ORİJİNAL MAKALE / ORIGINAL ARTICLE
Balıkesir Sağlık Bilimleri Dergisi / BAUN Sağ Bil Derg
Balıkesir Health Sciences Journal / BAUN Health Sci J
ISSN: 2146-9601- e ISSN: 2147-2238
Doi: https://doi.org/10.53424/balikesirsbd.1534185

The Relationship Between Consanguinity and Other Factors with Gross Motor Function Levels in Children with Neuromotor Developmental Delay

Bilgehan KOLUTEK AY[1], Mustafa TUNA[2]

[1] Sütçü İmam University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation
[2] Şanlıurfa Training and Research Hospital, Department of Physical Medicine and Rehabilitation

Geliş Tarihi / Received: *15.08.2024,* ***Kabul Tarihi / Accepted:*** *25.03.2025*

ABSTRACT

Objective: It is well established that consanguinity is a risk factor for neuromotor developmental delay. In our clinical observations, we have noted that children with neuromotor delay, and consanguineous parents tend to have more delayed gross motor skills. This study aimed to investigate the frequency of consanguinity in children with neuromotor developmental delay, and whether there is any relationship between consanguinity, gross motor function classification, and other parameters. **Materials and Methods:** Two hundred and six paediatric patients diagnosed with neuromotor developmental delay and referred to the rehabilitation clinic were included in the study. In the children included in the study, consanguinity and gross motor function levels were evaluated in conjunction with diagnosis, gestational age, birth weight, and various maternal and paternal factors, and inter-group comparisons were made. **Results:** 68% of the patients had a history of consanguinity. 65.5% of the children had a history of incubator care, 35.4% had a history of asphyxia, and 30.1% had a history of epilepsy. Upon reviewing the diagnoses, 63.6% were diagnosed with cerebral palsy, and 13.6% were diagnosed with axial hypotonia. Furthermore, no significant relationship was found between incubator care, asphyxia, epilepsy, neuromotor developmental delay, and consanguinity with gross motor classification. **Conclusion:** In our study, no significant relationship was found between consanguinity, gross motor classification, and other parameters in children with neuromotor developmental delay. Further studies are required to determine whether consanguineous marriage influences motor classification in neuromotor developmental delay.

Keywords: Consanguinity, Motor Skills Disorders, Neurodevelopmental Disorders.

Nöromotor Gelişim Geriliği Olan Çocuklarda Akraba Evliliği ve Diğer Faktörlerin Kaba Motor Fonksiyon Düzeyleri ile İlişkisi

ÖZ

Amaç: Akraba evliliğinin nöromotor gelişim geriliği için bir risk faktörü olduğu iyi bilinmektedir. Klinik gözlemlerimizde ebeveynlerinde akrabalık bulunan nöro-motor geriliği olan çocukların, kaba motor seviyesinin daha geride olduğunu gözlemledik. Bu çalışmada nöromotor gelişim geriliği olan çocuklarda akraba evliliği sıklığı ve kaba motor fonksiyon sınıflaması ile akraba evliliği ve diğer parametreler arasında bir ilişki olup olmadığı incelendi. **Gereç ve Yöntem:** Nöro-motor gelişim geriliği tanısı almış, rehabilitasyon polikliniğine başvuran 206 çocuk hasta çalışmaya dahil edildi. Çalışmaya dahil edilen çocuklarda akraba evliliği ve kaba motor fonksiyon düzeyleri; tanı, doğum haftası, doğum ağırlığı, çeşitli maternal ve paternal faktörler ile birlikte değerlendirilerek gruplar arası karşılaştırmalar yapıldı. **Bulgular:** Hastaların %68'inde akraba evliliği vardı. Çocukların %65,5'inde küvöz öyküsü, %35,4'ünde asfiksi öyküsü ve %30,1'inde epilepsi öyküsü vardı. Hastaların tanıları incelendiğinde %63,6'sında serebral palsi, %13,6'sında aksiyel hipotoni, saptandı. Ayrıca, küvözde kalma, asfiksi, epilepsi, nöromotor gelişim geriliği ve akraba evliliği ile kaba motor sınıflaması arasında anlamlı bir ilişki bulunmadı. **Sonuç:** Çalışmamızda nöromotor gelişim geriliği olan çocuklarda kaba motor sınıflaması ile akraba evliliği ve diğer parametreler arasında anlamlı ilişki bulunamadı. Bu konuda yapılacak ileri çalışmalar konunun aydınlatılmasına yardımcı olacaktır.

Anahtar Kelimeler: Kan Bağı, Motor Beceri Bozuklukları, Nörogelişimsel Bozukluklar.

Sorumlu Yazar / Corresponding Author: Bilgehan KOLUTEK AY, Sütçü İmam University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Kahramanmaraş, Türkiye.
E-mail: bilgehankolutek@gmail.com

Bu makaleye atıf yapmak için / Cite this article: Kolutek Ay, B., & Tuna, M. (2025). The relationship between consanguinity and other factors with gross motor function levels in children with neuromotor developmental delay. *BAUN Health Sci J, 14*(2), 288-294. https://doi.org/10.53424/balikesirsbd.1534185

BAUN Health Sci J, OPEN ACCESS https://dergipark.org.tr/tr/pub/balikesirsbd
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INTRODUCTION

Neuromotor development is a process that starts from the intrauterine period and continues until adulthood. The most important feature that distinguishes children and adults from each other is that children show continuous growth and development. While growth is the increase in body volume and mass, development is the change in the functions of cells and tissues (Çarman, 2016).

The increase in the use and skills of large muscle groups of the body indicates gross motor development, while the increase in the use of small muscle groups that provide functions such as writing, grasping small objects or toys indicates fine motor development (Yimenicioglu et al., 2023). Neuromotor development in children progresses from gross motor movements to fine motor movements, from cranial to caudal and from center to peripheral. The chronological age of the child should be taken into account when evaluating neuromotor developmental stages (Çarman, 2016; Yimenicioğlu et al., 2023).

While biological factors play a role in the early stages of neuromotor development, environmental factors gain greater importance in the later stages. Neuromotor developmental delay may occur due to many risk factors in prenatal, perinatal and postnatal periods. Neuromotor developmental delay may occur in children due to genetic syndromes, premature birth history, asphyxia, low birth weight, twins, intrauterine infection history, maternal systemic disease or smoking history (Caesar et al., 2023; Çelik, 2021; Hsieh at al., 2023).

In clinical practice, we observed that children with motor retardation whose parents had a consanguineous marriage had severe gross motor classifications. We aimed to identify the factors associated with the level of motor delay and contribute to the literature with the results of this study. So, we investigated the frequency of consanguineous marriage in children with neuromotor developmental delay in Şanlıurfa, where consanguineous marriages are common, and whether there is a relationship between gross motor level and consanguineous marriage and the other parameters.

MATERIALS AND METHODS

Study type

This cross-sectional descriptive study was conducted in Şanlıurfa Training and Research Hospital.

Study group

Children, who were diagnosed with neuromotor developmental retardation by a Paediatric Neurology physician and referred to the Physical Medicine and Rehabilitation Outpatient Clinic for rehabilitation, were included in this study.

Patients who had not yet been diagnosed, those with orthopaedic disabilities but without neuromotor delay, children with one or both step-parents, as well as children who have lost one or both parents and those whose parents did not provide consent for participation were excluded from the study.

Due to the descriptive and cross-sectional nature of the study, no specific sample size calculation was made. After obtaining the study approval, all patients who met the criteria during the study period (four months) were included in the study.

Procedures

Gender, mode of delivery, birth weight, incubator history, maternal gestational age, number of pregnancies, epilepsy history, similar disease history in siblings, family pregnancy planning, mother's folic acid use history, mother's systemic disease history were questioned and recorded in all of the children included in the study. The patients included in the study were considered as consanguineous if they married second-degree relatives, while those who neither knew each other before marriage nor lived in the same village were considered as non-consanguineous. Couples who were not related to each other but lived in the same village and were married were not included in the study. The gross motor function level of the children included in the study was evaluated according to the Gross Motor Functions Classification System. Gross motor classification was evaluated as age appropriate. Gross motor classification system is easy, simple and can be applied in a short time, and the general classification that divides the severity of disability into five levels for all ages is as follows.

LEVEL I: Can mobilize independently and without support in the community without restriction.

LEVEL II: Can ambulate in the community with restrictions

LEVEL III: Walks indoors using hand-held mobility devices but requires a wheelchair to ambulate in the community.

LEVEL IV: Self-movement is limited. Can use a motorized mobility vehicle.

LEVEL V: They are transported at home and in the community in a manual wheelchair. They are completely dependent on others (Palisano et al., 1997).

Statistical analysis

Analyzes were evaluated in 22 package programs of SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL). In the study, descriptive data were shown as n and % values in categorical data and mean±standard deviation (Mean±SD) values in continuous data. Chi-square analysis (Pearson Chi-square) was used to compare categorical variables between groups. Conformity of continuous variables to normal distribution was evaluated by Kolmogorov-Smirnov test. The Kruskal Wallis test was used to compare more than two groups. The statistical significance level in the analyses was accepted as $p<0.05$.

Ethical approval

Written permission was obtained from the Harran University Faculty of Medicine Clinical Research Ethics Committee and the institution where the study was conducted prior to data collection. In addition, all study participants' parents were informed about the nature of the study and that participation was on a voluntary basis.

Informed consent was obtained from all participants' parents.

RESULTS

206 patients with a mean age of 5.0±4.6 (min=1, max=13) years were included in the study, and 44.7% of the patients were female and 55.3% were male. There was consanguineous marriage in 68% of the patients' parents. 56.8% of the deliveries were caesarean section and 43.2% were normal deliveries. 38.8% of the mothers had a history of abortion and 18.4% had a history of multiple pregnancy. 11.2% of the mothers had a history of smoking during pregnancy and 16% had a history of additional disease. 60.2% of the patients had planned delivery and the mother had a history of folic acid use. 65.5% of the children had a history of incubator, 35.4% had a history of asphyxia and 30.1% had a history of epilepsy. When the diagnoses of the patients were examined, 63.6% had Cerebral Palsy (CP), 13.6% had a genetic disease that could cause central hypotonia (CH), 7.3% had Neural Tube Defect (NTD), 3.4% had Muscular Dystrophy (MD) and Spinal Muscular Atrophy (SMA) and 12.1% had Metabolic Disease (MDs).

Table 1. General characteristics of patients and parental factors.

		Number	%
Age, mean ±Standard Deviation			5.0±4.6
Gender	Female	92	44.7
	Male	114	55.3
Consanguineous marriage	Yes	140	68.0
	No	66	32.0
Father smoking history	Yes	113	54.9
	No	93	45.1
Type of birth	Cesarean section	117	56.8
	Vaginal	89	43.2
There is a history of abortion in the mother	Yes	80	38.8
	No	126	61.2
Multiple pregnancy history	Yes	38	18.4
	No	168	81.6
Smoking before and during pregnancy	Yes	23	11.2
	No	183	88.8
Mother's history of additional disease	Yes	33	16.0
	No	173	84.0
History of similar illness in siblings	Yes	55	26.7
	No	151	73.3
Pregnancy planning and use of folic acid	Yes	124	60.2
	No	82	39.8
Father's history of drug use during pregnancy planning	Yes	22	10.7
	No	184	89.3
Incubator story	Yes	135	65.5
	No	71	34.5
Perinatal Asphyxia	Yes	73	35.4
	No	133	64.6
History of epilepsy	Yes	62	30.1
	No	144	69.9
Diagnosis	Cerebral Palsy	131	63.6
	Central hypotonia	28	13.6
	Neural Tube Defect	15	7.3
	MD and SMA	7	3.4
	Metabolic Disease	25	12.1
Cerebral Palsy Classification	Diplegic	43	32.8
	Hemiplegic	27	20.6
	Tetraplegic	44	33.6
	Mixed type	17	13.0
Gross motor classification	1	13	6.3
	2	32	15.5
	3	30	14.6
	4	44	21.4
	5	87	42.2

MD: Muscular Dystrophy, SMA: Spinal Muscular Atrophy

It was observed that these MDs included Phenylketonuria(n=10), Mucopolysaccharidosis (n=7), Gaucher disease (n=4), Fatty Acid Oxidase Deficiencies (n=4), and Galactosemia (n=3). It was determined that 32.8% of CP patients were diplegic, 20.6% hemiplegic, 33.6% tetraplegic and 13% mixed type. When the gross motor classification of the patients was examined, 6.3% was level 1, 15.5% was level 2, 14.6% was level 3, 21.4% was level 4 and 42.2% was level 5 was (Table 1).

The classification of patients with CP showed significant difference among gross motor retardation levels ($p<0.001$). Gross motor retardation was lower in diplegic, and hemiplegic CP types compared to mixed and tetraplegic CP types. However, no statistically significant relationship was found between gross motor retardation and consanguinity or other parameters ($p>0.05$) (Table 2).

Table 2. Comparison of gross motor classifications of categorical parameters.

		1	2	3	4	5	p*
		N (%)	N (%)	N (%)	N (%)	N (%)	
Gender	Female	6 (6.5)	19 (20.7)	13 (14.1)	24 (26.1)	30 (32.6)	0.084
	Male	7 (6.1)	13 (11.4)	17 (14.9)	20 (17.5)	57 (50.0)	
Consanguineous marriage	Yes	8 (5.7)	20 (14.3)	18 (12.9)	30 (21.4)	64 (45.7)	0.590
	No	5 (7.6)	12 (18.2)	12 (18.2)	14 (21.2)	23 (34.8)	
Type of birth	Cesarean Section	7 (6.0)	14 (12.0)	14 (12.0)	28 (23.9)	54 (46.2)	0.254
	Vaginal	6 (6.7)	18 (20.2)	16 (18.0)	16 (18.0)	33 (37.1)	
Maternal abortion history	Yes	5 (6.3)	13 (16.3)	6 (7.5)	14 (17.5)	42 (52.5)	0.069
	No	8 (6.3)	19 (15.1)	24 (19.0)	30 (23.8)	45 (35.7)	
Multiple pregnancy history	Yes	3 (7.9)	8 (21.1)	3 (7.9)	11 (28.9)	13 (34.2)	0.344
	No	10 (6.0)	24 (14.3)	27 (16.1)	33 (19.6)	74 (44.0)	
Smoking during pregnancy	Yes	1 (4.3)	4 (17.4)	3 (13.0)	6 (26.1)	9 (39.1)	0.965
	No	12 (6.6)	28 (15.3)	27 (14.8)	38 (20.8)	78 (42.6)	
Mother's history of additional disease	Yes	3 (9.1)	4 (12.1)	7 (21.2)	6 (18.2)	13 (39.4)	0.694
	No	10 (5.8)	28 (16.2)	23 (13.3)	38 (22.0)	74 (42.8)	
Similar illness in siblings	Yes	3 (5.5)	8 (14.5)	6 (10.9)	14 (25.5)	24 (43.6)	0.836
	No	10 (6.6)	24 (15.9)	24 (15.9)	30 (19.9)	63 (41.7)	
Pregnancy planning and use of folic acid	Yes	8 (6.5)	17 (13.7)	17 (13.7)	28 (22.6)	54 (43.5)	0.882
	No	5 (6.1)	15 (18.3)	13 (15.9)	16 (19.5)	33 (40.2)	
Incubator story	Yes	10 (7.4)	14 (10.4)	19 (14.1)	29 (21.5)	63 (46.7)	0.053
	No	3 (4.2)	18 (25.4)	11 (15.5)	15 (21.1)	24 (33.8)	
Perinatal asphyxia	Yes	2 (2.7)	14 (19.2)	10 (13.7)	19 (26.0)	28 (38.4)	0.301
	No	11 (8.3)	18 (13.5)	20 (15.0)	25 (18.8)	59 (44.4)	
History of epilepsy	Yes	2 (3.2)	12 (19.4)	7 (11.3)	11 (17.7)	30 (48.4)	0.385
	No	11 (7.6)	20 (13.9)	23 (16.0)	33 (22.9)	57 (39.6)	
Diagnosis	Cerebral Palsy	11 (8.4)	24 (18.3)	16 (12.2)	29 (22.1)	51 (38.9)	0.277
	Central Hypotonia	1 (3.6)	4 (14.3)	8 (28.6)	6 (21.4)	9 (32.1)	
	Neural Tube Defect	1 (6.7)	1 (6.7)	1 (6.7)	2 (13.3)	10 (66.7)	
	MD And SMA	0 (0.0)	0 (0.0)	0 (0.0)	3 (42.9)	4 (57.1)	
	Metabolic Disease	0 (0.0)	3 (12.0)	5 (20.0)	4 (16.0)	13 (52.0)	
CP classification	Diplegic	6 (14.0)	6 (14.0)	7 (16.3)	13 (30.2)	11 (25.6)	**<0.001**
	Hemiplegic	5 (18.5)	13 (48.1)	4 (14.8)	5 (18.5)	0 (0.0)	
	Tetraplegic	0 (0.0)	1 (2.3)	2 (4.5)	10 (22.7)	31 (70.5)	
	Mixed Type	0 (0.0)	4 (23.5)	3 (17.6)	1 (5.9)	9 (52.9)	

* Chi-square analysis was applied. CP: Cerebral Palsy, MD: Muscular Dystrophy, SMA: Spinal Muscular Atrophy N: Number

There was a significant difference between gross motor classifications in terms of age (p=0.019). This difference was due to the difference among type 1 and type 2 and type 3 and among type 1 and type 2 and type 4. There was no significant difference between the gross motor classes in terms of other measurement parameters (p>0.05) (Table 3). 60.7% of the patients with consanguineous parents had a diagnosis of CP, while 69.7% of the patients without consanguineous parents had a diagnosis of CP. In both groups, the most common diagnosis was CP, and the distribution of disease diagnoses was similar. No statistically significant relationship was found between consanguineous marriage and the diagnosis of the disease (Table 4).

Table 3. Comparison of measurement parameters of gross motor classification.

	1	2	3	4	5	p*
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Age	7.4±5.2[a]	6.0±4.5[a]	3.8±4.1[b]	4.1±4.4[b.c]	5.0±4.6[a.b.c]	**0.019**
Father Age at Birth	33.2±6.9	31.0±9.3	31.7±7.0	31.0±6.8	32.2±7.4	0.575
Mother Age at Birth	31.7±7.6	25.8±6.8	27.6±8.3	26.0±5.7	27.0±5.7	0.118
Birth Order	3.8±2.5	3.7±2.6	3.9±2.3	3.6±2.3	3.9±2.2	0.891
Birth Week	37.2±3.7	36.7±4.7	36.0±3.9	36.2±4.4	37.1±3.7	0.545
Days of spent in incubator	22.8±32.8	12.9±20.2	25.0±33.3	30.3±38.7	31.0±40.8	0.095
Birth weight (grams)	2420.4±929.2	2416.3±876.4	2495.3±776.5	2832.5±3078.0	2508.7±808.7	0.959

Kruskal Wallis analyses was applied. a,b,c: Group where the difference originated. SD: Standard deviation

Table 4. Comparison of diagnosis frequency based on consanguineous marriage.

	Yes	No	p*
	N (%)	N (%)	
Cerebral palsy	85 (60.7)	46 (69.7)	0.400
Central hypotonia	20 (14.3)	8 (12.1)	
Neural tube defect	11 (7.9)	4 (6.1)	
MD and SMA	7 (5.0)	0 (0)	
Metabolic disease	17 (12.1)	8 (12.1)	

* Chi-square analysis was applied. MD: Muscular Dystrophy, SMA: Spinal Muscular Atrophy N: Number

DISCUSSION

Neuromotor development is a process that starts from the intrauterine period and continues until adulthood. Many risk factors that cause this process to stop may cause neuromotor developmental delay (Çelik, 2021). After neuromotor developmental retardation occurs, the effort and cost for treatment is very high. For this reason, protective-preventive approaches are of great importance in terms of preventing neuromotor developmental retardation. In order to be successful in this area, it is necessary to know the factors that prepare neuromotor developmental delay and how they can be controlled (Kleigman, Stanton, Geme, Schor & Behrman, 2015). In this study, we examined the patients with neuromotor developmental delay and examined the frequency of consanguineous marriage, the relationship between consanguineous marriage and gross motor level, and whether some factors have an effect on the level of gross motor function.

Consanguineous marriage was present in 68% of the parents of the patients included in our study. In another study, consanguineous marriages were also found at a high rate in the Arab society, which shares a culture similar to ours (Mushta et al., 2022). In addition, consanguineous marriages are common in Turkish culture and the frequency of genetic diseases is higher than in other societies.

There was no statistically significant relationship between the diagnoses of our cases included in the study and consanguineous marriage.

Prolongation of labor and decreased Apgar score are seen as risk factors for neuromotor developmental retardation (Aslan, Çalkavur, 2022). In our study, 56.8% of the patients had a history of caesarean section and 43.2% of them had a vaginal delivery, and no significant relationship was found between delivery type and gross motor function level. In addition, no significant relationship was found between the birth type of consanguineous marriage and the gross motor classification system.

In many studies, it is known that the mother's smoking or systemic disease is a risk factor for neuromotor developmental delay (Asif et al., 2022; Kahn, Talat &Malik, 2022). In our study, 11.2% of the mothers had a history of smoking during

pregnancy and 16% had a history of additional disease. Although no significant relationship was found in our study, a study conducted in Türkiye demonstrated that consanguinity, maternal anaemia during pregnancy, and maternal occupational status were associated with the age at which children began to walk independently in healthy children (Yalçın, Yurdakök, Tezel & Özbaş, 2012). This situation highlights the importance of maternal factors, which were also investigated in our study.

In studies, asphyxia, incubator and epilepsy history are known to be risk factors for neuromotor developmental delay (Asif et al., 2022; Aslan, Çalkavur, 2022; Kahn et al., 2022). In our study, 65.5% of the children had a history of incubator, 35.4% had a history of perinatal asphyxia and 30.1% had a history of epilepsy, which was consistent with the literature. There was no statistically significant relationship between neuromotor developmental retardation stage and these risk factors. In a study conducted in Türkiye on children with CP, no significant relationship was found between consanguinity and the presence of epilepsy in CP patients. However, it was shown that the gross motor classification was more impaired in the group of patients with epileptic cerebral palsy (Karatoprak, Sözen & Saltık, 2019). It was shown that prematurity and low birth weight are risk factors for developmental delay (Kerimoglu et al., 2004) In our study, no significant relationship was found between low birth weight and prematurity and neuromotor developmental delay stage. Gross motor retardation is more common in those with a history of asphyxia and low birth weight (Diabelkova et al., 2022). Our study was not compatible with the literature and no relationship was found between the level of gross motor retardation and these risk factors. It may be due to the presence of neuromotor retardation and multiple risk factors in all the patients included in this study.

In our study, a significant relationship was found between gross motor classification level and CP classification, which is compatible with the literature. It was expected that the gross motor level of diplegic and hemiplegic CPs was better than tetraplegic and mixed type CPs. Again, no relationship was found between CP and consanguineous marriage. While diplegic CP is seen more frequently in the normal literature, the rate of tetraplegic CP is higher in countries where consanguineous marriages are common, such as our country. In our study, the rate of tetraplegic CP was 33.6%, which was consistent with studies conducted in Pakistan and Arabia (Kahn et al., 2022; Keramat et al., 2022; Mushta et al., 2022).

In a study comparing Israeli and Arab children with CP, it was found that the prevalence of wheelchair-dependent children at GMFCS levels 4 and 5 was higher in the Arab population, and one of the possible reasons for this could be the higher rate of consanguinity within the Arab community. This finding appears to be consistent with our clinical observations (Blumenfeld, Ben-Pazi, Ornoy, Josef & Shohat, 2020).

History of prematurity and asphyxia is common in multiple pregnancies. This may cause neuromotor developmental delay and low gross motor classification system level in one and/or both twins. There are studies reporting a relationship between multiple pregnancy and neuromotor developmental delay (Chen et al., 2023; Christensen, Chau, Synnes, Grunau &Miller, 2021). In our study, no significant relationship was found between multiple pregnancy and neuromotor developmental delay stage.

Although in our clinical observations, we have noticed that children with consanguineous parents have more severe gross motor impairments, several factors may explain why this was not statistically significant in the study. These factors include the small sample size, the study being conducted at a single centre, and covering a limited time. Other possible contributing factors include maternal self-care and nutritional status during pregnancy, the child's nutritional status, whether the child received breast milk, and individual circumstances such as socio-economic conditions.

Limitation of the study

The retrospective nature of the study, its cross-sectional design, being conducted at a single centre, the small sample size, the measurement of gross motor level through instant examination rather than monitoring the limited number of similar studies in the literature, and the short duration of the study are among the limitations.

CONCLUSION

More research is needed on the epidemiology of children and adolescents with neuromotor developmental delay. In recent years, the number of individuals with neuromotor developmental delay has increased significantly. These registries provide a platform for epidemiological research, a sampling framework for clinical research, and can also provide information on healthcare planning and delivery.

Acknowledgement

We would like to thank Assoc. Prof. Dr. Muhammed Seyithanoğlu for his support in the statistical analysis of the study.

Conflict of Interest

The authors declare no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

Author Contributions

Plan, design: BKA; **Material, methods and data collection:** BKA, MT; **Data analysis and comments:** BKA, MT; **Writing and corrections:** BKA, MT.

Funding
None

Ethical Approval
Institution: Harran University Ethics Committee
Date: 28.11.2022
Approval no: HRU/22.23.03

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