

Retrospective Investigation of the Incidence of Patients with Neural Tube Defects During the Pandemic Period, Single Center Study

Pandemi Döneminde Nöral Tüp Defektli Hastaların İnsidansının Retrospektif İncelenmesi, Tek Merkezli Çalışma

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Özet

Amaç: Bu çalışmadaki amaç, Covid 19 döneminde alınan tedbirler sonucunda; açık alanlara çıkma yasağına bağlı immobilizasyon, maske kullanılmasına bağlı karbondioksit retansiyonu, uygun gebelik kontrollerinin zamanında yapılamaması ve hastalık döneminde gebeler üzerindeki strese bağlı faktörlerin hem Türk toplumunda hem de mültecilerde nöral tüp defekti insidansında bir artış yapıp yapmadığının araştırılmasıdır. Çalışmamız bu alanda yapılan ilk epidemiyolojik çalışmadır.

Gereç ve Yöntemler: Çalışmadaki veriler tek merkezli Şanlıurfa Eğitim Araştırma Hastanesi arşivinden elde edilmiştir. Bu çalışmada 01.01.2018-31.12.2019 tarihleri ile 01.01.2020-31.12.2021 tarihleri arası hastane arşivinde yer alan canlı doğumlar ve nöral tüp defekti nedeniyle opere edilen hastalar incelenmiştir.

Bulgular: Türk toplumunda 2018, 2019, 2020 ve 2021 yıllarında nöral tüp defekti insidansı sırası ile %0.077, %0.186, %0.298 ve %0.436 olarak bulunmuştur. Bu yıllar arasında istatistiksel açıdan anlamlı farklılık görülmüştür ($p<0.001$) (2018 ile diğer yıllar). Suriye kökenli mültecilerde 2018, 2019, 2020 ve 2021 yıllarında nöral tüp defekti insidansı sırası ile %0.148, %0.145, %0.483 ve %0.603 olarak bulunmuştur. Suriye kökenli mültecilerde belirtilen yıllar arasında istatistiksel açıdan anlamlı farklılık görülmüştür ($p<0.001$) (2019 ile 2020 ve 2019 ile 2021). 2020 senesinde Suriye kökenli mültecilerde nöral tüp defekti insidansı (%0.483) Türk toplumundaki nöral tüp defekti insidansından (%0.298) anlamlı şekilde yüksek bulunmuştur ($p=0.039$).

Sonuçlar: Pandeminin getirdiği kısıtlamalara bağlı nöral tüp defektinde artış meydana geldiğini saptadık. Cinsiyetler arası insidans artışı benzer idi. Hem Türklere hem de Suriyelilerde, 2020 yılı haricindeki yıllarda insidans oranları benzer idi.

Anahtar kelimeler: Nöral tüp defekti, Covid 19, Pandemi

Abstract

Objective: Our aim in this study is as a result of the measures taken during the Covid 19 epidemic period; investigate whether factors related to immobilization due to the ban on going outdoors, carbon dioxide retention due to the use of masks, inability to perform appropriate pregnancy visits on time and stress-related factors on pregnant women during the disease period increase the incidence of neural tube defects in both Turkish society and Syrian refugees living in Turkey.

Materials and Methods: The data in the study were obtained from the archive of the single-center Şanlıurfa Research and Training Hospital. In this study, live births in the hospital archive between 01.01.2018-31.12.2019 and 01.01.2020-31.12.2021 and patients who were operated for neural tube defects were examined.

Results: In the Turkish population, the incidence of neural tube defects in 2018, 2019, 2020 and 2021 was found to be 0.077%, 0.186%, 0.298% and 0.436%, respectively. There was a statistically significant difference between these years ($p<0.001$) (2018 and other years). The incidence of neural tube defects in refugees of Syrian origin in 2018, 2019, 2020 and 2021 was found to be 0.148%, 0.145%, 0.483% and 0.603%, respectively. There was a statistically significant difference between the years specified in refugees of Syrian origin ($p<0.001$) (2019 vs 2020 and 2019 vs. 2021). In 2020, the incidence of neural tube defects in refugees of Syrian origin (0.483%) was found to be significantly higher than the incidence of neural tube defects in the Turkish population (0.298%) ($p=0.039$).

Conclusion: We detected an increase in neural tube defects due to the restrictions brought by the pandemic. The incidence increase between the sexes was similar. Incidence rates were similar in both Turks and Syrians in the years except 2020.

Keywords: Neural tube defekt, Covid 19, Pandemic

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INTRODUCTION

Neural tube defect (NTD) is the most common congenital malformation of the brain and spinal cord. In the first weeks of pregnancy the neural tube closes. If the closure is delayed due to the organizational disorder between the neural, bone and mesenchymal tissue and the skin, a neural tube defect occurs. Among these anomalies, spina bifida occulta is the most common but spina bifida cystica, encephalocele, anencephaly, dermal sinus, tethered cord syndrome, syringomyelia, diastematomyelia and lipoma may occur. Anencephaly and encephalocele are incompatible with life and are lost in the intrauterine and early neonatal period. With the improvements of pediatric neurosurgery and intensive care developments, patients with neural tube defects are increasing. Among the causes of childhood disability, this is the one of the most common disease after cerebral palsy. It is also the most common congenital anomaly after congenital cardiac defects (1,2).

NTD has no definite etiological factor. In general, the opinion that it occurs due to the influence of environmental factors is common in those with genetic predisposition. It has been shown that maternal folate deficiency increases NTD, and incidence of NTD are significantly reduced with increasing folate level. However, the elimination of folic acid deficiency did not completely eliminate NTD and suggested that there may be other factors. In many studies, parental education, socioeconomic status, gestational age, maternal drug history, diabetes, obesity, hyperthermia and infection history during early pregnancy have been investigated and NTD has been found to be associated with these (2,3).

Its incidence may vary depending on geographical variation, genetic and environmental factors. Although the incidence is high in those with genetic predisposition, it is usually 0.1-0.2%. Similar results were found in incidence studies conducted in our country (1).

Due to the high contagiousness and mortality of Covid 19 infection spreading rapidly around the world, the health system had to focus on the patients affected by this disease (4). In order to prevent the spread of the disease, widespread precautions have been taken by the governments, and curfew, compulsory use of masks and staying at home for the risk groups are some of them. In addition, the anxiety of getting infected by Covid 19 has created a high stress level on people.

Our aim in this study is as a result of the measures taken during the Covid 19 epidemic period; investigate whether factors related to immobilization due to the ban on going outdoors, carbon dioxide retention due to the use of masks, inability to perform appropriate pregnancy visits on time and stress-related factors on

pregnant women during the disease period increase the incidence of neural tube defects in both Turkish society and Syrian refugees living in Turkey.

MATERIALS AND METHODS

The data used in our study are single-centered and were obtained in the archive of our hospital. After receiving the ethics committee approval for our study, the number of live births, patients diagnosed and operated due to spina bifida between 01.01.2018-31.12.2019 and 01.01.2020-31.12.2021, were examined. Only live births were screened in our study; stillbirths and abortions were not included. The reflection of the Covid 19 pandemic on neural tube defects was statistically examined.

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 are shown with n and % values in categorical data. Chi-square analysis (Pearson Chi-square) was used to compare categorical variables between groups. As a result of the chi-square analysis, Bonferroni correction was made to determine where the significance originates from. The statistical significance value in the analyzes was accepted as $p < 0.05$.

RESULTS

The study was conducted by evaluating the incidence of children who were born with neural tube defect of Turkish and Syrian refugees born between 2018-2021.

The incidence of NTD in Turkish was 0.077% in 2018, 0.186% in 2019, 0.298% in 2020 and 0.436% in 2021. There was a statistically significant difference among years in the Turkish ($p < 0.001$). The statistically important difference is among 2018 and all the other following years and between 2019 and 2021.

The incidence of NTD in Syrian refugees was 0.148% in 2018, 0.145% in 2019, 0.483% in 2020 and 0.603% in 2021. There was a statistically significant difference between years in the Syrian refugees ($p < 0.001$). The statistically important difference exists between the 2019 and 2020, within 2019 and 2021 (**Table 1**).

In 2020, the NTD rate in Syrians (0.483%) was found to be significantly higher than the NTD rate in Turks (0.298%) ($p = 0.039$). There was no significant difference in the incidence of NTD between races in the other years ($p > 0.05$) (**Table 2, Figure 1**).

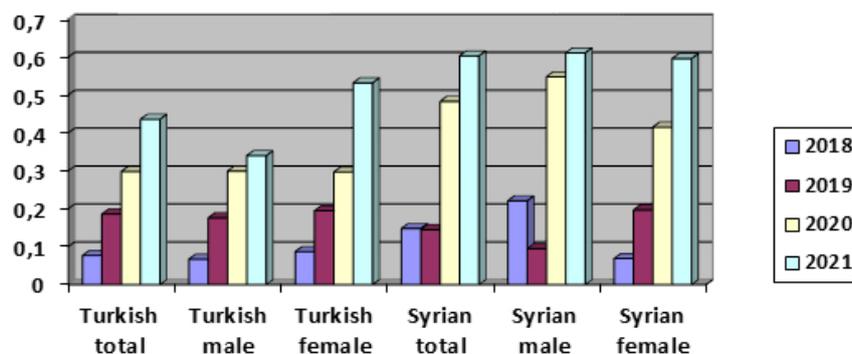
Table 1. NTD incidence by years

	2018	2019	2020	2021	P
	%	%	%	%	
Turkish Total	0.077 ^a	0.186 ^b	0.298 ^{b,c}	0.436 ^c	<0.001
Turkish Male	0.067 ^a	0.176 ^{a,b}	0.299 ^b	0.340 ^b	<0.001
Turkish Female	0.087 ^a	0.195 ^{a,b}	0.297 ^{b,c}	0.532 ^c	<0.001
Syrian Total	0.148 ^a	0.145 ^a	0.483 ^b	0.603 ^b	<0.001
Syrian Male	0.221 ^{a,b}	0.095 ^b	0.548 ^a	0.611 ^a	0.001
Syrian Female	0.069 ^a	0.197 ^{a,b}	0.415 ^b	0.596 ^b	0.002

Note: Same letters shows no significant difference among years, different letters shows significant difference among years.

Table2. Comparison of NTD incidence between races by year

		NTD	NO NTD	P
		Number (%)	Number (%)	
2018	Turkish	18 (0.077)	23402 (99.923)	0.102
	Syrian	9 (0.148)	6074 (99.852)	
2019	Turkish	42 (0.186)	22592 (99.814)	0.499
	Syrian	9 (0.145)	6202 (99.855)	
2020	Turkish	58 (0.298)	19400 (99.702)	0.039
	Syrian	26 (0.483)	5362 (99.517)	
2021	Turkish	92 (0.436)	21005 (99.564)	0.112
	Syrian	32 (0.603)	5273 (99.397)	

**Figure 1.** NTD incidence among years

DISCUSSION

Spinal dysraphism occurs as a result of failure of the spinal canal to close due to a congenital malformation of the neural tube. The central nervous system begins with the formation of the neural plate in the third week of pregnancy. Clefts are formed from the folds around the neural plate and merge into the midline. The neural tube, whose frontal part is swollen and caudal part is weak, thickens and closes, forming the first shape of the brain and spinal cord. Failure of the neural tube to close causes spinal dysraphisms. While spina bifida oc-

culta occurs only due to a bony closure defect, spina bifida aperta occurs due to the failure of the meningeal sheath, spine, subcutaneous muscle layer and neural tissue to be protected by the skin, and the cerebrospinal fluid to be closed with or without protection by a membrane after neurolation damage (1,2,5).

There is no single etiological factor responsible in the formation of neural tube defects, it develops as a result of a multifactorial etiology with the contribution of genetic and environmental factors. The most important proven cause of neural tube defect is maternal folic acid

deficiency. However, teratogenic drugs such as alcohol, valproic acid, carbamazepine, methotrexate, diuretics, antihistamines, sulfonamides and maternal fever history during pregnancy, malnutrition, low socio-economic status, gestational diabetes, infectious diseases and stress factors may also cause neural tube defects (6,7).

The incidence of spinal bifida in the world has been found to be between 0.5-2 per 1000 live births. In our study, the frequency of spina bifida in the absence of Covid 19 (2018-2019) was found to be similar in both Turkish race (0.077 -0.186) and Syrian refugee (0.148-0.145), while there was a very significant increase in the frequency of neural tube defects in both Turkish populations (0.298-0.436) and Syrian refugees (0.483-0.603) during the COVID-19 period (2020-2021). The increase in the incidence of spinal bifida was similar in both Turkish population and Syrian refugees.

The Covid 19 virus, spreading rapidly in China and causing serious mortality and morbidity has caused a significant disruption to the health system (8). Because of high spread rate and high lethality of the virus governments have taken some precautions such as a curfew, mandatory use of masks, and the risky group not leaving the house unless necessary. This situation created an important stress factor on pregnant women. The first Covid 19 case in our country was seen in March 2020 and measures similar to the above precautions were taken. In our study, in which we investigated the effectiveness of all these measures on the incidence of neural tube defects, we found that the incidence of neural tube defect was significantly affected in the last period of 2020 and in 2021 in both Turkish race and Syrian refugees. This increase in incidence may have been due to the single policies of the countries, the virus infection itself, or maternal stress factors. For whatever reason, the pandemic itself can be considered a risk factor for neural tube defect. Our study only investigated the incidence of neural tube defects, and an increase may have occurred in congenital malformations, cerebral palsy, miscarriages, cardiovascular or respiratory system diseases due to the pandemic. More research is needed on these issues.

Neural tube defect is the inability of the spinal canal to close due to malformations. There are many risk factors in its etiology and it is formed as a result of the interaction of genetic and environmental factors. We detected an increase in neural tube defects due to the handicaps brought by the pandemic in people with genetic predisposition. Governments should change their policies and take measures to prevent an increase in the incidence of diseases in future pandemics.

Ethics Committee Approval: Ethical approval for this study was obtained from the Harran University (HRU) Clinical Research Ethic Committee. We started work after the approval of the Ethics Committee (Date 18.04.2022, Decision number: HRU/ 22.08.15). Helsinki declaration principles were followed.

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Declaration of Competing Interest: None

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