The Seroepidemiology of Varicella Zoster Virus (VZV) in Different Age Groups in Tehran, Iran

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ABSTRACT

Varicella zoster virus (VZV), the causative agent of chickenpox and shingles, can cause severe systemic infections of the CNS and the respiratory tract in immunocompetent individuals as well as in immunocompromised patients. The aim of this cross-sectional study was to assess the prevalence of antibody Varicella zoster virus in different age groups. The enzyme linked immunosorbent assay (ELISA) method was used to assess the presence of anti-VZV antibody.

A total of 635 serum samples were collected. Age specific prevalence of IgG antibody to VZV showed a progressive increase with age in both males and females. The overall seroprevalence rate was 83.6%. Prevalence of antibodies was 59.7% in the age group of less than 10 years, 60.4% in 10-14 years, 87.5% in 15-19 years, 88% in 20-24 years, 89.4% in 25-29 years and 87.9% in 30-39 years.

The data show that children should be considered as a target group for prevention programs against VZV infection.

Keywords: Prevalence; Vaccination; Varicella Zoster Virus

INTRODUCTION

Varicella zoster virus (VZV) is the etiologic agent of primary varicella (chickenpox) in childhood, establishing a latent infection that may re activate to cause herpes zoster (shingles). VZV infections are usually benign, but serious and occasionally fatal infections do occur. Among children, varicella is usually a self-limited disease. Adolescents, adults, and immunocompromised persons, usually have more severe disease and are at higher risk for complications. Primary sub clinical infection with VZV is rare for persons of all ages. VZV causes a systemic infection that usually results in lifetime immunity. In otherwise healthy persons, clinical illness after exposure is rare; such illness is more likely to occur among immunocompromised persons.

Varicella has worldwide distribution with an annual incidence estimated to be equal to the birth cohort. However, there is considerable interest in the disease due to epidemiological variations between geographic location, especially between temperate and tropical regions of the world. In temperate countries, varicella is considered to be a childhood disease with almost universal seroconversion by early adolescence. Nearly 100% seropositivity to VZV has been documented by 11-13 years of age in USA. The epidemiology is less well understood in tropical areas, where a relatively large proportion of adults in some countries are seronegative. The varicella virus vaccine is composed of the Oak strain of live, attenuated VZV. The Oak strain was isolated in Japan in the early 1970s from vesicular fluid in a healthy child with natural varicella and was attenuated through sequential propagation in cultures of human embryonic lung cells, embryonic guinea-pig cells and human diploid cells (WI-38). Varicella virus vaccine was first licensed for use among high-risk children in several European countries in 1984, in Japan in 1986,
and in Korea in 1988. In Japan and Korea, licensure was extended to healthy children in 1989. The varicella virus vaccine licensed in the United States in 1995, and Canada in 1998. With the availability of vaccines against varicella, recently has been renewed interest in the epidemiology of this disease. The epidemiology of VZV has important implications for future vaccine strategies. Many countries are currently studying the possibility of mass vaccination against varicella. Low vaccine coverage can result in an increase in the average age of primary infection, with a concomitant increase in severity of varicella in adult age groups, and especially in pregnant women, where infection can have adverse sequel for both the mother and unborn child. The levels of coverage estimated in countries with current VZV vaccination (approximately 25%), will have little impact on the age distribution of disease. However, with increasing coverage, morbidity amongst adults is likely to increase, and vaccination is only predicted to decrease morbidity in both adults and children at around 70% coverage. Thus, it is important that universal vaccination against VZV is introduced in a region or country only if the attainment of very high coverage can be assured. No data on frequency and character of VZV infection have been published in Iran. The objective of this study was to provide a comprehensive picture of the pre-vaccine immunological status of the varicella zoster virus in Iran to aid in the design of immunization programs.

MATERIALS AND METHODS

This cross sectional study was carried out to identify seroprevalence of VZV in different age groups from October 2003 to January 2005. The study population consisted of 635 healthy male and female volunteers from 1 to 60 years old.

Subjects were checked for inclusion and exclusion criteria, a questionnaire was completed including background and family history of varicella. The exclusion criteria were: acute infectious disease, recent administration of immunoglobulin, blood products or immunosuppressive therapy.

Samples were collected and stored at –20 °C until tested for varicella antibodies. Anti-VZV specific antibodies were detected using a commercially available ELISA (EIAGen Varicella Zoster IgG Biochem Immunosystems), which according to manufacturer has a sensitivity of 90.9% and a specificity of 100%. Sera were classified as negative if the OD was less then 0.90 and as positive if higher than 1.10; sera with OD reproducibly between 0.90 and 1.10 were classified as borderline. The statistical comparison of data was performed using the \( \chi^2 \) test.

RESULTS

A total of 635 serum samples collected from October 2003 to January 2005, were tested; 3.8% of these samples had borderline results and were not considered in the data analysis. The overall seroprevalence rate was 83.6%. Seroprevalence was 59.7% in the age group of less than 10 years, 60.4 % in 10-14 years, 87.5 % in 15-19 years, 88 % in 20-24 years, 89.4 % in 25-29 years and 87.9 % in 30-39 years (Figure 1).

The seroprevalence rate of VZV increased with age (Table 1). The seroprevalence rate of females of reproductive age was 80.9% in 15-39 years group. There was significant relation between the presence of VZV antibodies and age (p=0.000). There was no significance difference between the presence of VZV antibodies and sex (p=0.47).

Table 1. Number of sera tested and percentage positive for varicella IgG antibody by age group.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number of sample</th>
<th>% Positivity</th>
<th>95% Confidence interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>77</td>
<td>59.7</td>
<td>48.7-70.7</td>
</tr>
<tr>
<td>10-14</td>
<td>51</td>
<td>60.4</td>
<td>47-73.8</td>
</tr>
<tr>
<td>15-19</td>
<td>104</td>
<td>87.5</td>
<td>81-93.9</td>
</tr>
<tr>
<td>20-24</td>
<td>151</td>
<td>88</td>
<td>82.8-93</td>
</tr>
<tr>
<td>25-29</td>
<td>47</td>
<td>89.4</td>
<td>80.6-98.2</td>
</tr>
<tr>
<td>30-39</td>
<td>107</td>
<td>87.9</td>
<td>81.7-94</td>
</tr>
<tr>
<td>≥40</td>
<td>74</td>
<td>86.5</td>
<td>78.6-94.3</td>
</tr>
</tbody>
</table>

Figure 1. Varicella Zoster Virus seroprevalence by age group in Tehran, Iran.
DISCUSSION

The different epidemiology of primary varicella infection between tropical and temperate countries is a known fact; VZV seropositivity is observed earlier in temperate countries and later in life in tropical countries. Our results reveal that prevalence of antibodies to varicella gradually increases throughout childhood, adolescence and adulthood. An overall seropositivity rate from 59.7% in less than 10 years group to 60.4% at age 10-14 years, which increased to nearly 90% at the age of 30 years. Our results are comparable to those reported for other tropical countries.

In the United Arab Emirate, the overall adult seroprevalence rate was 81.3%. The rate among Emirati citizens increased with age; <10 years, 45.8%; 11–20 years, 68.4%; 21–30 years, 89.5%; 31–40 years, 94.7%; and > 41 years, 88.9%.16

In India, overall seropositivity of anti-VZV antibody was 68.22%. The age related seroprevalence rate of anti-VZV antibodies was 29% in the age group of 1-5 years, 51.1% in 5-10 years, 71.7% in 11-15 years, 79.8% in 16-20 years, 88.1% in 21-30 years and 91.1% in 31-40 years.17 In Singapore, investigators found that only 41% of those aged 15-24 years had protective antibodies and >90% seroprevalence was not reached until 35 years of age.18 In Thailand, two groups reported that many adolescence and young adults lack protective antibodies, with seroprevalence reaching >90% seroprevalence only in those over 30 years.19 Similar results have been reported from Malaysia and the Philippines with only 50-60% seroprevalence below 15 years of age.20 Reports from tropical countries indicate that varicella occurs in adults more frequently and apparently with severe clinical manifestations.21

This is in contrast to temperate countries, where studies have reported near universal seropositivity by early adolescence. Swiss and American studies have reported that over 90% of individuals in Europe and the United States acquire immunity before adolescence. For the USA reports mention 100% seropositivity by the age of 13 years or only 6% susceptible between 11 to 19 in temperate countries.3 In the UK >90% of individuals were infected by the age of 15 years;15 there was 80% seropositivity by the age of 7 years in Spanish children22 and 83% seroconversion by the age of 9 years in Japanese children.23 On the other hand, studies in Turkey, Australia and Italy, reported levels of immunity by the ages of 10-14 years 85%, 83% and 82% respectively.24-27

It is postulated that high ambient temperature and humidity in the tropics decreases VZV transmission by inactivating the virus in the cutaneous lesions. Alternatively, it is possible that because of high prevalence of certain other childhood viruses in tropical countries, there is interference with the transmission of VZV and the age of varicella infection is postponed.28

In conclusion, although VZV seroprevalence increases with age in the population studied. A significant proportion of adolescence are still susceptible to varicella infection. In older individuals, the disease is more severe and prolonged and has a 15-25 times higher mortality than in children.29

The percentage of cases notified among young adults may be a cause for alarm since the clinical course of varicella is generally more serious in adults and the incidence of complications is higher. Among specific population groups [e.g. among individuals with chronic, renal failure or lymphoproliferative diseases; and immunocompromised individuals in general] varicella can be most severe or fatal.30,31

The percentage of females of reproductive age who do not have specific anti-VZV antibodies (19.1% among the 15-39 years age-group) indicates the risk of having pregnant woman susceptible to VZV.

Since the majority of VZV infections occur during the early childhood, the best option to reduce the circulation of wild type VZV in the population would be the immunization of young children.

These data are also fundamental for evaluating the suitability of establishing mass varicella vaccination programs. Mass vaccination against VZV should be introduced only if very high coverage can be assured. The impact that a mass vaccination program among children 12-18 months of age could have on the epidemiological trend of the infection must be carefully considered. In fact, programs that fail to reach high levels of coverage could lead to an increase in the mean age of acquisition of the infection, which should be avoided for communicable diseases in general and especially for varicella.32,33

The data presented in table 1 and figure 1 clearly indicate that this virus is circulating among the people in the city, infecting and multiplying in the bodies of
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the very young who are susceptible and boosting the immune response of those who had previously been exposed to the virus, thus rising their serum antibody levels and prolonging the duration of their immunity.

REFERENCES