaların 9-11 yaş civarında yürümeyi kaybettiğini belirtti. DMD'li bir hastanın izleminde rol oynayan pediatri yandalları ve pediatri dışı bölümler açısından katılımcıların %50 ve daha fazlasının yeterli bilgisi olmadığı kaydedildi.

Sonuç: Bu çalışma ile pediatrik hasta takip ve tedavisinde önemli rol oynayan geniş bir hekim grubu değerlendirilerek DMD'nin genetik ve klinik özellikleri ve hastalık yönetimindeki önemli noktaların öğrenim faaliyetleri ile geliştirilmesinin gerekliliği dikkati çekmiştir.

Anahtar Sözcükler: Tutum, Duchenne musküler distrofi, Bilgi düzeyi, Nöromusküler hastalık, Nadir hastalık

INTRODUCTION

Duchenne muscular dystrophies (DMD), also known as dystrophinopathies, are the most common neuromuscular diseases of childhood resulting from X-linked mutations in the dystrophin gene (1-3). The dystrophin gene codes the main skeletal frame protein dystrophin, located on the cytoplasmic surface of the skeletal and cardiac muscle cell membranes. Mutations causing a loss of gene function cause progressive and fatal muscle weakness (1-3). Patients with DMD are followed up by the pediatricians throughout their lifetime for numerous comorbidities such as progressive skeletal muscle weakness starting from the pelvic girdle and cardiac involvement (1-3). These patients are routinely followed up by pediatric neurology and physical therapy and rehabilitation departments for muscle strength and function, and adverse effect management and rehabilitation of sleep disorders. Cardiac functions are followed up by pediatric cardiology while scoliosis, contractures, and bone fractures are followed up by the orthopedics department. Respiratory problems, spirometry evaluation, and sleep studies in addition to ventilator support in the advanced stages of the disease are managed by the department of respiratory pediatrics. The pediatric endocrinology department manages growth, pubertal development, and bone metabolism while the pediatric gastroenterology department is involved in feeding, chewing, swallowing, constipation, gastroesophageal reflux, gastroparesis, and possible gastrostomy placement in the advanced stages of the disease. Pediatrics, social pediatrics and healthy child clinics provide follow up for the continuity of routine health services such as vaccination (1,2)

The medical genetics and/or pediatric genetics department also plays an important role in the detection of carriers and providing genetic counseling to families (1,2). Pediatricians and pediatric clinics are crucial for the management of this chronic-progressive disease which has an early childhood onset and benefits from supportive treatments that have a positive effect on survival and life quality with new gene-based treatment options are discovered every day. Thus, pediatricians and pediatric residents are expected to have detailed knowledge of diagnostic and management features of DMD in addition to the routine treatment options along with the natural course of the disease. The knowledge levels and attitudes towards the disease and coping strategies of the patients and parents on hereditary neuromuscular diseases have been subject to numerous studies (4-6). However, no study concerning the knowledge levels, attitudes, and practices of the medical doctors with the most frequent exposure to this disease – pediatricians and pediatric residents – could be found in the literature. This study aims to identify the knowledge levels, attitudes, and practices of pediatric residents and pediatricians concerning DMD using a structured questionnaire prepared by the authors.

MATERIAL and METHODS

This prospective cross-sectional questionnaire study evaluated Turkish pediatricians and pediatric residents from private hospitals and clinics, government hospitals, and university clinics from 10th to 20th June 2020. The questionnaire was prepared by four researchers to evaluate knowledge, attitude, and practice of pediatric patients with DMD and was submitted via Google Forms (Alphabet, Mountain View, CA, USA). A random sampling method has been used in the study. The questionnaire form was filled in by 197 pediatricians and pediatric residents from all parts of the country. Informed consent was obtained online by adding the "Informed Consent Form" to the questionnaire prepared via Google Forms. The first two questions were about the professional title and the duration of work in that title followed by 15 open-ended, structured, and multiple-choice questions targeted to measure knowledge, attitude, and practice about DMD. Of the questions, 3 were

about the hereditary pattern and genetic features of the disease, 1 was about pathophysiology, 3 were about clinical features, 1 was about laboratory findings, 1 was about vaccination, 5 were about follow-up features and 1 was about treatment. Four of the answers (one question for genetics, one for clinics, one for treatment, one for management) were codified as dichotomous variables, namely as yes/No/unknown or correct/false/unknown responses, or in general (n:11) as categorical variables, when a multiple-choice selection had been requested. To ensure that all questions were answered, a choice for "No opinion" was added and the participants were not allowed to take the next question before answering the current one.

The ethics committee approval was obtained from the Turkish Ministry of Health, Antalya Research and Education Hospital non-interventional studies ethics committee on 06 May 2021 with ethical approval number: 6/19. The study has been conducted in accordance with the Helsinki guidelines.

Statistical analyses

All answers and datas were performed as the number of cases (n) and percentages (%) by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States).

RESULTS

The study was completed with 106 (53.8 %) pediatricians, 27 (13.7 %) pediatrics subspecialty fellows, and 64 (32.5 %) pediatric residents with a total of 197 responders (Figure 1).

The work experience was distributed as follows: 10.7 % (n:21) had less than 6 months, 18.8 % had more than 10 years, 39.1 % (n:77) had more than 5 years. The distribution of work duration in pediatrics was as follows: 7.6 % (n:15) between 6 months and 1 year, 21.3 % (n:42) between 1 and 3 years, 21.3 % (n:42) between 3 and 5 years.

The answers given to three questions concerning the inheritance pattern and genetic features of DMD have been summarized in figure (Figure 2). 97.5 % of the responders knew that it was a genetic disease, 74.6% (n:147) chose X-linked inheritance and 42.6% (n:84) stated that it could affect both genders.

93.3% (n:185) of the responders correctly chose dystrophin to "Which muscle protein deficiency causes DMD?" aimed at questioning the knowledge about the pathophysiological mechansims. On the other hand, 1% (n:2) of the responders chose dysferlin, 1.5% (n:3) chose sarcoglycan while 3.6% (n:7) had no opinion. No responders chose laminin or emerin.

Questions about clinical and laboratory features of DMD patients and answers have been summarized in table (Table I).

The participants were asked "Which of the following is not recommended in the follow-up of DMD patients?" to evaluate the knowledge about vaccination program in DMD patients. Two (1%) of the responders stated that questioning the vaccination history was not necessary at the time of diagnosis, 4 (2%) stated that pneumococcal vaccine was not recommended, 44 (22.3%) stated that the routine vaccination schedule as advised by the ministry of health could not be implanted and 15 (7.6 %) stated that they had no opinion on the vaccination of DMD patients. 131 (66.5%) of the patients believed that it was not necessary to inform the parents and family practitioner about avoiding attenuated vaccines.

Questions concerning bone metabolism, pubertal growth, respiratory and sleep problems, the necessity for genetic

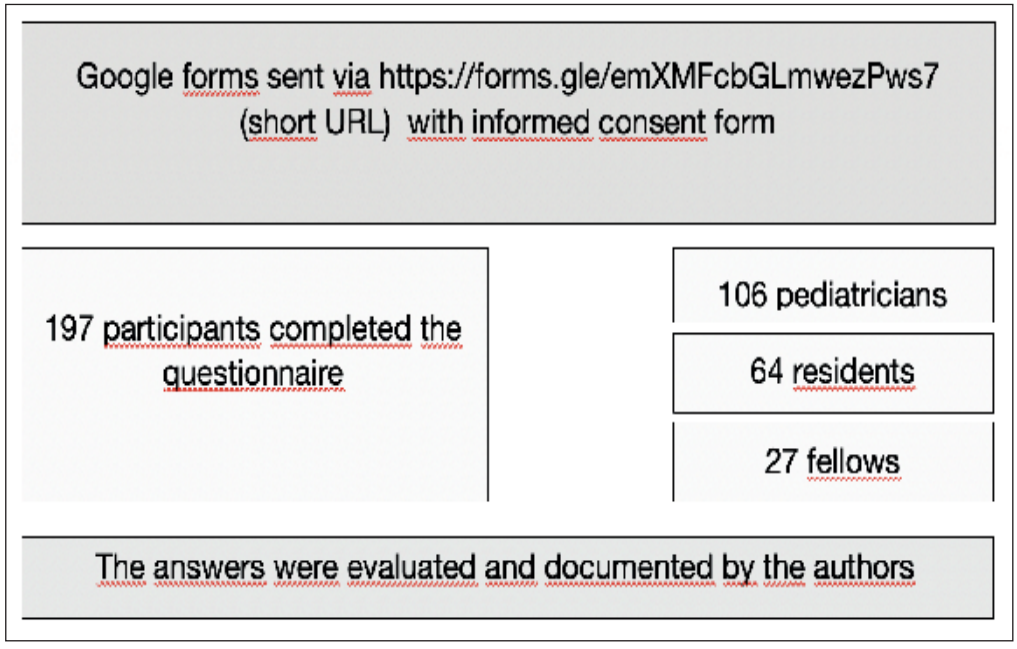

Figure 1: Flowchart of the study.

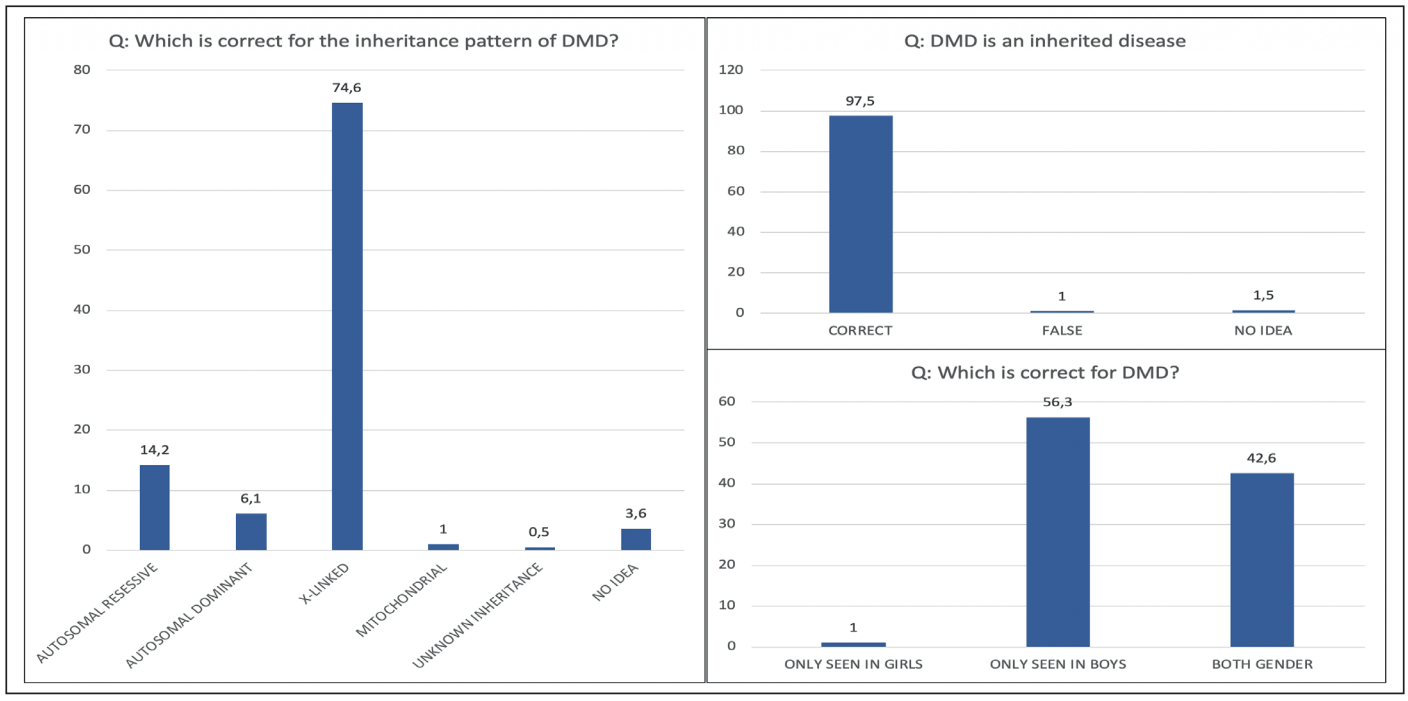

Figure 2: Questions and answers on inheritance pattern and genetic features of DMD.

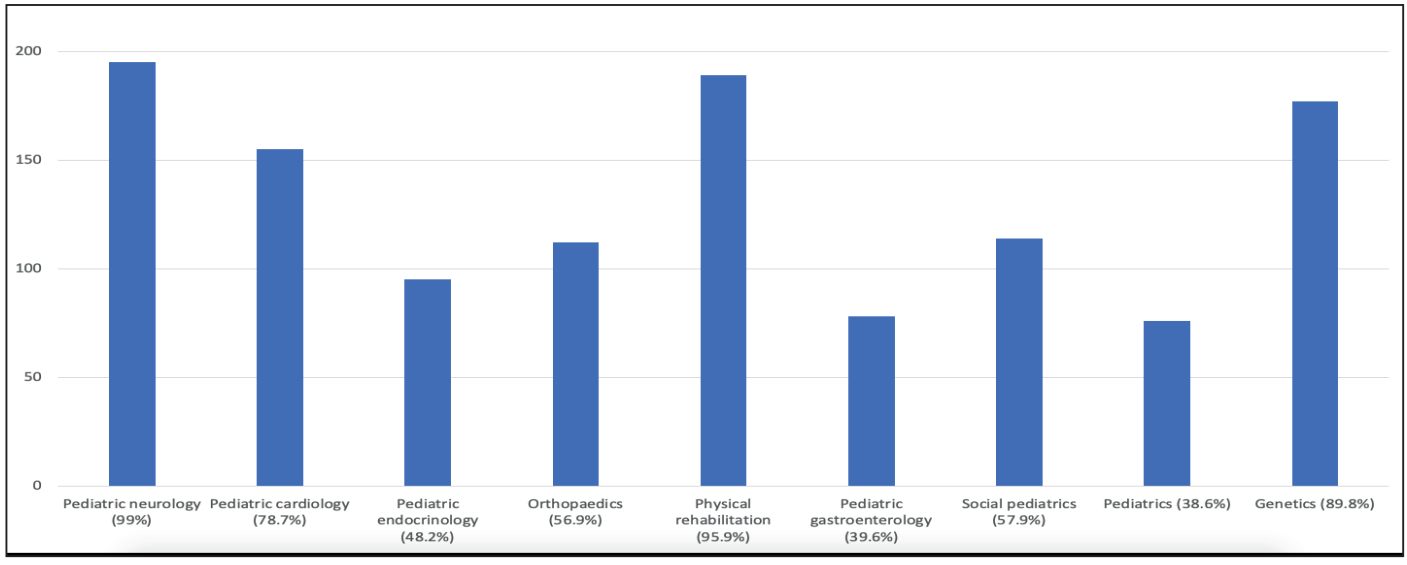

Figure 3: Distribution of answers concerning which subspecialty should follow up patients with DMD.

counseling, and treatment options and their answers have been summarized in table (Table II).

Questions about which pediatric subspecialty should manage DMD and their answers have been summarized in figure (Figure 3). 195 (99%) of the participants agreed on pediatric neurology while the second most popular opinion was physical therapy and rehabilitation with 189 (95.9%) answers. 76 (38.9%) of the responders who consisted of pediatric residents and specialists stated that general pediatrics should also participate in the follow-up.

DISCUSSION

Although rare, DMD is the most frequent hereditary neuromuscular disease and a timely diagnosis decreases future morbidity and comorbidity, while the fact that appropriate management and the consistently increasing number of new treatments increase the quality of life and lower the disease severity point to the importance of guidance by physicians. This survey study has revealed that 26.4% of doctors receiving education on pediatrics could not correctly identify the inheritance pattern of the disease, and 57.3% of them were not aware of the fact

Table I: Questions about clinical and laboratory features of patients with DMD and answers of the participants.

Questions and choices	Answers (%,n)
Which of the following is correct for DMD patients?	
They can never walk	0.5 (n=1)
They can never run	6.6 (n=13)
They can never sit without support	0.5 (n=1)
They lose the ability to walk between 9-11 years of age	91.9 (n=181)
No opinion	0.5 (n=1)
Which of the following is not one of the symptoms and findings of DMD?	
Frequent falls	2 (n=4)
Difficulty climbing stairs	1.5 (n=3)
Difficulty walking	23.9 (n=47)
Fasciculation in the tongue	72.1 (n=142)
Difficulty standing up from sitting position	0.5 (n=1)
No opinion	-
Muscle weakness in DMD starts from the pelvic girdle	
True	68 (n=134)
False	22.8 (n=45)
No opinion	9.1 (n=18)
Which of the following is not a laboratory finding in DMD?	
Elevated serum creatinine kinase (CK)	0.5 (n= 1)
Elevated serum Lactate dehydrogenase (LDH)	1.5 (n= 3)
Elevated serum liver function tests (ALT,AST)	5.1 (n= 10)
Low serum vitamin B12 levels	76.1 (n= 150)
Elevated serum aldolase levels	11.7 (n= 29)
No opinion	5.1 (n= 10)

CK: *Creatinine kinase,* ***ALT:*** *Alanine aminotransferase,* ***AST:*** *Aspartate aminotransferase*

Table II: Questions about bone metabolism, pubertal growth, respiratory and sleep problems, the necessity for genetic counseling, and treatment options of DMD patients and answers of the participants.

Questions and choices	Responses (%,n)
Which of the following is not recommended in the follow up of DMD patients?	
Evaluation of growth every 6 months	1 (n=2)
Evaluation of bone metabolism when the patient loses the ability to walk	71.1 (n=140)
Evaluation of pubertal growth every 6 months	19.3 (n=38)
Evaluation of Vitamin D and calcium intake starting at the time of diagnosis	3.6 (n=7)
No opinion	5.1 (n=10)
Which of the following is incorrect for DMD?	
The most frequent causes of death are lung involvement, infection, and cardiomyopathy	9.1 (n=16)
Cardiac evaluation should be performed at the time of diagnosis	5.1 (n=10)
Lung capacity should continually be evaluated	1.5 (n=3)
Regular rehabilitation, endocrine, gastroenterology, and orthopedic should be performed after diagnosis	6.1 (n=12)
Glucocorticoids should be avoided in DMD patients	70.1 (n=138)
Genetic counselling should be provided to the families of DMD patients	
True	99.5 (n=196)
False	-
No opinion	0.05 (n=1)
Which of the following symptoms in a DMD patient points to a sleep disorder?	
Headache while or after waking up in the morning	1.5 (n=3)
Inactivity and loss of concentration and	8.1 (n=16)
Sweating during night or sleep	1 (n=2)
Loss of appetite	-
All choices point to a sleep disorder	83.8 (n=165)
No opinion	5.6 (n=11)
The curative treatment for DMD has not been found yet	
True	82.7 (n=163)
False	9.6 (n=19)
No opinion	7.6 (n=15)

that it affects both genders. Autosomal recessive inheritance is more common in rare diseases could have misled 14.2% of the participants. On the other hand, this situation may have been caused by the belief that a disease with an X-linked pattern would have resulted in asymptomatic carriers in females. However, DMD can be observed in 1: 50.000.000 live female births (7,8). Girls may be symptomatic carriers when they are affected by homozygous mutations in the dystrophin gene, with the partial or total expression of the abnormal gene and also, carriers are symptomatic due to chromosomal translocations, Turner syndrome, or abnormal X chromosome or X inactivation (1,7). Diagnosis and follow-up of symptomatic/asymptomatic girls is as important as the necessity for genetic counseling for these girls given the fact that they may become mothers in the future (9). 99.5% of the participants of this study have proven their sensibility by stating that genetic counseling was important for these patients.

Although serious progress has been made in the diagnosis and management of DMD in the last decade, there is still a large interval between the onset of symptoms, and genetic confirmation (10,11). In the literature, the mean age of diagnosis of DMD is 4.3-4.11 years and the mean total delay in diagnosis is 19.2-30 months (11). The most important factor that can shorten this interval in our country is the knowledge of pediatricians and pediatric residents on clinical and laboratory findings (11,12). In our study, 91.9% of the responders stated that DMD patients lost their ability to walk around 9-11 years of age, 72.1% stated that tongue fasciculations were not part of the physical examination, 68% stated that muscle weakness originated from the pelvic girdle, while 34.4% reported symptoms which were not part of DMD as symptoms that could be observed and reported that tongue fasciculations which are related to anterior motor horn involvement could

be observed in DMD which is a myopathy. On the other hand, while elevations of enzymes like ALT, AST, aldolase, LDH, and CK are expected and directly related to the diagnosis of DMD, 5.1% of the responders had no opinion and 18.8% reported vitamin B12 deficiency as a laboratory finding directly associated with DMD. This points out the fact that 23.9% of the responders lack sufficient knowledge about laboratory findings associated with DMD. Although not in the screening program of our country, evaluation of CK levels in the first 3 years of life can help early diagnosis which is recommended in other countries (11). Elevated levels of muscle enzymes like AST, ALT, LDH in addition to CK is another finding of the disease (1,2). This points to the fact that CK levels should be evaluated in patients with elevated liver function tests.

In the diagnosis and management guideline by Birnkrant et al, evaluation of pubertal status every six months in addition to vitamin D and calcium supplementation starting at the time of diagnosis is advised (1,2). 71.1% of the responders gave the correct answer about this subject. According to the mentioned guideline, cardiac evaluation should be performed at the time of diagnosis, lung capacity should be regularly measured and routine rehabilitation, endocrinology, gastroenterology, and orthopedic follow up should be initiated However, 5.1%, 1.5% and 6.1% of the responders respectively did not provide the correct response. Additionally, 9.1% of the responders are not correctly informed about the fact that the most frequent cause of death in DMD is pulmonary involvement-infection and cardiomyopathy. This is important about the importance of follow-up concerning pulmonary infection, respiratory, and cardiac functions. The frequency of sleep disorders in children and adolescents with DMD has been reported as 20-65% which is higher than the healthy population (13). Thus clinicians should question the DMD patients and their families on sleep disorder symptoms. However, due to the design of the study, we were not able to evaluate if the clinicians questioned the patients on sleep disorder-related symptoms. 83.3% of the responders were familiar with these symptoms.

More than 90% of the responders believed pediatric neurology and physical therapy and rehabilitation departments should manage these patients. However, the responders had a low level of awareness about the fact that departments such as pediatric cardiology, endocrinology, gastroenterology and orthopedics should also participate in the management.

Treatment of DMD is centered on glucocorticoids, prevention of contractures, and medical care of cardiomyopathy, and respiratory compromise. However, nearly 30% of the responders believed that glucocorticoids should be avoided in patients with DMD. This points to a low level of awareness concerning the use of glucocorticoids which has been extensively researched and found to help pulmonary functions, slowed the progress of cardiomyopathy, delayed the onset of scoliosis and reduced mortality (1,2,14). Until the last decade, hereditary neuromuscular diseases including DMD were believed to be incurable and the aim was to provide supportive therapy to reduce morbidity and mortality. With the advancement of molecular diagnosis and targeted treatment, the necessity of increased competency within the physicians who play the primary role in the diagnosis and treatment of these patients become more evident.

On the other hand, we would like to emphasize that this study can not fully evaluate all knowledge and attitudes of the clinicians. The responses were limited to the knowledge questioned or the choices provided in the survey since the questions were close-ended and most of them had multiple choices. Such questions provide an easier assessment since they are easy to answer and less time-consuming thus provide coherent and regular responses. However, the studies encompassing a wider range of physicians which question knowledge and management with open-ended questions are necessary. Our study shows that pediatricians and pediatric fellows should read more material on routine management and follow-up in DMD and more time should be allocated to this disease in learning activities.

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