

Prevalence of muscular dystrophy in patients with muscular disorders in Tehran, Iran

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Abstract

Muscular dystrophy is a group of diseases that is characterized by progressive muscle wasting and the weakness of variable distribution and severity. On the basis of the distribution of predominant muscle weakness, there are many different kinds of muscular dystrophy. Some dystrophies are especially frequent in certain populations. There are no studies on the prevalence of muscular dystrophy in Iran. This study was aimed to survey the prevalence of muscular dystrophy among Iranian patients with muscular disorders. This analytical cross-sectional study was conducted on 1000 patients with musculoskeletal disorders who visited the dystrophy association of Bou-Ali Hospital (Tehran) from June 2014 to June 2016. Patients' data were extracted using a checklist that included age, gender, age of onset, family history, findings from clinical diagnostic tests and types of muscular dystrophy. The clinical findings were the results of genetic tests; EMG-NCV; para-clinical findings, including LDH and CPK; and pathological findings. All data were analyzed by SPSS V.22 (IBM Inc., NY) with Chi Square and One way ANOVA tests. All analyses were performed with $P = 0.05$ considered as the threshold of statistical significant. Out of the 337 patients studied, 262 (77.7%) were male and 75 (22.3%) were female. Subjects had a mean (\pm SD) age of 26.08 (\pm 11.86) years with an age range of 3 to 59 years. The most common types of muscular dystrophy were found to be Duchenne dystrophy (131 cases, 38.9%), limb-girdle dystrophy (91 cases, 27%), Becker dystrophy (58 cases, 17.2%), FSHD dystrophy (31 cases, 9.2%), and SMA (26 cases, 7.7%), respectively. The results showed that a statistically significant relationship between dystrophy types and gender, age, family history, age of diagnosis, CPK and LDH levels ($P < 0.001$). There were no statistical relationship between dystrophy types and pathological findings ($P = 0.57$), EMG-NCV test results ($P = 0.062$), and genetic findings ($P = 0.06$). Since muscular dystrophies often appear during the first decade of life, any information in regard to their prevalence can contribute to better planning and provisioning of required services, as well as better treatment or control of the condition. The results also showed that genetic tests, para-clinical tests, pathology analysis, and EMG-NCV tests can serve as good diagnostic tools for different varieties of dystrophy. Thus, facilitation of these diagnostic tests, particularly the genetic tests, can lead to a faster and more accurate diagnosis of dystrophy, especially in people with a family history of the disease.

Key Words: Prevalence, Muscular Dystrophy, Muscular Disorders, Iran.

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Muscular dystrophy is a group of diseases that is characterized by progressive muscle wasting and the weakness of variable distribution and severity. In muscular dystrophy, abnormal genes (mutations) interfere with the production of the proteins needed to form healthy muscle.^{1,2} On the basis of the distribution of predominant muscle weakness, there are many different kinds of muscular dystrophy, including congenital forms:

Duchenne and Becker; Emery-Dreifuss; distal; facioscapulo-humeral; oculopharyngeal; spinal muscular atrophy (SMA), and limb-girdle, which is the most heterogeneous group.^{3,4} The main sign of muscular dystrophy is progressive muscle weakness. Specific signs and symptoms begin at different ages and in different muscle groups, depending on the type of muscular dystrophy. In Duchenne muscular dystrophy, onset is in

early childhood. Signs and symptoms typically appear between the ages of 2 and 3 and may include frequent falls, difficulty getting up from a lying or sitting position, trouble running and jumping, muscle pain and stiffness, and learning disabilities.⁵⁻⁷ In Becker muscular dystrophy, signs and symptoms are similar to those of Duchenne muscular dystrophy, but are typically milder and progress more slowly. In other types of muscular dystrophy, signs can vary and may include the inability to relax muscles (myotonic), muscle weakness in the face and shoulders (Facioscapulohumeral or FSHD), and may affect hip and shoulder muscles (limb-girdle).⁸⁻¹⁶ On the basis of some studies, incidence at birth of Duchenne muscular dystrophy is around 300×10^{-6} , and its prevalence in the population (in terms of the total male population) is around 60×10^{-6} . Also, based on a detailed study from Sweden, the prevalence of muscular dystrophy in children under the age of 16 years was estimated to be 25×10^{-6} for congenital muscular dystrophy, 8×10^{-6} for limb-girdle muscular dystrophy, 8×10^{-6} for FSHD muscular dystrophy, and (only in boys) 16×10^{-6} for Becker muscular dystrophy.^{17,18} Muscular dystrophy occurs in both sexes and in all ages and races. People with a family history of muscular dystrophy are at a higher risk of developing the disease or passing it onto their children. Related to causes of these diseases, certain genes are involved in making proteins that protect muscle fibers from damage. Muscular dystrophy occurs when one of these genes is defective. Each form of muscular dystrophy is caused by a genetic mutation particular to a specific type of the disease. Many of these mutations are inherited. Some, however, occur spontaneously in the mother's egg or the developing embryo and can be passed onto the next generation.¹⁹⁻²¹ Some different methods can be used to diagnose the various types of muscular dystrophy, such as a Serum creatine kinase (CPK) test, an electromyography (EMG) test, a nerve conduction velocity (NCV) test, a genetic test, and a muscle biopsy. Damaged muscles release enzymes, such as creatine kinase, into the blood. In a person who has not had a traumatic injury, high blood levels of CPK suggest a muscle disease, such as muscular dystrophy. In an EMG test, an electrode needle is inserted into the muscle to be tested and changes in the pattern of electrical activity can confirm a muscular disease. In genetic testing, blood samples can be examined for mutations in some of the genes that cause different types of muscular dystrophy. Also, related to a muscle biopsy, a small piece of muscle can be removed through an incision or with a hollow needle. Analysis of the tissue sample can distinguish muscular dystrophies from other muscle diseases.²²⁻²⁴ Some dystrophies are especially frequent in certain populations but are rare elsewhere: for example, autosomal dominant distal muscular dystrophy in Scandinavia, Fukuyama muscular dystrophy in Japan, oculopharyngeal muscular dystrophy in French Canada, and several autosomal recessive limb-girdle muscular

dystrophies in communities in Brazil, North America, and the Middle East.^{1,25} There are no more studies regarding the prevalence of muscular dystrophy in Iran. This study was aimed to survey the prevalence of muscular dystrophy among Iranian patients with muscular disorders.

Materials and Methods

The analytical cross-sectional study was conducted on 1000 patients with musculoskeletal disorders who visited the dystrophy association of Bou-Ali Hospital (Tehran) from June 2014 to June 2016. Subjects were selected by convenient sampling. Inclusion criteria were having any type of muscular dystrophy of unknown etiology, an age of less than 60 years, and the absence of systemic musculoskeletal disorders. All subjects were asked to fill a consent form in advance. In the first stage, 1,000 people with muscular dystrophy of unknown etiology were included in the study. After reviewing the medical files, 337 cases were found eligible for further investigation, and the rest were excluded. The data collection tool was a two-part questionnaire: The first part pertained to demographic information (age, gender); the second part was dedicated to clinical information, including the age of onset, family history of disease, findings from clinical diagnostic tests, and the type of dystrophy. The enquired clinical findings were the results of genetic tests; EMG-NCV; paraclinical findings, including LDH and CPK; and pathological findings. Exclusion criteria included any deficiency in a patient's medical records and a patient's refusal to participate. This study was disclosed to and approved by the ethics and research committees of the faculty of medicine of Islamic Azad University-Tehran Medical Branch. The collected data was analyzed with SPSS V.22 (IBM Inc., NY). The chi-square test was used to quantify the qualitative variables and determine their relationship with dystrophy types and the one-way ANOVA was used to analyze this relationship for two-state quantitative variables. All analyses were performed with $P = 0.05$ considered as the threshold of statistical significant.

Results and Discussion

Out of the 337 patients studied, 262 (77.7%) were male and 75 (22.3%) were female. Subjects had a mean (\pm SD) age of 26.08 (\pm 11.86) years, with youngest being 3 years old the oldest being 59 years. Analysis of family history of muscular diseases showed that 99 patients (29.44%) had a close relative with muscular dystrophy. The mean (\pm SD) age of onset was 10.52 (\pm 7.97) years, with the lowest being 1 year and the highest being 38 years. The most common types of muscular dystrophy were found to be Duchenne dystrophy (131 cases, 38.9%), limb-girdle dystrophy (91 cases, 27%), Becker dystrophy (58 cases, 17.2%), FSHD dystrophy (31 cases, 9.2%), and SMA (26 cases, 7.7%), in that order. The chi-square test showed that the dystrophy type had a significant relationship with gender and family history of disease (P

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Table 1. Associations between Demographic Variables and Types of Dystrophy

		Types of Dystrophy						P value
		Duchenne N (%)	Limb-Girdle N (%)	Becker N (%)	Facioscapulohumeral N (%)	Spinal Muscular Atrophy N (%)	Total N (%)	
Gender	Male	127 (48.47)	43 (16.41)	53 (20.22)	22 (8.40)	17 (6.49)	262 (100)	$P < 0.001$
	Female	4 (5.33)	48 (64)	5 (6.66)	9 (12)	9 (12)	75 (100)	
Family History	Positive	14 (14.14)	43 (43.43)	23 (23.23)	10 (10.10)	9 (9.90)	99 (100)	$P < 0.001$
	Negative	117 (49.15)	48 (20.16)	35 (14.70)	21 (8.82)	17 (7.14)	238 (100)	
Age of Patients	0-10	20 (83.33)	0 (0)	0 (0)	0 (0)	4 (16.66)	24 (100)	$P < 0.001$
	10-20	75 (72.11)	10 (9.61)	12 (11.53)	4 (3.84)	3 (2.88)	104 (100)	
	20-30	29 (31.18)	25 (26.88)	20 (21.50)	12 (12.90)	7 (7.52)	93 (100)	
	30-40	6 (7.5)	39 (48.75)	17 (21.25)	9 (11.25)	9 (11.25)	80 (100)	
	40-50	1 (4.34)	13 (56.52)	3 (13.04)	5 (21.73)	1 (4.34)	23 (100)	
	50-60	0 (0)	4 (30.76)	6 (46.15)	1 (7.7)	2 (15.38)	13 (100)	
Age of Onset	0-10	123 (63.40)	23 (11.85)	26 (13.40)	5 (2.57)	17 (8.76)	194 (100)	$P < 0.001$
	10-20	8 (7.84)	44 (43.13)	23 (22.54)	20 (19.60)	7 (6.86)	102 (100)	
	20-30	0 (0)	20 (55.55)	9 (25)	6 (16.66)	1 (2.77)	36 (100)	
	30-40	0 (0)	4 (80)	0 (0)	0 (0)	1 (20)	5 (100)	
	40-50	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
	50-60	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	

< 0.001) (Table 1). Also, a statistically significant relationship was found between dystrophy type and a patient's age and age of onset ($P < 0.001$). A review of pathologic findings showed that 263 subjects (78%) had tested positive in pathological tests and 74 subjects (22%) had tested negative. EMG-NCV test results confirmed the presence of muscular dystrophy in 306 patients (90.8%). A review of genetic test results showed that genetic evidence confirms the presence of muscular dystrophy in 246 (73%) patients, but not in the remaining 91 (27%) cases. Analysis of paraclinical findings (CPK and LDH) revealed a statically significant relationship between dystrophy type and CPK and LDH levels ($P < 0.001$). The subjects had a mean (\pm SD) CPK and LDH of 5182.09 (\pm 7001.92) U/l and 2831.69 (\pm 1157.66) U/l, respectively, which were several times higher than normal. Statistical analysis showed no significant relationship between dystrophy type and the pathological findings ($P = 0.57$), EMG-NCV test results ($P = 0.062$),

or genetic findings ($P = 0.06$) (Table 2). Our study of 337 patients with muscular dystrophy (who visited Bou-Ali Hospital in Tehran) found the most common types of this disorder to be Duchenne dystrophy, limb-girdle, Becker dystrophy, FSHD dystrophy, and SMA, in that order. The incident of dystrophy was found to have a statistically significant relationship with gender and family history, as it was more prevalent among males than females and also more prevalent among people with a family history of dystrophy. In terms of the prevalence of dystrophy types, our results are consistent with the results of Paul et al.,²⁵ which showed the higher prevalence of Duchenne dystrophy than Becker dystrophy in the United States,²⁶ and with the meta-analysis of Mah et al.,²⁶ which reported that Duchenne dystrophy is more prevalent than Becker.²⁷ In a study by Norwood et al.²⁸ on the prevalence of gene-related muscle disorders, the most common types of dystrophy were reported to be myotonic (28.6%), FSHD (10.7%), limb-girdle (6.2%),

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Table 2. Associations between Genetic Tests, Pathology, and EMG-NCV Test Results and Types of Dystrophy

		Types of Dystrophy						P value
		Duchenne N (%)	Limb- Girdle N (%)	Becker N (%)	Facioscapulohumer al N (%)	Spinal Muscular Atrophy N (%)	Total N (%)	
Genetic Test	Positive	107 (43.50)	62 (25.20)	37 (15.04)	21 (8.53)	19 (7.72)	246 (100)	0.06
	Negative	24 (26.37)	29 (31.86)	21 (23.07)	10 (10.99)	7 (7.69)	91 (100)	
Pathology Test	Positive	101 (38.40)	72 (27.37)	48 (18.25)	21 (7.99)	21 (7.99)	263 (100)	0.57
	Negative	30 (40.54)	19 (25.67)	10 (13.51)	10 (13.51)	5 (6.75)	74 (100)	
EMG-NCV Test	Positive	117 (38.23)	86 (28.10)	55 (17.97)	28 (9.15)	20 (6.53)	306 (100)	0.062
	Negative	14 (45.16)	5 (16.12)	3 (9.67)	3 (9.67)	6 (19.35)	31(100)	

and SMA (5.1%). In our study, the prevalence of limb-girdle dystrophy was 27%, which is higher than the figure reported by Norwood et al.,²⁸ but our observations in regard to prevalence of FSHD dystrophy and SMA are largely consistent with their findings.²⁸ A systematic review of the literature on the prevalence of dystrophy types by Theadom et al.²⁹ has also reported that myotonic dystrophy, Duchenne dystrophy, and FSHD dystrophy are the most common types of this disorder. In that study, myotonic dystrophy was reported as the most prevalent type of dystrophy, but our data showed Duchenne dystrophy to be the most common type.²⁹ Our results regarding the prevalence of dystrophy types are also consistent with the results of a study by Leth et al.,³⁰ which showed that Duchenne dystrophy, limb-girdle dystrophy, and FSHD dystrophy are the most common types of dystrophy in Denmark.³⁰ In a study by Ballo et al.,³¹ 46% of people with Duchenne dystrophy and Becker dystrophy had a family history of these disorders. However, in our study, only 29.40% of subjects had such family history. Also, in Ballo et al.'s study, 60% of patients who had Becker dystrophy (20 cases) had a positive family history, but in our study, this figure was 40%. This difference is probably due to differences in the sample size and the type of dystrophies examined.³¹ In our study, dystrophy type was found to have a statistically significant relationship with gender, as it was more prevalent among men than women. In this respect, our results are consistent with the results of Dogan et al.,³² which report that gender can affect dystrophy phenotype and severity and that men are more frequently affected by the disease than women.³² We also found a statistically significant relationship between the age of onset and dystrophy type. Our results showed that, statistically, Duchenne dystrophy appears during the first decade of life (at ages less than 10 years), Becker

dystrophy appears during the first and second decades (at ages less than 20 years), FSHD dystrophy appears during the second decade (at ages between 10 and 20 years), limb-girdle dystrophy appears during the first three decades (at ages less than 30 years), and SMA appears during the first decade of life (at ages less than 10 years). In a study by Mahjneh et al.,³³ limb-girdle dystrophy was reported to emerge during the first three decades of life, which is in agreement with our results.³³ In the study by Ballo et al.,³² diagnosis of Duchenne dystrophy was confirmed in about 42% of cases by genetic test results. In our study, this figure was about 73% for all types of dystrophy and about 81% for Duchenne dystrophy alone.³⁴ In a study by Hallwirth-Pillay et al.³⁴ and in a group of 68 patients with Duchenne dystrophy and Becker dystrophy, about 57% of diagnoses were confirmed by genetic test results, which is lower than the figure obtained in our study.³⁵ Also, in a study by Chung et al.³⁵ on the prevalence of muscular dystrophy in Chinese children based on the results of genetic and EMG-NCV tests, it was found that 228 (68%) of the 332 studied children had gene-related muscular dystrophies. An epidemiological study by El-Tallawy et al.³⁶ on muscular dystrophies in Egypt found that more than 80% of subjects had an elevated CPK (> 225 IU/l), which is consistent with our results, which showed elevated CPK in about 88.8% of patients. In this study, we investigated the prevalence of muscular dystrophy in an Iranian population. Duchenne dystrophy, limb-girdle dystrophy, Becker dystrophy, FSHD, and SMA were found to be the most common types of dystrophy among subjects. The results showed a significant relationship between the incident of dystrophy and age, gender, and family history of the disease. Since these dystrophies often appear during the first decade of life, any information in regard to their prevalence can contribute to better planning and

provisioning of required services, as well as better treatment or control of the condition. The results also showed that genetic tests, paraclinical tests, pathology analysis, and EMG-NCV tests can serve as good diagnostic tools for different varieties of dystrophy. Thus, facilitation of these diagnostic tests, particularly the genetic tests, can lead to a faster and more accurate diagnosis of dystrophy, especially in people with a family history of the disease.

List of acronyms

SMA - Muscular atrophy
 FSHD - Facioscapulohumeral or
 CPK - Serum creatine kinase
 EMG - Electromyography
 NCV - nerve conduction velocity

Author's contributions

Each author contributed in equal part to the manuscript.

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Conflict of Interest

The authors declare no conflicts of interests.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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