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Research Article

PHYSICAL CAPACITY OF SPINA BIFIDA AND FACTORS AFFECTING DURING PREGNANCY: A CASE CONTROL STUDY

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***Abstract**: It was aimed to evaluate the physical characteristics of the cases with spina bifida and to review the factors that may affect the etiology of the disease. 48 cases with spina bifida and 48 control groups in other disease groups evaluated. A physiotherapist physically evaluated the cases after their personal information was obtained. A survey form examining the possible factors in the etiology of spina bifida was applied to the families. It was found in the physical examination of the cases that 45.8% had hydrocephalus, and 41.7% had movement restriction due to muscle weakness. When the two groups were compared, lower level of maternal literacy, residence in a rural area, undergoing an infectious disease during pregnancy, drug utilization during pregnancy, and not utilizing folic acids during pregnancy were significantly higher than the control group ($p< 0.05$). Spina bifida was increased by place of residence of family (OR: 2.8, CI: 1.11-7.08), infectious disease during pregnancy (OR: 5.0, CI: 1.05-24.05), and not using folic acid during pregnancy (OR: 3.8, CI: 1.04-13.76). Spina bifida was more common in females and caused extensive leg limitations. It was observed that education, place of residence and conditions experienced during pregnancy had an impact on the disease.*

***Keywords:** Folic Acid, Motor Activity, Joint Range of Motion, Pregnancy Complications, Public Health*

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1. Introduction

Spina bifida is a disease that causes common and treatable neuromuscular dysfunction due to congenital malformation of neural tube development. It is a defect that occurs as a result of incomplete closure of the vertebra and neural tube between the 21st and 28th days of the embryonic period of the central nervous system [1].

The types and severity of the disease may vary depending on the affected parts of the body. Spina bifida occulta (defect in the vertebral arch but no herniation), meningocele (protrusion of the dura and arachnoid without containing neural elements), and myelomeningocele (herniation of the spinal nerves from the large posterior defect in the dura) are the most common types of disease [2].

Spina bifida is more common in females than in males. Its incidence throughout the world is between 0.3-10 per 1000 live births. It is determined as 0.3/1000 in Japan, 1/1000 in Europe, and 2-4/1000 in the United States. Its incidence in Turkey is defined as 3 per 1000 live births [3].

Problems such as low back pain, paraplegia, hydrocephalus, and dysfunctions in bladder and intestines occur in spina bifida depending on the level of neurological damage. The most common clinical findings accompanying the disease are lower extremity muscular strength loss, hip instability, knee contractures, foot-ankle deformities and the development of scoliosis over time [4].

Many factors play a role in the development of the disease, although their direct causes are not known. These factors are associated with high fever during pregnancy, hypertension, diabetes mellitus, malnutrition, some medications, obesity, environmental pollutants, past disease history, mother's age less than 20 and higher than 35, failure to receive prenatal care, low socioeconomic level and the folic acid deficiency [5].

The World Health Organization recommends regular prenatal care and utilization of 400 mcg folic acid supplements per day during pregnancy to prevent health problems such as spina bifida [6]. Diagnosed children are referred to a specialist healthcare team for their follow-up and treatment to be planned. Physiotherapy programs are applied to help independent movement, prevent deformity and strengthen leg muscles [7].

This study aims to identify cases of spina bifida and determine their current functionality levels and the factors that may affect the disease.

2. Materials and Methods

2.1. Type of Study

This study is a case-control type of clinical research.

2.2. Population and Sample of Study

The study was carried out with the participation of 48 cases with spina bifida between the ages of 0 and 2 evaluated in Diyarbakır Gazi Yaşargil Training and Research Hospital Pediatric Clinics and 48 control groups in other disease groups in response to each case.

The case group consisted of patients who were diagnosed in the Neonatal Intensive Care Unit between February 2019 and January 2020 (39 children) (n=39/Diyarbakır Gazi Yaşargil Training and Research Hospital number of live births per year = 21317), and who applied to the Physiotherapy and Rehabilitation Department from the centers outside for physiotherapy needs (9 children). The control group was formed through random selection among the children in the same age group between the same dates, did not have any diseases related to the neuromuscular system, and were hospitalized for any other reason (Child Diseases Service 1, Service 2).

2.3. Data Collection Tools and Implementation of the Study

Personal information (age, gender, etc.) of the children involved in the study was recorded. Spina bifida data were obtained from patient records and the diagnosing pediatrician and neurosurgeon. A physiotherapist evaluated the children in the case group through physical examination. During the physical examination, the physiotherapist assessed the patients' motor development levels, normal joint range of motion, muscle tone, muscle atrophy, and muscle strength tests. The own statement of individuals completed the Survey Form issued by the researchers by scanning the relevant literature by talking face-to-face with the mothers of the children in both groups voluntarily. Questions about parental information (age, gender, occupation, marital status, education, consanguineous marriage) and factors that may cause spina bifida disease were asked in this survey form.

2.4. Ethical Aspects of the Study

Approval of the Ethical Research Board of Dicle University Faculty of Medicine was obtained to conduct the study (Date: 25.01.2018, No: 30). Permission was obtained from the Chief Physician Office of Diyarbakır Gazi Yaşargil Training and Research Hospital to conduct the study. The mothers of each child were informed about the study and signed a written informed consent form indicating that they agreed to participate.

2.5. Evaluation of Data

The survey data were recorded in a computer environment and evaluated with the SPSS 21.0 package program during statistical analysis. The numbers and percentages were given together in the tables. Chi-Square test and logistic regression analysis were used during statistical analyses. Odds ratio (OR) and confidence interval (CI) values are given in logistic regression analysis. $p< 0.05$ was accepted as the significance level.

3. Results

66.7% (n=32) of the cases were female, and 45.8% (n=22) were between 0-6 months. It was observed that 52.1% (n=25) of the cases in the control group were male and 60.4% (n=29) were between 0-6 months. When they were considered individually, it was observed that the gender, age, ages of mothers, and occupation status of fathers in the case and control groups were similar ($p> 0.05$) (Table 1).

Besides, it was determined that all mothers in both groups were housewives, 50.0% of them were illiterate, and 35.4% of the families resided in rural areas.

Table 1. Demographic characteristics of the cases and control groups

	Spina Bifida		Control Group		Total		Significance[a]
	n	%	n	%	n	%	p
Gender							
Male	16	33.3	25	52.1	41	42.7	>0.05
Female	32	66.7	23	47.9	55	57.3	
Age							
Smaller than 6 months	22	45.8	29	60.4	51	53.1	>0.05
6-12 months old	17	35.4	5	10.4	22	22.9	
12-24 months old	9	18.8	14	29.2	23	24.0	
Mother's Age Group							
Age of 18 and below	2	4.2	1	2.1	3	3.1	>0.05
Age of 19-34	31	64.6	39	81.3	70	72.9	
Age of 35 and above	15	31.3	8	16.7	23	24.0	
Father's Occupation							
Worker	24	50.0	19	39.6	43	44.8	>0.05
Craftsman/Farmer	9	18.8	8	16.7	17	17.7	
Officer	2	27.1	8	16.7	10	10.4	
Unemployed	13	4.2	13	27.1	26	27.1	

[a] :Fischer exact chi-square test

The presence of spina bifida, which was diagnosed due to the births in the hospital, was found to be 1.8% (n=39/Diyarbakır Gazi Yaşargil Training and Research Hospital number of live births per year = 21317) (Figure 1).12.8% of these patients were in the meningocele (n=5) and 87.2% were in the myelomeningocele (n=34) type spina bifida group.

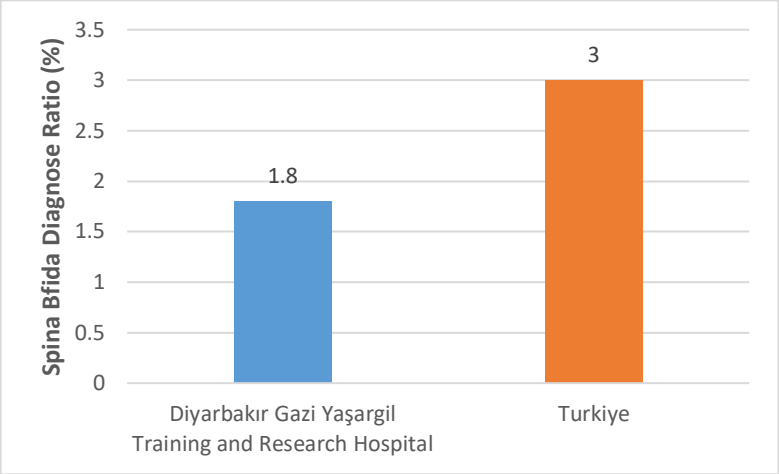

Figure 1. Incidence distribution of spina bifida in the study in Turkey

When the cases with spina bifida were evaluated in terms of physical examination, it was found that 45.8% (n=22) had hydrocephalus, 52.1% had high levels of lesions and 41.7% (n=20) had movement restriction due to muscular weakness. It was observed that the upper extremity joint range of motion was in average range values in 87.5% (n=42) of them. While the lower extremity range of motion was in the normal range in 54.2% (n=26) of them, it was found that the restrictions were mostly in the form of limitation in the whole leg (involvement of hip, knee, and feet together) with 20.8% (n=10) (Table 2).

Table 2. Physical Examination Evaluations of Children with Spina Bifida

	n	**%**
Level of Lesions		
High (L1 and higher)	25	52.1
Mid (L2-5)	19	39.6
Low (S1 and lower)	4	8.3
Hydrocephalus		
Yes	22	45.8
No	26	54.2
Muscular Strength		
Complete	28	58.3
Restricted	20	41.7
Upper Extremity Joint Range of Motion		
Normal Range	42	87.5
Restricted	6	12.5
Lower Extremity Joint Range of Motion		
Open	26	54.2
Limitation in the whole leg[b]	10	20.8
Knee flexion contracture, hip flexion-abductor contracture	7	14.6
Gastrocnemius contracture	3	6.2
Foot deformities (pes plano valgus)	2	4.2

[b] Group with knee flexion contracture, hip flexion-abductor contracture and foot-ankle deformities

Low level of mothers' literacy (64.6%), residency in rural areas (79.2%), high fever/infectious disease during pregnancy (37.5%), drug utilization during pregnancy (27.1%) and not using folic acid during pregnancy (83.3%) was significantly higher in the case group than the control group (Table 3).

No relationship was determined between spina bifida and the consanguineous status of the parents, the presence of siblings with spina bifida, the mother's age, receiving prenatal care, exposure to radiation during pregnancy, and cigarette/alcohol/drug use during pregnancy (p>0.05).

Table 3. Some Factors That May Affect the Etiology of Spina Bifida Disease

	Spina Bifida		**Control Group**		**Significance[a] p**
	n	**%**	**n**	**%**	
Education Level of Mother					
Illiterate	31	64.6	17	35.4	**0.019***
Literate	9	18.8	11	22.9	
Primary-secondary school	7	14.6	16	33.3	
High school	1	2.1	4	8.3	
Place of Residence of Family					
City	10	20.8	22	45.8	**0.009****
Rural area	38	79.2	26	54.2	
Affinity Status of Mother and Father					
No	28	58.3	22	45.8	>0.05
Yes	20	41.7	26	54.2	
Prenatal Care					
Yes	37	77.1	41	85.4	>0.05
No	11	22.9	7	14.6	
Infectious Disease During Pregnancy					
Yes	18	37.5	3	6.2	**0.001****
No	30	62.5	45	93.8	
Drug Utilization During Pregnancy					
Yes	13	27.1	1	2.1	**0.002****
No	35	72.9	47	97.9	
Status of Using Folic Acid During Pregnancy					
Yes	8	16.7	19	39.6	**0.013***
No	40	83.3	29	60.4	
Smoking During Pregnancy					
Yes	8	16.7	6	12.5	>0.05
No	40	83.3	42	87.5	

[a]:Fischer exact chi-square test;*p<0.05; **p<0.01

Spina bifida was increased by place of residence of family (OR: 2.8, C: 1.11-7.08), infectious disease during pregnancy (OR: 5.0, CI: 1.05-24.05), and not using folic acid during pregnancy (OR: 3.8, CI: 1.04-13.76) (Table 4).

Table 4. Factors associated with Spina Bifida

					95% CI	
	B	**S.E.**	**p**	**OR**	**Lower**	**Upper**
Mother's Age	0.023	0.056	0.673	1.024	0.918	1.142
Place of Residence of Family	1.033	0.471	**0.028***	2.811	1.116	7.081
Education Level of Mother	-1.520	1.708	0.373	0.219	0.008	6.220
Infectious Disease During Pregnancy	1.616	0.798	**0.043***	5.034	1.053	24.058
Drug Utilization During Pregnancy	2.347	1.241	0.059	10.457	0.918	119.167
Using Folic Acid During Pregnancy	1.335	0.657	**0.042***	3.801	1.049	13.766

S.E.: Standard Error; OR: Odds ratio; CI: Confidence interval; Logistic regression analysis; *:p< 0.05

4. Discussion

Preventive health services, which are the basis of public health, are the primary, secondary and tertiary prevention methods that can be applied to prevent the development of Neural Tube Defect (NTD) and the unwanted complications that may develop due to it. The most important, safe and effective method in primary prevention is maternal folic acid supplementation. In addition, screening, early diagnosis and treatment have an important place in secondary prevention. It is known that folate has a direct role in the closure of the neural tube [8, 9]. It is essential for the course of the disease to detect the cases with spina bifida in the early period, to minimize the neurological damages that may occur, and to identify the factors that may affect the disease.

It was found that 66.7% of the cases with spina bifida in the study were females. Saygi et al. found in the study they conducted in Turkey that the rate of females with spina bifida was 51.2% [10]. In a survey conducted in Northern Ireland, the rate of females (68%) was higher [11]. In the study, it was observed that the presence of spina bifida was more in females than in males in line with the literature.

The incidence of spina bifida was found to be 01.8% in the study. In a survey conducted in Afyon, it was reported that spina bifida/ meningocele/ meningomyelocele types were found at the rate of 2%o [12]. Its incidence in Turkey was reported to be 3/1000 [3]. While it is 6.1/1000 in Ethiopia, it varies between 1 and 3 per 1000 births throughout Africa [13]. It was found to be 2.92/10000 in a study conducted in Germany [14]. The incidence of spina bifida varies by regions and countries. The fact that the rate in the study is lower than the average in Turkey may be because the study was limited to only the births in the hospitals and the cases that reach the hospital.

It was found in the physical examination of the cases that 45.8% of them had hydrocephalus. Singh et al. reported that hydrocephalus is the most common lesion observed in patients with spina bifida [15]. Since the presence of hydrocephalus may affect the functionality of children in the subsequent stages of the disease, treatment in the early period is required.

It was determined that the upper extremity range of motion is restricted in 12.5% of the cases. Kumari and Singh reported in their study that congenital malformations affecting the upper extremity were 14% [16]. Windman et al. found that shoulder and upper arm muscular strength was lower in patients with spina bifida compared to the healthy control group [17]. Evaluation of the upper extremity is a criterion that should not be missed during physical examination. In the study, it was observed that the lower extremity range of motion was in the form of restriction in the whole leg, knee-hip involvement, and foot-ankle deformities. It was reported in the studies that the most common lower extremity problems accompanying the disease were hip instabilities, knee contractures, and foot-ankle deformities [4, 18]. All joint range of motion restrictions evaluated in the lower extremities will affect the mobility and walking levels of children in the future. Involving the children in physiotherapy and rehabilitation programs in the Neonatal Unit in the early stage may increase their functionality.

When both groups were compared, it was found that 64.6% of the mothers of the cases in the case group were illiterate. De Marco et al. reported in their study that the incidence of spina bifida decreases as the level of maternal education increases [19]. Ong et al. stated that a low maternal education level poses a high risk for spina bifida [20]. A low level of education may cause a low level of knowledge about the disease and insufficient use of healthcare services.

The fact that 79.2% of the families with children with spina bifida reside in rural areas was found to be closely related to the disease in the study. The prevalence of spina bifida is much higher, especially in rural areas of northern China than in urban areas [21]. In a survey conducted in Congo, it was reported that the farawayness of healthcare centers in rural areas is the most critical obstacle to

care [22]. This may be in association with the geographical location, environmental exposure, diet, and problems in accessing healthcare services. The difficulty in accessing rural areas causes the primary health care services, where public health services are carried out, not to be provided and these services not to be inspected regularly. The Ministry of Health should be able to provide primary health care services equally to all parts of the country.

It was found that 37.5% of the mothers in the case group had an infectious disease due to high fever or other reasons during pregnancy. During pregnancy, fever not only affects the mother, but it can also lead to fatal involvement, affect the outcome of the pregnancy, and increase morbidity and mortality. Although the mechanism by which the fever can affect the development of the neural tube is unknown, there is an increased correlation between maternal peripheral fever and neural tube defects [23, 24]. Screening, early diagnosis, and treatment have an important place in secondary prevention. Access to healthcare services and regular pregnancy follow-ups will ensure timely combat of such infectious diseases.

The utilization of various medications (analgesics, antihypertensives, antibiotics, etc.) during pregnancy was found to be higher (27.1% of the cases) than in the control group. Othman et al. reported that 26.3% of the mothers used medications (analgesics and herbal medicines) during pregnancy [25]. Kondo et al. reported in their study demonstrating the utilization of antiepileptic drugs without folic acid supplements that affected pregnancies resulted in 20.2 times higher risk [26]. The prevalence of congenital malformations should be reduced by preventing the unconscious utilization of medications by pregnant women and recommending the use of medicines, the efficacy of which was proven, as low as possible.

Not using folic acid during pregnancy was significantly higher than the control group with 83.3% of the mothers in the case group. They pointed out in their studies that Neural Tube Defects with increased mortality and morbidity risk such as spina bifida and anencephaly occur as a result of folic acid deficiency during the intrauterine development process [27, 28]. It is known that it is an important approach for women who may conceive to improve public health to eat foods fortified with folic acid or foods rich in folate to reduce the risk of birth defects [8, 29]. In Canada, compulsory fortification of selected foods with folic acid has been shown to reduce the incidence of neural tube defects by 46% [30]. There is no food fortification with folic acid in many countries, like Turkey. The Ministry of Health's proposals for food fortification with folic acid have been officially submitted to the Ministry of Agriculture and Forestry, and no regulation has been made on this issue yet [31]. Ministries need to start food fortification processes as soon as possible and offer this to the public at a low cost. Vitamin supplements are needed to achieve the recommended daily dose of Folic acid. The World Health Organization recommends folic acid supplements and folic acid-rich food consumption of 400 mcg per day or 2800 mcg per week during pregnancy to prevent such health problems [6]. Health authorities in Turkey can encourage the use of folic acid by providing free folic acid distribution support to pregnant women within the scope of primary health care services. In addition, it was determined half of the women (53.7%) did not hear or read about folic acid, and less educated women were more unaware of folic acid in the "Awareness and use of folic acid among reproductive age and pregnant women" study conducted in Turkey [32]. In our study, the insufficient use of folic acid in women in both groups may be related to this issue. Therefore, we think that the use of folic acid before pregnancy can be increased by increasing health literacy and more frequently informing expectant mothers before they become pregnant.

No relationship was found between the spina bifida and the consanguineous status of the parents and the mother's use of cigarettes/alcohol/drugs during pregnancy. It was also reported that consanguineous marriage is a risk factor for the incidence of spina bifida [15]. In a study performed in Turkey, it was stated that no correlation was found between consanguineous marriage and spina bifida

[33]. The result of the study complies with the results of the study in Turkey. In the study, while none of the mothers used alcohol and drugs during pregnancy, 16.7% of the case group used cigarettes. It was observed that there is no correlation between smoking and alcohol intake levels in terms of the risks of spina bifida [34, 35].

5. Conclusion

Spina bifida was more common in females and caused hydrocephalus and extensive leg limitations. It was observed that the education level of the mother, place of residence, undergoing infectious diseases during pregnancy, utilization of medications during pregnancy and not using folic acid during pregnancy are effective on spina bifida.

It is very clear that expectant mothers are regularly informed, and called for doctor's control, health literacy will be increased, the use of folic acid before and after pregnancy will be increased, and the disease incidence will decrease compared to the previous ones. In addition, the complications, morbidity, and mortality that may develop with these children by timely and appropriate interventions and their inclusion in physiotherapy and rehabilitation programs starting from the earliest period will significantly decrease.

Ethical statement:

Approval of the Ethical Research Board of Dicle University Faculty of Medicine was obtained to conduct the study (Date: 25.01.2018, No: 30).

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Authors' contributions:

S.E.: Conceptualization, data collection and translation. M.Ar.: Design of the study, statistical analysis, and writing of the study. M.As.: Resources and validation. G.S.: Validation and writing-review & editing.

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