SEROEPIDEMIOLOGY OF VARICELLA-ZOSTER IN PAKISTAN

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Abstract. The availability of safe and effective vaccines has renewed interest in the epidemiology of varicella worldwide. To date published data on the epidemiology of varicella in Pakistan is very scarce. Therefore, we conducted a study to determine the age-specific seroprevalence rate of varicella-zoster virus (VZV) antibodies in Pakistan. Between December 1997 and March 1998, 1,509 healthy volunteers aged between 1 month and 30 years were recruited from the Islamabad, Karachi, Lahore and Rawalpindi areas. Demographic information, socioeconomic status and past medical history were obtained by questionnaire. Serum samples were assayed for IgG antibodies against VZV by enzyme-linked immunosorbent assay. Overall 41.8% (600/1,435) of those tested were found to be seropositive for VZV antibodies. No difference was found in results obtained from the different cities. A higher seroprevalence was observed among women (45.2%) compared to men (39.6%). Seroprevalence rates increased with age and were 28.4% in those aged 0-5 years, 41.5% in the 6-10 year age group, 42.5% in the 11-15 year age group, 46.7% in the 16-20 year age group and 53.6% in those aged 21-30 years. Socioeconomic status was not a significant risk factor for VZV seropositivity. This is the first report of the seroepidemiology of VZV in Pakistan. The results indicate that seroprevalence of VZV increases with age in the Pakistani population studied. As in other tropical countries, there is greater susceptibility to varicella among the adolescent and young adult population. The results of this study suggest that these at-risk groups should be included in vaccination programs aimed at reducing the public health impact of varicella.

INTRODUCTION

Primary infection with the varicella-zoster virus (VZV) results in chickenpox. This is a highly infectious disease that occurs most frequently in children. In most healthy children the infection is self-limiting with few complications and low mortality. The disease may also occur in adolescents and adults where complications are much more severe and the risk of mortality is greatly increased (Guess *et al*, 1986; Preblud, 1981). The risk of complications is also increased in immunocompromized people and pregnant women (Nathwani, 1993; Feldman *et al*, 1975).

Although chickenpox is common worldwide, the epidemiology of the disease varies markedly between tropical and temperate regions of the world. In temperate countries such as the UK and USA, chickenpox presents mainly in childhood and is commonly a mild disease. Over 90% of the population are seropositive by the time they reach adolescence (Wharton, 1996). In tropical countries, however, children are less likely to be infected with VZV, leaving a large proportion of the young adult population susceptible to infection and disease (Wharton, 1996).

Safe and effective vaccines against chickenpox, based on the Oka strain, are available, and licensed in several countries (White, 1996). Despite the renewed interest in the epidemiology of varicella worldwide, there is to date no published data on the epidemiology of varicella in Pakistan. Such data are needed to serve as baseline epidemiologic data that can be used to draw up an immunization policy based on exact information.

MATERIALS AND METHODS

A cross-sectional multi-center study was carried out from December 1997 to March 1998. Six study centers were used to prospectively recruit healthy subjects from four different areas of Pakistan. The centers were located in Islamabad, Karachi, Lahore and Rawalpindi.

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The study population was randomly selected from a variety of locations according to age group. Children aged 1 month to 3 years were recruited from baby clinics, while children aged 3-15 years were recruited from various schools. Subjects aged 16-30 years were recruited from banks, offices, factories and universities. Informed consent was signed by each volunteer, or the parent/guardian in the case of infants and children. A questionnaire was completed for each case and included details of age, sex, address, past history of chickenpox and monthly collective income of the household. Subjects with a history of chickenpox were excluded from the study.

The monthly household income was used to classify subjects into one of three socioeconomic groups. A collective household income of more than RS15,000 per month defined the upper class, RS5,000-15,000 identified middle class households and an income of less than RS5,000 per month was taken as representative of lower class households.

Blood was collected from each subject, 5 ml from infants and children and 10 ml from adults. The serum from all samples was separated, labeled and stored at -70ºC until analyzed at the central laboratory. A commercial ELISA kit (Genzyme Virotech, Germany) was used according to the manufacturers instructions to detect VZV antibodies in the serum samples.

A descriptive data analysis was performed. The seroprevalence rates were calculated with the 95% confidence intervals.

RESULTS

A total of 1,509 volunteers were recruited. Of these, 74 were excluded because of missing data or age-ineligibility. The demographic characteristics of the study population are shown in Table 1.

Of the total 1,435 samples analysed 600 (41.8%) were positive for anti-VZV IgG. A similar pattern of seropositivity was seen in all study centers (data not shown). Overall, the proportion of subjects that were anti-VZV positive increased with age (Table 2). The most marked increase was between the two

Table 1
Demographic characteristics of the study population.

	Number	% of total
Age group (years)		
0-5	317	22.1
6-10	316	22.0
11-15	327	22.8
16-20	212	14.8
21-30	263	18.3
Gender		
Female	546	38.0
Male	866	60.3
Unknown	23	1.6
Socioeconomic group		
High	435	30.3
Middle	523	36.4
Low	477	33.2

Table 2
The proportion of particular age-groups seropositive for VZV prevalence in Pakistan by socioeconomic group.

Age group (years)	All (N=1,435)		High (N=435)		Middle (N=523)		Low (N=477)	
	% SP	95% CI	% SP	95% CI	% SP	95% CI	% SP	95% CI
0-5	28.4	23.5-33.7	28.3	20.0-37.9	31.1	22.9-40.2	25.0	16.6-35.1
6-10	41.5	36.0-47.1	43.5	33.2-54.2	34.2	25.6-43.7	47.3	37.7-57.0
11-15	42.5	37.1-48.1	40.2	30.6-50.4	42.4	33.3-51.8	44.9	35.2-54.8
16-20	46.7	39.8-53.7	55.7	43.3-67.6	38.6	27.2-51.0	45.8	34.0-58.0
21-30	53.6	47.7-59.8	50.8	38.1-63.4	50.0	39.9-60.1	59.4	48.9-69.3
Total	41.8	39.2-44.4	42.1	37.4-46.9	39.0	34.8-43.3	44.7	40.1-49.2

%SP = percentage seropositive subjects; 95% CI = confidence intervals

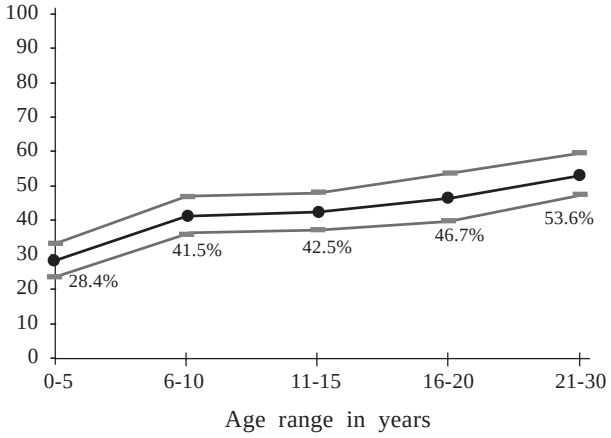

Fig 1–Varicella Zoster virus age-specific seroprevalence rate, with 95% confidence intervals.

first age categories and from then on the increase was more gradual (Fig 1). The seroprevalence rate in males was 39.6% compared with 45.2% in females (not significant).

Socioeconomic analysis (Table 2) of the study population suggested that there were no differences in seroprevalence between the socioeconomic groups either overall or when stratified into age-groups.

DISCUSSION

This report is the first description of the seroprevalence of VZV in Pakistan, and indicated that approximately 50% of adolescents and young adults remain susceptible to VZV.

The overall age-specific seroprevalence pattern reported in this study is similar to those reported previously from tropical countries with lower seroprevalence rates for adolescents and young adults. For the 0-5 year age group we observed a seroprevalence rate of less than 30%. By the time people reach adolescence about half the population is still susceptible to VZV infection and this remains the case until the age of 30 years. These values are similar, albeit even lower, to those obtained in tropical countries such as Singapore and Thailand (Lee, 1998). However, Pakistan has a hot dry climate and can thus not be considered a typical tropical country with a hot and humid climate. Further, the results differ markedly from results reported from temperate countries such as UK (Fairley and Miller, 1996) and USA (Muench *et al*, 1986) where more than 90% of the population are seropositive already by 15 years of age.

Reasons for the observed differences between temperate and tropical countries remain obscure. There are however a number of hypotheses which attempt to explain late seroconversion in the tropics. One proposal is that transmission of the virus is affected by high ambient temperatures and humidity which may reduce survival of the virus in respiratory droplets (Garnett *et al*, 1993). Our findings suggest that heat is the more important factor in the equation. Other theories include the observation that frequent infections with other viruses might interfere with the acquisition of chickenpox in childhood (Sinha, 1976) or that closely related infections might lead to cross-immunity (Edson *et al*, 1985). None of these theories on its own adequately explains the mechanism of transmission of chickenpox in tropical areas.

It is acknowledged that varicella not only has important health, economic and social costs (Brunell, 1993; Preblud, 1986; Yawn *et al*, 1997) but that the age-distribution of varicella seroprevalence has important implications for vaccination policy. Indeed, in the USA, the Advisory Committee on Immunization Practices (ACIP) has recently updated its guidelines (CDC, 1999). It not only recommends the use of varicella vaccine for young children, immunodeficient individuals, as well as adolescents and non-pregnant women of childbearing age with no history of chickenpox, but also recommends that the vaccine be used for postexposure prophylaxis and outbreak control.

In conclusion, VZV seroprevalence in Pakistan exhibits a pattern typical for tropical countries, with seroconversion occurring in adolescents and young adults. It is in these age groups that there is a greater risk of morbidity and mortality. Late seroconversion will also increase the possibility of fetal damage and disease during the natal and perinatal period as a consequence of infection with the virus in women of reproductive age. Given the increasing risk with age and the associated risk of serious complications these results support the introduction of varicella vaccination for susceptible adolescents and adults, as well as young children.

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