# Varicella Zoster Seroprevalence in Children less than 5 years old

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**Summary**

**This study was designed to evaluate the age-specific varicella-zoster virus (VZV) seroprevalence in children less than 5 years old who presented at a healthy child outpatient clinic and to compare the results with the data from other countries. The study was a cross-sectional study determining the prevalence of serum IgG against VZV in children who presented to the Healthy Child Outpatient Clinic of the Gazi University Medical Faculty and who were aged between 9 months and 5 years, in the 3rd–97th percentile as regards height and weight, not suffering from any disease, and without a history of vaccination against varicella. The information on the children was obtained from a questionnaire, by physical examination, and from patient files. Serum samples were obtained from babies and children at 9, 15, 24, 36, 48, and 60 months. The 295 serum samples were kept at −20°C following centrifugation until used for serologic analysis (ELISA). The 292 children of the study group consisted of 168 males (57.5 per cent) and 124 females (42.5 per cent). VZV antibodies were found to be positive in 65 children aged between 9 months and 5 years (22.3 per cent); 22.0 per cent in males and 22.6 per cent in females with no statistically significant difference between the sexes ($p > 0.05$). The VZV seroprevalence was highest at the 48th and 60th months and this difference was statistically significant ($p = 0.000$).**

**Key words: children, seroprevalence, varicella-zoster virus**

## Introduction

Varicella is a mild disease in children but can have a severe and complicated course in adolescents, young adults, and in those with immune deficiency. It can also have a negative influence on school performance by affecting attendance.[1]

Both cellular and humoral responses develop in those who suffer from the disease. Antibodies specific to varicella-zoster virus (VZV) appear 4 days after natural infection, reaching their peak levels on the 4th to 8th week and decreasing gradually after remaining at a high level for 6–8 months. These protective antibodies do not disappear completely and are present throughout life. Varicella antibodies are transferred through the placenta but their levels decrease after 6–9 months and disappear at around the age of 12 months, after which sensitivity to the disease develops.[2–4]

**Acknowledgements**

This research was supported by the Research Fund of Gazi University. This study was permitted by the Ethics Committee of Gazi University. TF 01/2001-30

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Varicella is encountered in children less than 10 years old in temperate zones but mostly in older children in tropical countries.[1] The Turkish Ministry of Health data indicate that the disease is encountered in the 5–9-year-old age group in Turkey.[5] Kanra, *et al*. have found a VZV seroprevalence of 85 per cent in 10-year-old children in a study carried out in nine Turkish states.[6]

A live virus vaccine for the disease was developed in 1974. A small number of countries are currently employing this vaccine in their routine vaccination programs[1] but it is not available in Turkey's universal vaccination program.[5] The seroepidemiology of the disease would be expected to change in those countries using the vaccine widely. It is necessary to know the seroprevalence of the disease before including the vaccine in a country's routine vaccination program.

This study was designed to evaluate the age-specific VZV seroprevalence in children less than 5 years old who presented at a healthy child outpatient clinic and to compare the results with data from other countries.

## Materials and Methods

This study was a cross-sectional study to determine the prevalence of serum IgG against VZV in children who presented to the Healthy Child Outpatient

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doi: 10.1093/tropej/fmh102 Advance Access Published on 14 April 2005

Clinic of the Gazi University Medical Faculty and who were aged between 9 months and 5 years, in the 3rd–97th percentile as regards height and weight, not suffering from any disease, and without a history of vaccination against varicella. The outpatient clinic is located in a region in the city center where families are mostly of middle socio-economic status, with an average of two children per family, and a very small percentage (3.2 per cent) of children attending day-care facilities. The information on the children was obtained from a questionnaire, by physical examination, and from patient files. Serum samples were obtained from babies and children at 9, 15, 24, 36, 48, and 60 months.

The 295 serum samples were kept at $-20^{\circ}C$ following centrifugation until used for serologic analysis. The IgG levels were measured with the Trinity Biotech VZV IgG ELISA kit. Three serum samples were excluded from the study as their results were borderline and they could not be tested again.

The binomial exact test was used to calculate the confidence interval for the seropositivity rates by age group and the chi-squared test was employed to compare seropositivity by age and sex.

## Results

The 292 children of the study group consisted of 168 males (57.5 per cent) and 124 females (42.5 per cent). Table 1 shows the seropositivity data for VZV.

VZV antibodies were found to be positive in 65 children aged between 9 months and 5 years (22.3 per cent); 22.0 per cent males and 22.6 per cent females with no statistically significant difference between the sexes ($p > 0.05$).

The VZV seroprevalence was highest at the 48th and 60th months and this difference was statistically significant ($p = 0.000$). Figure 1 shows the VZV antibody seroprevalence.

TABLE 1
*VZV antibody prevalence in Turkey by age and sex*

| Age group | Sex (*n*) | Seropositivity no. (%) | 95% CI | $p$[a] |
|---|---|---|---|---|
| 9 months | M (17) | 0 (–) | (0.00–23.52) | NS |
| | F (14) | 1 (7.1) | (0.00–21.42) | NS |
| 15 months | M (14) | 0 (–) | (0.00–28.57) | NS |
| | F (18) | 1 (5.6) | (0.00–16.66) | NS |
| 24 months | M (33) | 6 (18.2) | (6.06–33.33) | NS |
| | F (28) | 3 (10.7) | (0.00–25.00) | NS |
| 36 months | M (44) | 8 (18.2) | (6.81–29.54) | NS |
| | F (19) | 4 (21.1) | (5.26–42.10) | NS |
| 48 months | M (41) | 15 (36.6) | (21.95–51.21) | NS |
| | F (21) | 10 (47.6) | (28.57–66.66) | NS |
| 60 months | M (19) | 8 (42.1) | (21.05–63.15) | NS |
| | F (24) | 9 (37.5) | (20.83–58.33) | NS |
| Total | M (168) | 37 (22.0) | (16.07–28.57) | NS |
| | F (124) | 28 (22.6) | (15.32–29.83) | NS |

[a] $\chi^2$ test: $\chi^2 = 34.7$; $p = 0.000$.
NS: not significant; $p > 0.05 = \text{NS}$.

## Discussion

We found the VZV seropositivity rate in children under 5 years old to be 22.3 per cent. A linear increase in seropositivity is noted when evaluated by age. Another study from Turkey has also revealed an increasing seropositivity rate with age, although the age-related seropositivity rates were higher than ours at 32.5 per cent for 1–3 years and 59.4 per cent for 4–6 years.[6] Our study investigated the younger age groups in more detail. The increase in seropositivity with age has been shown in studies from various countries. The rates determined in various studies are 33.6 per cent for 2–3-year-olds and 62.5 per cent for 4–5-year-olds in Germany;[2] 11 per cent for age 1 and 46 per cent for age 5 in Switzerland;[8] 21.2 per cent for 1–4-year-olds and 56.9 per cent for 5–9-year-olds in Bolivia;[9] 35.29 per cent for age 1 and 80.19 per cent for age 5 in Belgium;[11] and 85 per cent for age 1 and 92.5 per cent for age 4 in Spain.[17]

In our study, 32.6 per cent of the 5-year-old group were positive for VZV antibodies. This rate is lower than the seropositivity rate for similar age groups found in some European studies investigating seroprevalance. The same rate for 5-year-old children was determined as 80.19 per cent in Belgium,[11] 46 per cent in Switzerland,[8] 62.5 per cent for 4–5-year-olds in Germany,[2] 85 per cent for 6–9-year-olds in Catalonia,[7] and 50 per cent for 3-year-olds in England.[19] Seropositivity for children under 5 years old has been determined to be less than 15 per cent in India,[16] 28.4 per cent in Pakistan,[13] and 21.2 per cent in Bolivia.[9] These data are consistent with the knowledge that VZV infection is seen in older age groups in hotter countries when compared with temperate countries. A previous study from Turkey found a seropositivity rate of 59.4 per cent for

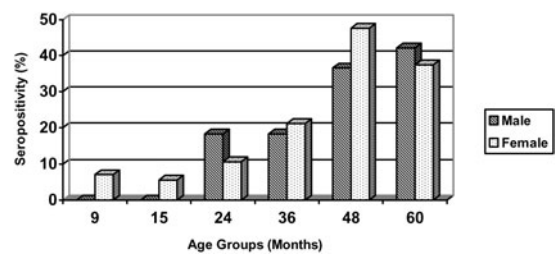


FIG. 1. VZV antibody seroprevalence in children 5 years old and younger.

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4–6-year-olds.[6] Some studies have postulated that the VZV seroprevalence in adolescents and young adults in southern Europe is lower than the rates for northern and central Europe.[8] The location of Turkey in southern Europe may explain the seroprevalence rate for the first 5 years being lower than that of most European countries. A study from Italy has found an immunity rate of 82.1 per cent in the 10–19-year-old age group.[15]

Our study was carried out in an urban area with small families where a low percentage of children attend day-care facilities and are mostly looked after at home. The decreased contact between children less than 5 years old may have decreased the transmission of the disease and shifted the infection age upwards. With the increased number of preschool facilities in Turkey we might expect a seroepidemiology similar to that of European countries in the future. Increased contact between preschool children has been shown to push the disease age downwards.[19]

Our study did not find any difference in seropositivity by sex. Other studies found similar results.[4,6,9,11]

Two studies mentioned that the age of the patients has been increasing in the USA and UK.[20–22] Another study carried out in the UK during the same period has not confirmed these findings.[19] It is not possible to postulate an upward shift as Turkey and most European and Asian countries do not have adequate historical seroepidemiological data.

This study revealed that 60.2 per cent of children older than 5 years are sensitive to VZV. It is known that the disease is especially severe in children younger than 1 year and older than 15 years and that it can lead to lost school days in older children.[23] In light of these findings, adding the varicella vaccine to the universal vaccination program should be considered for older children in our country with a high percentage of the population sensitive to the virus. The same consideration applies to tropical countries where the age of the patients is higher. Our country and many countries in tropical zones have a large population of children and limited economic means. Including a vaccine in the universal program can only happen if vaccine production is of sufficient quantity and at a reasonable cost for large populations. It is difficult to say that these conditions have been met for the varicella vaccine. The WHO emphasizes that a country needs to have achieved a high percentage of vaccination before a new vaccine is added to universal childhood vaccination programs. In Turkey and many tropical countries, the rate of vaccination for vaccines included in the EPI is 80 per cent or even lower. The inadequate administration of a new vaccine could, therefore, cause more harm than good by shifting the age at which the disease is seen upwards. A coverage of 97 per cent is required for the varicella vaccine to eliminate endogenous transmission. Catch-up vaccination programs for adults will also be needed in this case to prevent the shift towards the older age groups. However, there is evidence showing increased availability of preschools and kindergartens in Turkey.[24] When the rapid transmission of the disease is taken into account, this will shift varicella to younger ages where the disease is relatively benign.

In conclusion, where protection by a vaccine is possible it is, of course, best to prevent a disease by universal vaccination. Countries need to employ strategies that would rapidly increase the vaccination rates for vaccines within the context of EPI, and to at least stop interventions to vaccinate some sections of the community (those living in the cities, the affluent, etc) that would shift the disease to older age groups and increase the complication rate before the vaccination rate is at a desirable level. The higher cost of new vaccines necessitates efforts to decrease their costs and for most countries to increase their health budget.

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