

Seroepidemiology of *Varicella Zoster Virus* Infection among 1-70 year individuals in Iran

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Abstract

Background: *Varicella zoster virus* (VZV) causes varicella and, later in the life of the infected person, can reactivate to cause Herpes zoster (HZ). The objective of this study was the investigation of anti *Varicella zoster virus* IgG antibodies in infants and adults in Shiraz, southern Iran.

Methods: A cross-sectional, age and population-based seroprevalence study was conducted in 2008 on 843 subjects, ages ranging from 1 to 70 years old. IgG antibodies against VZV were measured with a commercially available enzyme-linked immunosorbent assay (ELISA).

Results: The seroprevalence of *Varicella zoster* antibodies increased with age, being 25.3% in 1-5 year age group, 43.1% in 6-10 year group, 73.5% in 11-15 year group and 86% in adult population.

Conclusion: The majority of VZV infections occurred during childhood. The best policy to prevent the circulation of wild type VZV in the population and reduction of the rate of complicated cases is the immunization of 5 year old children and those younger. VZV vaccine should be incorporated in the conventional childhood vaccination plan in Iran.

Keywords: *Varicella Zoster Virus*; Seroepidemiology; Susceptibility; Vaccination; Iran

Introduction

Varicella zoster virus (VZV) is responsible for the two distinct diseases; *Varicella* (chicken pox) and *Herpes zoster* (HZ). *Varicella*, caused by VZV primary infection, is not usually so severe in itself. However, it may result in severe complications and in some cases death in healthy and immunocompromised individuals.¹

Primary infection in pregnant women during the first 20 weeks of gestation could be associated with congenital infection and anomalies in 2% of fetuses. The VZV infection within the third trimester of gestation or close to delivery time can cause severe *Varicella* infection in neonates.² Furthermore, the latent infection established in individuals following

Varicella may become active due to a variety of reasons including aging, and immunosuppression and result in HZ.³

Varicella and its consequential complications could be prevented through active immunization by a live attenuated vaccine (VZV oka strain).⁴ The vaccine has been available since 1970s and has proved very effective, as demonstrated in a wide range of international studies.^{5,6} It is of little complications and can bring about long standing immunity. In addition, it has been found that *Herpes zoster* is of equal or less frequency in vaccinated patients compared with those infected by the wild type virus.^{7,8} In many countries, the vaccine is now used for universal vaccination in children, however, in Iran it is not yet practiced across the nation.⁹

The present study seeks to determine the prevalence rate of natural infection with VZV through seroepidemiological tests among a population of 1-70 years old individuals in Shiraz, southern Iran. The findings could be of importance to the controlling of VZV infection.

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Materials and Methods

The minimum sample sizes from different age groups with 95% confidence interval and 5% alpha error were calculated using the seroepidemiologic findings from other countries¹⁰⁻¹² and the existing little data reported from Iran.^{13,14} From May to September 2008, 843 blood samples were collected from the individuals referred to Nemazee Hospital clinics affiliated to Shiraz University of Medical Sciences, for routine medical examination check up. It is worth mentioning that written informed consents were obtained from the cases or their guardians prior to the study and were reviewed and approved by the Ethics Committee of Professor Alborzi Clinical Microbiology Research Center, Shiraz University of Medical Sciences. The mean age was 22 years (range, 1 to 70 years) and there were 413 (49%) males and 430 (51%) females. The inclusion criteria were lack of present history of symptomatic infectious disease and being in normal immunity status. Five ml blood samples were collected from the subjects and following serum separation, coding and indexing they were stored at -20°C till examination.

IgG antibodies against VZV were measured using a commercially available ELISA (enzyme linked immunosorbent assay) test kit (IBL, Hamburg, Germany). The manufacturer's protocols were followed during the procedures. All sera with equivocal results for VZV antibodies (2.5 %) were retested for confirmation using the same assay and considered to be negative if still indeterminate.

To compare the prevalence rates among different age groups, Chi-Square test was used and *p*-values less than 0.05 were considered statistically signifi-

cant. The prevalence of anti *Varicella* antibodies for the age groups and its 95% confidence intervals (CI) for each, in comparison with the results of all other groups were calculated. Epi Info software was used for all statistical calculation.

Results

The sample consisted of 843 individuals, 399 (47.3%) infants (≤ 15 years) and 444 (52.7%) adults ($16 \geq$ years). VZV serology was positive in 559 (66.3%) of the 843 studied individuals; 275 (66.5%) in males and 284 (66%) in females; and 284 (33.7) were seronegative or susceptible to the infection (Table 1). Meanwhile, 177 (44.4 %) of the infants had antibodies against VZV and 222 (55.6%) of them remained susceptible to the infection but susceptibility rate in adults was 14%. The prevalence of *Varicella* antibodies increased with age (Figure 1). In the 1-5 year age group, only 25.3% were infected. This proportion grew up to 43.16% in the 6-10 year age group and increased to 73.5% in 11-15 year age group. In young adults between 16 and 20 years of age, the rate was 83.2%. In those over 20 years, 86.9% were infected. No difference in prevalence was observed with respect to gender. The population susceptible to the infection decreased from 66.2% in the 1-10 year old to 14% in the adults. 16.8% of the patients, aged 16-20 years were susceptible to the infection.

Discussion

Incorporation of *Varicella* vaccine into the national

Table 1: Serorevalence of antivariella antibodies according to gender and age in Shiraz

Variable	Prevalence: No (%)	Total	OR (95% CI)	P
Gender				
Female	284 (66.0)	430	0.98 (0.73-1.31)	0.870
Male	275 (66.5)	413		
Age (years)				
1-5	39 (25.3)	154	9.07 (5.96-13.86)	0.001
6-10	60 (43.1)	139	3.2 (2.17-4.73)	0.001
11-15	78 (73.5)	106	0.67 (0.42-1.09)	0.090
16-20	84 (83.2)	101	0.36 (0.2-0.64)	0.001
21-30	82 (84.5)	97	0.32 (0.18-0.59)	0.001
31-40	68 (88.3)	77	0.24 (0.11-0.5)	0.001
41-50	81 (88)	92	0.24 (0.12-0.47)	0.001
51-70	67 (87)	77	0.27 (0.13-0.55)	0.001
Total	559 (66.3)	843		

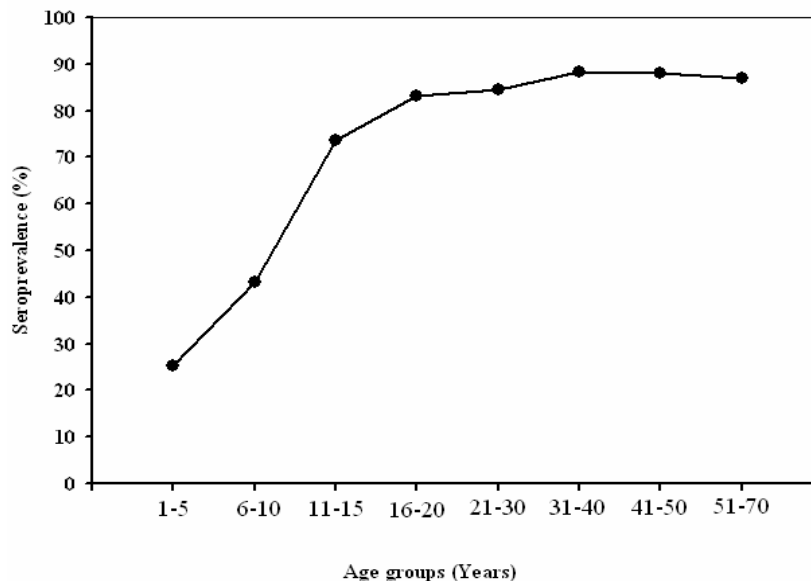


Fig. 1: Age-specific seroprevalence of antibodies to *Varicella zoster virus* (VZV) in Shiraz, southern Iran

routine immunization program is being deliberated in several countries.⁹ To do so, knowledge of the epidemiology of VZV infection is essential to making proper decision, arranging nationwide program and measuring the effects of the vaccine.

Investigation of VZV seroprevalence, as pursued in the present study can serve as a means of gathering epidemiologic data. As the findings showed, the prevalence of VZV and age were positively correlated, i.e. the older the population, the greater the prevalence was. Yet, 55.6% of children and 14% of adults are found susceptible to VZV infection. Susceptibility in these two groups, as demonstrated in this study, is lower than expected and is a little bit different from those reported in some other countries; 46% for 5 years old in Switzerland,¹⁵ 75% for the 5–9 year old in Spain,¹⁶ 82–83% for the 10–14 year old in Italy,¹⁷ and 94% for the 10–11 year old in Germany.¹⁸ In the Netherlands, seropositivity increased sharply with age from 18.4 for 0-1 year old to 48.9%, 59.0%, 75.7% and 93.0% for 2, 3, 4 and 5 years old, respectively and varied between 97.5% and 100% for the older age groups.¹⁹ An important report from Tehran showed the seroprevalence of anti VZV antibodies in children and in age is relatively higher than present study (59.7% positivity in 0-10 to 87.5% among 15-19 years old vs. 25.3% and 73.5% positivity among 1-5 and 11-15 years respectively).¹⁴ This may be re-

lated to the difference between two locations.

Geographically, Shiraz with temperate condition is located in the distal margin of the Zagros range which is of tropical climate. During summer time, the average temperature in this city rises up to 42°C which might be the reason why the prevalence is lower than expected. Geographical difference of VZV antibody seroprevalence among children had been reported previously.²⁰

The results of the study have revealed two important points. First, the prevalence of the infection with wild type VZV among Iranian population seems rather high. Second, a remarkable proportion of children and adults are still at the risk of VZV infection. Natural infection in both children and adults may lead to hospitalization with severe condition and even death. Vaccination against VZV is very helpful in such scenarios. Considering the vaccination schedule in the US, we understand that it has resulted in the decrease of 80-85% of the VZV disease. Moreover, 95% of the severe cases have been prevented. Vaccination has also caused the incidence rate to decline by 57-90%, hospitalization by 75-88%, and mortality by 74%.²¹

Meanwhile, in view of the high rate of VZV among Iranian population, the potential rate of HZ could be high accordingly. The HZ induced by the wild type can be very severe and associated with complications such as neuralgia, wound secondary infection and meningitis, particularly when occurring

to the elderly. Also, the transplant recipients and malignancy sufferers are highly at risk.^{22,23} The reported studies have also demonstrated that out of 100,000 individuals with HZ, 4.4-16.1 cases are hospitalized.^{24,25} The bulk of literature indicates no increase in the overall incidence of HZ, and some indicate even a decrease in it.^{7, 26, 27} Recently, it has been suggested that booster doses of VZV vaccine with higher titers can remarkably reduce the incidence of HZ and the associated complications in people over 60 years.^{28,29} Also it was shown that the severity of HZ among the population vaccinated against VZV is lower, compared to the cases induced by the wild type virus. In the former, the progression of the infection is milder.^{29,30}

Taking into account the present findings, it is highly suggested that universal vaccination of

children against VZV be implemented across the nation. In doing so, the complications due to the incidence of wild type in the population can be reduced which would be cost effective consequently.

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Conflict of interest: None declared.

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