

# Varicella Seroprevalence in Pediatric Populations: Results from a Single-Center Study

## Pediatric Popülasyonlarda Varisella Seroprevalansı: Tek Merkezli Bir Çalışmanın Sonuçları

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### ABSTRACT

**Objective:** Varicella is a highly contagious illness with potentially severe complications, especially in young children. In Turkey, the varicella vaccine was integrated into the Universal Varicella Vaccination program in 2013, targeting 12-month-old infants. While officially reported varicella cases have decreased considerably in the past two decades, underreporting remains a challenge. This study aimed to investigate varicella seropositivity in a tertiary center.

**Material and Methods:** A qualitative immunoassay, the enzyme-linked immunosorbent assay (ELISA), was employed to detect anti-varicella antibodies. Serum samples were collected from individuals aged 4 to 18 residing in Turkey. Information on vaccination records, varicella history, and disease notification was also collected.

**Results:** The varicella IgG antibody records were accessed for a total of 90 children. The overall prevalence of positive varicella antibodies was 58.0% (n=47) in the study population. Seropositivity rates were 67.2% for the 4-6 age group and 30% for the 7-12 age group. Notably, the 4-6 age group showed a significant association between seropositivity and age [ $p=0.005$ ; OR=4.85; 95%CI (1.614-14.569)].

**Conclusion:** The seropositivity rate of 58% for chickenpox is concerning. In light of this, conducting more extensive studies will provide valuable guidance. It may be worth considering the administration of an additional dose of the varicella vaccine within the age range of 4-6 years. Further research is necessary to assess the potential benefits and feasibility of implementing such a vaccination strategy.

**Key Words:** Pediatric, Seropositivity, Turkey, Varicella

### ÖZ

**Amaç:** Varisella, özellikle küçük çocuklarda potansiyel olarak ciddi komplikasyonları olan oldukça bulaşıcı bir hastalıktır. Türkiye'de su çiçeği aşısı, 2013 yılında 12 aylık bebekleri hedef alan Ulusal Suçiçeği Aşısı programına entegre edildi. Resmi olarak rapor edilen su çiçeği vakaları son yirmi yılda önemli ölçüde azalmış olsa da, eksik raporlama hala bir sorun olmaya devam ediyor. Bu çalışmada üçüncü basamak bir merkezde suçiçeği seropozitifliğinin araştırılması amaçlanmıştır.

**Gereç ve Yöntemler:** Kalitatif bir immünolojik test olan enzim bağımlı immüno-sorbent testi (ELISA), anti-varisella antikorlarını tespit etmek için kullanılmıştır. Türkiye'de ikamet eden 4-18 yaş arası bireylerden serum örnekleri toplandı. Aşı kayıtları, su çiçeği geçmişi ve hastalık bildirimine ilişkin bilgiler de toplanmıştır.



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**Bulgular:** Toplam 90 çocuğun su çiçeği IgG antikorları kayıtlarına erişildi. Çalışma popülasyonunda pozitif su çiçeği antikorlarının genel prevalansı %58.0 (n=47)'di. Seropozitiflik oranları 4-6 yaş grubunda %67.2, 7-12 yaş grubunda ise %30 olarak belirlendi. Özellikle 4-6 yaş grubu seropozitiflik ile yaş arasında anlamlı bir ilişki gösterdi [p=0.005; OR=4.85; 95%CI (1.614-14.569)].

**Sonuç:** Suçiçeği için %58'lik seropozitiflik oranı endişe vericidir. Bunun ışığında daha kapsamlı çalışmaların yapılması değerli bir yol gösterici olacaktır. 4-6 yaş aralığında ek doz su çiçeği aşısı yapılması düşünülebilir. Böyle bir aşılama stratejisinin uygulanmasının potansiyel faydalarını ve fizibilitesini değerlendirmek için daha fazla araştırma yapılması gerekmektedir.

**Anahtar Sözcükler:** Pediatrik, Seropozitiflik, Türkiye, Suçiçeği

## INTRODUCTION

Varicella-zoster virus (VZV) is a member of the herpesvirus family responsible for causing the itchy rash of chickenpox (varicella) in children and the painful blistering rash called herpes zoster (HZ) or shingles in older or immunocompromised individuals. After infection, the virus can remain dormant in the dorsal root ganglia for the individual's entire life until it is reactivated (1).

The administration of the varicella vaccine is an effective preventive measure to significantly reduce the incidence of varicella. Before the widespread availability of the vaccine, Europe reported approximately 5.5 million varicella cases annually, with 80% of unvaccinated children and adolescents showing positive serum anti-VZV IgG (2,3). Similarly, in the United States, approximately 4 million cases were reported each year before the vaccine became widely accessible (4). However, since the introduction of a single-dose vaccination for children aged 12-18 months in 1996, the incidence of varicella decreased by about 90% by 2005 (5).

According to the World Health Organization (WHO), VZV infects at least 140 million people worldwide annually, imposing significant social and economic burdens (6). To address this, the WHO has recommended the inclusion of varicella vaccines in routine childhood immunization programs. In 1995, The Centers for Disease Control and Prevention (CDC) also advised that individuals of all ages, including children, adolescents, and adults, receive two doses of the varicella vaccine as a precautionary measure against the disease (7). The first vaccine dose is typically administered to children between 12 and 15 months of age, with the second dose given to children aged 4 to 6 years.

Despite the success of varicella vaccination programs in reducing the incidence of the disease, cases of varicella infection continue to occur both domestically and internationally, as reported in several studies (6,8). These studies have demonstrated the protective effect of both one-dose and two-dose varicella vaccines. The findings indicate that the protection rates for one-dose varicella vaccine are 72.98%, while the protection rates for two-dose varicella vaccine are 100 (9). Although a single dose of the vaccine has shown to provide approximately 97% protection against severe and moderate chickenpox infections, its efficacy against any degree of severity is lower, ranging from 80-85%. Therefore, it is possible for children who receive a single dose of the vaccine to still contract a chickenpox infection. On the other hand, administering two doses of the

chickenpox vaccine has been reported to significantly reduce the incidence of chickenpox cases (9).

The objective of the present study was to assess the prevalence of varicella antibody seropositivity in healthy children aged 4-12 years who had a single dose of varicella vaccine at 12 months of age.

## MATERIALS and METHODS

In this study, a retrospective evaluation was conducted on the records of a total of 90 children who underwent testing for varicella IgG at Başkent University. Due to incomplete vaccination records for five children and chronic illnesses in four others, these nine children were excluded from the study. A total of 81 children have been vaccinated with only one dose of varicella vaccine at 12 months of age. These 81 children had attended the clinic for routine well-child check-ups and had received a single-dose varicella vaccine according to the standard vaccination schedule implemented in our country.

The study received approval from the Başkent University Faculty of Medicine Ethics Committee (project number: KA 23/244-19.07.2023) before its commencement.

### Varicella Vaccination Strategy in Turkey

In Turkey, the varicella vaccination strategy involves including the varicella vaccine in the national vaccination calendar since 2013. According to the vaccination schedule, children in Turkey receive the varicella vaccine at the age of one year.

### Detection of Anti-Varicella-Zoster Virus (VZV) IgG Antibodies

The Enzyme-linked immunosorbent assay (ELISA) test kit, ARCHITECT-in, was used to determine the presence of anti-VZV IgG antibodies in the samples. The manufacturer's instructions were followed, and established threshold values were used to interpret the results. Each test result was considered independent. Samples with a  $\Delta A$  value below the threshold were classified as negative, and those above the threshold were classified as positive. The manufacturer's information indicated that anti-VZV IgG concentrations of  $\geq 11$  NTU,  $\geq 9$  to  $<11$  NTU, and  $<9$  NTU were classified as positive, equivocal, and negative results, respectively. It was observed that all patients who had borderline or negative Varicella IgG levels had received the varicella vaccine.

## Statistical Analysis

Data obtained from questionnaires were analyzed using IBM SPSS Statistics version 22.0 (SPSS Inc., Armonk, NY, IBM Corp., USA) software package. Descriptive statistics such as frequency, percentage, mean, and standard deviation were used to present the data. The normal distribution of variables was evaluated using the Shapiro-Wilk test, with p-values below 0.050 considered statistically significant. To assess differences between groups, the Mann-Whitney U test was employed. For categorical data, either the Chi-square significance test or Fisher's exact test was used. Additionally, univariate and multivariate logistic regression analysis was conducted to investigate the factors influencing viral seropositivity. Results were considered statistically significant if they achieved a confidence level of 95% or a margin of error of 0.05."

## RESULTS

The study included 81 healthy children with a mean age of 6.0 ± 2.1 years. Of the participants, 43.2% were female (n=41), 75.3% (n=61) were aged between 4-6 years, and 24.7% (n=20) were aged between 7-12 years. The distribution of boys and girls was similar across both age groups (p=0.843).

Upon analyzing the varicella seropositivity rates, it was found that 58% (n=47) of the participants tested positive for varicella IgG.

When comparing varicella seropositive and seronegative groups, no significant difference was found in terms of gender (p=0.831). However, a statistically significant difference was observed between the two groups in terms of age distribution (p=0.003) (Table I). The varicella seropositivity rate in the 4-6 age group was found to be 67.2%, while the rate in the 7-12 age group was 30%.

Table II presents the results of the logistic regression analysis, which aimed to identify the variables that predict varicella seropositivity rates. The analysis was conducted using two predictor variables: age group and gender. The results show that the age group variable was a significant predictor of varicella seropositivity rates [p=0.005; OR=4.85; 95%CI (1.614-14.569)]. Children in the 4-6 age group were 4.85 times

more likely to be seropositive for varicella than those in the 7-12 age group. On the other hand, gender was not a significant predictor of varicella seropositivity rates [p=0.636; OR=1.24; 95%CI (0.511-2.999)].

## DISCUSSION

Varicella, commonly known as chickenpox, is a viral infection that can lead to severe and life-threatening complications in children (10). To prevent the spread of this infection, it is crucial to be aware of its potential risks and take appropriate measures, such as vaccination and isolation of infected individuals. The present study found that the varicella seropositivity rate was 58% among healthy children in a tertiary center.

Bollaerts et al. (11) conducted a systematic review of 43 studies across 16 European countries to assess varicella seroprevalence before the implementation of universal childhood immunization. The results showed considerable variation in varicella seroprevalence among European countries during childhood, highlighting the need for tailored vaccination policies. In a study among adults in our country, Sac et al. (12) found a high seroprevalence of varicella (93%), indicating a relatively high level of immunity against varicella in the adult age group due to asymptomatic or undiagnosed infection. This information is crucial in developing vaccination strategies for maintaining and enhancing population immunity. Hu et al. (6) investigated varicella vaccination status among Chinese children aged 6-11 and found low two-dose vaccination rates among those with a history of varicella infection. The researchers recommended increasing the coverage of the varicella vaccine and including a two-dose regimen in the National Immunization Program of China.

Gabutti et al. (13) conducted a study in Italy to evaluate varicella seroprevalence and the impact of mandatory varicella vaccination for newborns. The findings indicated a high overall seroprevalence of varicella in Italy, with increasing seropositivity observed in younger age groups since the implementation of mandatory varicella vaccination for newborns in 2017. Taken together, the studies reviewed here reveal that varicella seropositivity rates are influenced by various factors, such as age, gender, vaccination status, and geographical location. The findings also demonstrate considerable variation in varicella seroprevalence across different countries and regions, indicating the need for tailored vaccination policies based on local epidemiological data. These insights are crucial in understanding the complex nature of varicella infection and developing effective strategies for preventing its spread and minimizing its associated risks. Further research is needed to explore the factors that contribute to the heterogeneity of varicella seroprevalence and to identify optimal vaccination strategies in different populations.

Our study revealed a significant difference in varicella IgG positivity rate between the 4-7 age group and the 7-12 age group,

**Table I: Comparison of the participant features according to varicella seropositivity**

	Varicella Seronegative	Varicella Seropositive	P
Age (m±SD) (years)	7±3	5±1	0.105
Age group*			
4-6 years	20 (32.8)	41 (67.2)	0.003 <sup>†</sup>
7-12 years	14 (70.0)	6 (30.0)	
Gender*			
Female	17 (39.5)	26 (60.5)	0.831
Male	17 (44.7)	21 (55.3)	

\*: n(%), †: p<0.050 is significant, m: mean, SD: standard deviation

**Table II: Univariate and multivariate logistic regression of the varicella seropositivity**

	Univariate Logistic Regression Analysis				Multivariate Logistic Regression Analysis			
	OR	CI 95%	beta	p	OR	CI 95%	beta	p
4-6 years	4.78	1.599-14.307	1.56	0.005	4.85	1.614-14.569	1.57	0.005
Gender	1.24	0.511-2.999	0.21	0.636	1.61	0.514-3.352	0.27	0.570

**OR:** Odds ratio, **CI:** confidence interval

with a higher rate observed in the younger age group. Zhang et al. (9) evaluated varicella seropositivity rates and protective effects of varicella vaccination in children aged 3-6 years. The study found a significant increase in positive antibodies with an increasing number of vaccine doses administered and a higher protection rate with two-dose vaccination compared to one-dose vaccination. Luan et al. (14) found a higher seroprevalence of anti-VZV IgG antibodies in Chinese children who had received varicella vaccination, indicating a positive impact of vaccination on the development of immunity against varicella. However, vaccination rates differed between genders, highlighting the need for targeted vaccination strategies.

Although our study had some limitations, such as a small sample size and the lack of examination of antibody levels in healthy children aged 12-18, we believe that our findings provide a valuable contribution to the field of varicella seroprevalence research in healthy children. By identifying the varicella seropositivity rates in our study population, we were able to shed light on the epidemiology of varicella in our community and provide insights into the potential impact of vaccination programs in our region.

In conclusion, while we acknowledge the limitations of our study, we believe that our findings provide important insights into the seroprevalence of varicella in healthy children and can serve as a starting point for further research in this area. We hope that our study will encourage continued investigation into the epidemiology of varicella and inform the development of effective vaccination programs to reduce the burden of this infection in our community and beyond.

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