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Depression Levels and Associated Factors in Individuals with Hereditary Neuromuscular Disease

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ABSTRACT

Objective: The purpose of this study was to determine depression and anxiety levels in individuals diagnosed with Hereditary Neuromuscular Diseases (HNMDs) with differing degrees of ambulation, and the factors affecting those levels. **Materials and Methods:** The study population in this descriptive study consisted of patients under follow-up with diagnoses of HNMD at the Gazi Yaşargil Education and Research Hospital muscular diseases clinic. One hundred fifty-nine patients with varying degrees of ambulation were included. The study data were collected using a sociodemographic data form, the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), and the Functional Ambulation Classification (FAC). **Results:** The participants' mean age was 21.03±9.35 years, and 55.3% were male. Physical ambulation levels were nonfunctional in 24.5% of participants, dependent on supervision in 15.7%, and independent in 59.7%. A significant part of the participants had moderate or severe anxiety levels. The general BAI score was 20.44±10.25, and the general BDI score was 21.03±9.35. Mild and severe depressive symptoms were present in 76.1% of the participants. Advanced age ($p<0.05$) and high physical dependence levels ($p<0.05$) emerged as significant variables adversely affecting depression and anxiety levels. **Conclusion:** It was concluded that especially advanced age and dependent physical ambulation level are important risk factors.

Keywords: Anxiety, Depression, Neuromuscular Disease.

Genetik Geçişli Nöromusküler Hastalığı Olan Bireylerin Depresyon Düzeyi ve İlişkili Faktörler

ÖZ

Amaç: Bu çalışmanın amacı, farklı ambulasyon düzeylerine sahip Genetik Geçişli Nöromusküler Hastalığı (GNMH) olan bireylerin depresyon ve anksiyete düzeyinin belirlenmesi ve etkileyen faktörlerin tespit edilmesidir. **Gereç ve Yöntem:** Tanımlayıcı olarak tasarlanan çalışmanın evrenini Gazi Yaşargil Eğitim Araştırma Hastanesi Kas Hastalıkları kliniğinde GNMH tanısı ile takip edilen hastalar oluşturmaktadır. Farklı ambulasyon seviyelerindeki 159 hastanın dahil edildiği çalışmanın verileri sosyodemografik veri formu, Beck Depresyon ölçeği (BDÖ), Beck Anksiyete ölçeği (BAÖ) ve Fiziksel Ambulasyon Skalası (FAS) aracılığı ile toplanmıştır. **Bulgular:** Çalışmaya katılanların yaş ortalaması 21.03 ± 9.35 ve %55.3'ü erkektir. Katılımcıların %24.5'i fonksiyonel olmayan, %15.7'si gözetimli bağımlı, %59.7'si tam bağımsız seviyesinde fiziksel ambulasyon düzeyine sahiptir. Çalışmaya katılanların önemli bölümü orta ve şiddetli düzeyde anksiyete seviyesine sahip olup, genel BAÖ puan ortalaması 20.44±10.25'tir. Katılımcıların BDÖ genel puan ortalaması 21.03±9.35'tir. Hafif ve ileri düzey depresyon belirtisi gösterenlerin oranı ise %76.1'dir. GNMH tanılı bireylerde ileri yaş ($p<0.05$) ve fiziksel bağımlılık düzeyinin yüksek olması ($p<0.05$) depresyon ve anksiyete düzeyini olumsuz etkileyen önemli değişkenler olarak tespit edilmiştir. **Sonuç:** Özellikle ileri yaş ve bağımlı fiziksel ambulasyon seviyesinin önemli birer risk faktörü olduğu sonucuna ulaşılmıştır.

Anahtar Kelimeler: Anksiyete, Depresyon, Nöromusküler Hastalık.

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INTRODUCTION

There are several types of hereditary neuromuscular disease (HNMD) (Dahlqvist et al., 2020; Deenen et al., 2015). Recent studies from the UK and Norway have reported HNMD prevalences of approximately 120 and 112/100,000, respectively (Carey et al., 2021; Müller et al., 2021). In some of these, patients are physically independent, but may be bed-bound in others. However, HNMD causes long-term function losses in almost all patients, even those with independent ambulation levels (Dahlqvist et al., 2020). Several cardiological, respiratory, and physical complications are known to occur in severe HNMD progressing with motor weaknesses (Finder, 2021). From that perspective, despite the rarity of HNMDs, they still represent an important public health problem by causing a rise in the dependent population. According to World Health Organization data, the global prevalence of depression is 4.4%, but can be as high as 5%, particularly in Africa (WHO, 2023). Chronic and physical diseases are risk factors affecting depression in addition to various sociodemographic variables such as sex and economic status (Bogdan et al., 2020; Liu & Tang, 2018; WHO, 2017). A study of patients with different HNMDs reported a prevalence of depression of 32.5% (Mori-Yoshimura et al., 2019), while a meta-analysis reported a depressed rate of 18% and an anxiety disorder rate of 24% (Pascual-Morena et al., 2022). However, while this can emerge in association with long-term therapeutic processes, it can also derive from patients' individual and environmental differences. In both cases, depression can adversely affect prognosis in patients with chronic disease and can also reduce therapeutic success (Aytap & Özer, 2021). This will impact on the treatment and rehabilitation of patients with HNMDs requiring long-term treatment and care. Determining the prevalence of depression and anxiety in HNMDs and factors associated with severity is therefore important in terms of the prognosis of HNMDs. The evaluation of several risk factors potentially associated with depression in individuals with HNMDs will contribute to their prolonged treatment and care. The HNMDs included in this study are rare entities. Studies have investigated diagnostic groups such as Duchene and Limb Girdle, which are relatively more common. However, in addition to these diagnostic groups, all seven diagnostic groups in the HNMD classification were included in the present study. This research is important in terms of identifying determinants of depression in patients with HNMDs, in whom depression is frequently observed.

MATERIALS AND METHODS

Study type

This was a descriptive study.

Place and time of research

This study was performed with adults with HNMD under follow-up at the Health Sciences University

Gazi Yaşargil Education and Research Hospital (HSUGYERH) muscular diseases clinic, Turkey. Research data were collected between 15.07.2021 and 05.05.2022.

The population / sample of the research

Patients aged 18 or over, diagnosed with HNMD and with no mental, visual, or hearing problem representing a difficulty to understanding, evaluating, or answering the questions in the research were included in the study. Epi Info software (7.4.2.0) was used to determine the sample power. Post power analysis based on the depression rate showed that 159 individuals would be representative at an 86% confidence interval a 5% margin of error (alpha: 0.05). The study population consisted of 304 individuals diagnosed with HNMD under follow-up at the HSUGYERH muscular diseases clinic. The authors aimed to contact all the study population, with no sampling being performed. Sixty-two of the patients under follow-up were excluded due to being younger than 18, and another 26 due to having disabilities representing an obstacle to communication. Data were finally collected from 159 of the 216 individuals meeting the inclusion criteria, a participation rate of 73.6%.

Variables

Independent variables of the study Functional Ambulation Classification (FAC) and sociodemographic characteristics; Dependent variables are The Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI).

Data collection tools

A sociodemographic data form, BAI, BDI, and the FAC were employed for data collection. The questionnaire employed in the research consisted of 54 questions, six investigating sociodemographic characteristics, 21 each for the BAI and BDI, and six evaluating the FAC.

Sociodemographic Data Form: This form, developed by the authors in line with the literature, investigated characteristics such as marital status, sex, age, and education, together with information concerning height and weight (Darmahkasih et al., 2020; Mori-Yoshimura et al., 2019; Pascual-Morena et al., 2022).

Beck Anxiety Inventory (BAI): The BAI evaluates the frequency of experienced anxiety symptoms and was developed by Beck et al. in 1988 (Beck et al., 1988). This Likert-type self-report scale consists of 21 items scored between 0 and 3. Higher total scores indicate higher levels of anxiety. The validity and reliability of the scale in Turkey were studied by Ulusoy et al., with a Cronbach alpha reliability coefficient of 0.807 being determined (Ulusoy et al., 1998). The Cronbach alpha reliability coefficient in the present measurement, applied to determine the degree of emotional tension such as anxiety and worry in individuals with HNMD, was 0.821.

Functional ambulation classification (FAC)

This scale applied by the authors to determine participants' functional abilities was developed at the

Massachusetts General Hospital, USA. The six-point scale evaluates how much assistance the individual requires from a device or other person during ambulation. Scoring is from 0 to 5. At level 0 the individual is unable to walk (non-functional) or requires a parallel bar or the assistance of several people to do so. At level 1, the individual is ambulated with the assistance of another person and walks with another person taking his weight on a flat surface. At level 2, the individual is ambulated with the occasional assistance of another person but not such as to take the patient's weight. At level 3, the individual can ambulate on a flat surface under the visual supervision of another person but without their physical support. At level 4, the patient can ambulate on a flat surface but not at all speeds, and not on stairs etc. At level 5, the individual can walk on all surfaces at a sufficient speed (Akdeniz et al., 2015).

Beck Depression Inventory (BDI): This self-report scale is the most frequently employed tool for measuring physical, emotional, and cognitive symptoms seen in depression in research and the clinical setting. It consists of 21 items, each scored between 0 and 3. Total possible scores range between 0 and 63 and show the severity of depression. The BDI was developed by Beck et al., with validity and reliability study for Turkey being conducted by Hisli (Bats & Brown, 1996; Hisli, 1989). Scores of 1-9 indicate minimal depression, 10-16 mild depression, 17-29 moderate depression, and 30-63 severe depression (Bats & Brown, 1996). The Cronbach alpha reliability coefficient in the Turkish-language validity and reliability study was 0.782, and 0.733 in the present study (Hisli, 1989).

Data collecting

The research data were collected by the researchers using the data collection form, face-to-face with the patients diagnosed with HNMD, at the HSUGYERH Muscular Diseases Polyclinic Muscle Diseases outpatient clinic.

Statistical analysis

Frequency, percentage, arithmetic mean, and standard deviation were used as descriptive methods

in the data analysis. The Kolmogorov-Smirnov test was applied to determine whether variables were normally distributed. The independent samples t test and One-Way Analysis of Variance (ANOVA) were applied to examine the change caused by independent variables in dependent variables. Turkey's test was applied to identify the source of significance in ANOVA tests yielding significant results. Spearman's correlation was used to determine correlations between total BAI and BDI scores and other numerical variables. p values lower than 0.05 were regarded as statistically significant.

Ethical considerations

Approval was received from the Batman University non-interventional clinical research ethical committee before commencement (No:2021/02-10 dated 28.05.2021). Written informed consent was obtained from all participants.

RESULTS

The largest proportion (30.2%) of participants in this study completed with 159 individuals were those diagnosed with limb-girdle muscular dystrophy (LGMD). Myotonic dystrophy (MD) was present in 34 participants, congenital myopathy in 23, and facioscapulohumeral muscular dystrophy (FSHM) in 26. The remaining less common HNMDs are shown in Table 1. In this study, 64.8% of participants were single, their mean age was 21.03 ± 9.35 , and 55.3% were male. Thirty-nine percent of participants were educated to high school or university level, while 24.5% were illiterate. Participants physical dependence was evaluated using the FAC. The results showed that 24.5% were non-functional, 15.7% were supervision-dependent, and 59.7% were either independent on a flat surface or completely independent in terms of ambulation (Table 1).

A significant proportion of the participants in this study had moderate or severity anxiety. The mean general BAI score was 20.44 ± 10.25 . The participants' mean general BDI score was 21.03 ± 9.35 .

Table 1. Sociodemographic characteristics (n=159).

Descriptive characteristic	n	%
Sex		
Male	88	55.3
Female	71	44.7
Marital status		
Single	103	64.8
Married	56	36.2
Education level		
No formal education	39	24.5
Elementary-middle school	58	36.5
High school-university	62	39.0

Table 1 (continued). Sociodemographic characteristics (n=159).

Diagnosis		
	n	%
Duchenne/Becker Muscular Dystrophy (DMD/BMD)	3	1.9
Limb-Girdle Muscular Dystrophy (LGMD)	48	30.2
Facioscapulohumeral Muscular Dystrophy (FSHM)	26	16.4
Myotonic Dystrophy (MD)	34	21.4
Congenital Myopathy (CM)	33	20.8
Other Myopathies	5	3.1
Hereditary Polyneuropathy (HP)	10	6.2
FAC		
Non-functional (FAC score: 0 and 1)	39	24.5
Supervision-dependent (FAC score: 2 and 3)	25	15.8
Independent on a Flat Surface and Completely Independent (FAC score: 4.5)	95	59.7
BAI		
Minimal (<7)	16	10.1
Mild (8-15)	40	25.2
Moderate (16-25)	57	35.8
Severe (>26)	35	28.9
BDI		
Minimal (<9)	38	23.9
Mild (10-16)	37	23.3
Moderate (17-29)	51	32.1
Severe (>30)	33	20.7

Mild or severe depressive symptoms were determined in 76.1% of the participants. Relationship between sociodemographic characteristics and various risk factors and mean BDI scores are shown in Table 2. No statistically significant relationship was found between sex and severity of depression in individuals with HNMD ($p=0.483$). However, women had significantly higher anxiety levels than men ($p=0.018$). No significant association was also found between participants' marital status, level of education, or body mass index and mean BDI or BAI scores. Mean BAI levels were significantly higher among individuals with HNMD aged 36 or over compared to those aged 18-24 ($p=0.040$). Analysis revealed a significant association between physical dependency and mean BDI ($p=0.007$) and BAI ($p=0.001$) scores. At post hoc analysis mean BDI and

BAI scores were significantly higher in the non-functional group (FAC score:0 and 1) compared to the independent on a flat surface and completely independent group (FAC score: 4 and 5), while no association was determined between the other groups. Weak negative correlation was detected between participants' physical ambulation levels and total BAI and BDI scores ($0.150 < r < 0.350$; $p < 0.005$). Weak positive correlation was observed between the age of patients with HNMD and total BAI scores ($0.150 < r < 0.350$; $p < 0.005$), while no correlation was found between BDI scores and age ($-0.150 < r < -0.150$; $p > 0.005$). No correlation was found between total BAI and BDI scores and the other parameters of Body Mass Index (BMI), age at diagnosis, or number of siblings ($-0.150 < r < -0.150$; $p > 0.005$) (Table 3).

Table 2. Correlations between sociodemographic characteristics and various risk factors and mean BDI Score (n=159).

Variables	Groups	n	BDI		BAI		Test/p values	
			Mean	SD	Mean	SD	BDI	BAI
Sex	Male	88	20.56	9.19	18.72	9.18	t:-0.703	t:-2.389
	Female	71	21.61	9.58	22.57	11.13	p:0.483	p:0.018
Marital status	Single	103	21.23	9.37	21.27	10.45	t:0.558	t:-1.579
	Married	53	20.35	9.05	18.54	9.70	p:0.578	p:0.116
Age	18-25 ^A	54	20.38	8.46	18.03	8.66	F:3.544 p:0.031 C>B	F:3.293 p:0.040 C>A
	26-35 ^B	44	18.63	7.97	20.06	11.17		
	Above 36 ^C	61	23.34	10.56	22.85	10.47		

Table 2 (Continued). Correlations between sociodemographic characteristics and various risk factors and mean BDI Score (n=159).

Education	No formal education	39	23.07	8.92	20.71	9.56	F:1.25 p:0.289	F:2.118 p:0.124
	Elementary-middle school	58	20.55	9.66	22.32	11.02		
	High school or university	62	20.20	9.28	18.51	9.72		
Body mass index (kg/m²)	>18.5	19	21.94	8.43	24.89	11.21	F:0.658 p:0.579	F:2.425 p:0.068
	18.5-24.99	86	20.98	8.72	19.46	9.49		
	25-24.99	39	21.84	10.20	21.87	10.77		
	< 25	15	18.06	11.78	16.73	10.45		
FAC	(FAC: 0-1) ^A	39	24.94	10.77	25.10	10.82	F:5.166 p:0.007 A>C	F:7.454 p:0.001 A>C
	(FAC:2-3) ^B	25	21.24	8.84	22.16	10.42		
	(FAC:4-5) ^C	95	19.37	8.43	18.08	9.28		

Table 3. Factors associated with BDI and BAI (n=159).

Variables	FAC		BMI		Age		Age at Diagnosis		Number of Siblings	
	r	p	r	p	r	p	r	p	r	p
BAI	-0.283	0.029	-0.029	0.719	0.175	0.027	-0.023	0.467	0.092	-0.248
BDI	-0.232	0.003	0.022	0.782	0.099	0.219	0.058	0.773	-0.017	0.836

DISCUSSION

A large part of the individuals diagnosed with HNMDs in this research (32.1%) exhibited moderate depression levels. Similarly, a study of patients with different HNMDs reported a prevalence of depression of 32.5% (Mori-Yoshimura et al., 2019), while a meta-analysis reported a depressed rate of 18% and an anxiety disorder rate of 24% (Pascual-Morena et al., 2022). Another study involving 47 patients diagnosed with muscular dystrophy (spinal muscular atrophy, LGMD, and FSHM) reported mild depression (32%) in a large proportion of participants, while a few exhibited moderate depressive symptoms (Winblad et al., 2010). Comparable research in the literature have also reported widespread occurrences of depression in such different HNMDs as LGMD (Peric et al., 2018), myasthenia gravis (MG) (Parada et al., 2014), and multiple sclerosis (Feng et al., 2020; Ozer et al., 2010). A meta-analysis of 38 studies of patients with MG determined a depression rate of 36% and an anxiety rate of 33% (Nadali et al., 2023). A study of patients with Duchene muscular dystrophy observed emotional/behavioral disorders at a rate of 38.7% (Darmahkasih et al., 2020). In another study, 23% of patients with LGMD and asymptomatic hyperckemia met the criteria for major depressive disorder (Feng et al., 2020). This and other studies indicate a high prevalence of depression in individuals with HNMDs. This makes it essential to prioritize interventions aimed at depression in psychological support activities specific to individuals with HNMD. Moderate (35.8%) or severe (28.9%) levels of anxiety were observed in the majority of individuals diagnosed with HNMD in the present study. Similarly, an anxiety rate of 40.0% and a depression rate of 25.2% were reported in patients with spinal

muscular atrophy (Yao et al., 2021). Research from Turkey determined a prevalence of trait anxiety of 20.5% in BMD, FSHM, LGMD, and MD (Ozer et al., 2010). High levels of anxiety can adversely affect individuals' psychological health by over-rising their adaptive coping mechanisms. Another finding of the present study, and one supported by the literature is the positive association (Parada et al., 2014) between anxiety and depression, showing that depression and anxiety are psychological disorders that should be considered together in psychological support studies for individuals with HNMDs. The sociodemographic variable of age groups was found to affect both depression and anxiety levels in individuals with HNMD in the present study. However, no relationship was found between anxiety and depression levels and education level, marital status, or body mass index. Similarly, only the age variable has been found to be associated with DM2, HMSN-I and amyotrophic lateral sclerosis has been shown to decline with age (Feng et al., 2020; Peric et al., 2018; Winter et al., 2010). Research has emphasized the link between depression and decreased quality of life in HNMDs (Feng et al., 2020; Messina et al., 2016; O'Dowd et al., 2021). This research shows that prognosis varies among the different disease groups in the study. For example, while prognosis is poor in patients with LGMD, there were also diseases with a better course in the study group, such as MD. However, subsequent function loss associated with muscle weakness applies in all HNMDs (Dahlqvist et al., 2020). During this process, complications or various negativities related to HNMD may be expected to occur with increasing age. Decreased quality of life with advancing age and increased disability due to the progressive nature of the disease may account for inadequacy of the individual's

current coping resources, and the increase in depression and anxiety. Women diagnosed with HNMDs had higher levels of anxiety than men in the present study. However, while mean depression levels were also higher among women, this was not statistically significant. Similar research confirms that anxiety and depressive disorders are more frequent among women in chronic diseases such as MG (Parada et al., 2014). The researchers suggested that women exposed to such chronic diseases also had a higher probability of reporting depression (Darmahkasih et al., 2020; Nadali et al., 2023). Even in the absence of any chronic disease, women's biology, psychological characteristics, methods of coping with problems, and societal and cultural position all make them more susceptible to depression. Susceptibility to depression and anxiety in such chronic diseases, particularly among women, must therefore be prioritized. Another important finding of the present study is that functional ambulation levels are a significant factor affecting depression and anxiety levels in patients with HNMDs. Hypotheses suggesting that the progressive nature of the illness contributes to the depressive state support the findings of the present study (Darmahkasih et al., 2020; Nadali et al., 2023). Several studies of both healthy individuals and various disease groups have shown that physical activity impacts positively on depression (Feng et al., 2020; Parada et al., 2014). A meta-analysis involving a large sample group with more than one chronic disease showed that physical health is a factor affecting depression levels (O'Dowd et al., 2021). From that perspective, depression and anxiety are an important risk factor, especially in individuals with HNMD who experience severe physical dependence (FAC: 0-1). No correlation was found between age at diagnosis of HNMD and anxiety or depression. Similarly, no relationship has been determined between age at diagnosis and anxiety or depression scores among patients with LGMD (Peric et al., 2018). However, in contrast to these findings, an association between age at onset and depression in patients with LGMD and asymptomatic hyperckemia (Feng et al., 2020). Another study reported negative correlation between age at diagnosis and anxiety levels in patients with MG, but no association was observed with depression (Parada et al., 2020). Research has produced inconsistent findings concerning age at diagnosis and depression and anxiety. More specific research is therefore needed to elucidate the effect mechanism of age at onset.

Limitations and Strengths of the Study

The important finding of the present study is that functional ambulation levels are a significant factor affecting depression and anxiety levels in patients with HNMDs. The inability to reach sufficient samples from some subgroups of HNMDs in this study is an important limitation. In addition, due to the cross-sectional nature of the study, it was not

possible to comment on the anxiety and depression levels of patients with HNMDs over time. Future research might usefully consider the effects of HNMDs in the long term. In addition, studies involving more samples from different HNMD subgroups may provide useful information about the rates of depression and anxiety among different groups.

CONCLUSION

The fact that the level of physical ambulation is an important determinant of depression in patients with HNMDs indicates that individuals with HNMDs who have physical limitations should be followed closely. It is important to follow the medical treatment at the primary and secondary prevention level in HNMDs patients who do not have physical limitations yet. When the loss of physical ambulation is irreversible in HNMDs patients, rehabilitation and psychosocial support for HNMDs patients with increased physical limitations may provide support in controlling depression. In addition, it may be a precaution to employ HNMDs whose physical ambulation level has reached the level of addiction in a profession they can carry out in order not to be separated from the society and to gain a place in the society. The physical therapy process of patients who have reached the level of physical addiction and informing their caregivers are important issues that should be done at the tertiary prevention level.

Conflict of Interest

The author declares no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Author Contributions

Plan, design: AT, HB, FA; **Material, methods and data collection:** AT, HB, FA; **Data analysis and comments:** AT, HB, FA; **Writing and corrections:** AT, HB, FA.

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