ORIGINAL CONTRIBUTIONS

SEROPREVALENCE OF VARICELLA ZOSTER VIRUS INFECTIONS IN COLOMBO DISTRICT, SRI LANKA

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ABSTRACT

BACKGROUND: *Although Varicella Zoster virus (VZV) infections occur worldwide, the epidemiology is remarkably different in tropical and temperate climates. VZV infections result in significant morbidity and mortality among adults in Sri Lanka.* ***AIMS:*** *For future VZV vaccination strategies, we set to determine the age-specific seroprevalence rate of VZV infections in Colombo, Sri Lanka.* ***MATERIALS AND METHODS:*** *The study was carried out from 1999 to 2000. Multi-stage cluster sampling technique was used to collect 913 blood samples, which were tested for the presence of VZV-specific IgG antibodies.* ***RESULTS:*** *VZV seroprevalence rates were markedly lower in all age groups when compared to temperate climates. The seroprevalence rates increased with age in both the rural and urban populations. Of those aged 60 years, only 50% in the rural population and 78.9% in the urban population were immune to VZV. Seroprevalence rates of VZV infections were significantly different between the urban and rural populations (P<0.001), with VZV-specific IgG antibodies detected in 47.5% in the urban population and 27.9% in the rural population. It was found that 56.2% (131) of females of childbearing age were nonimmune to VZV.* ***CONCLUSIONS:*** *These findings highlight the need for a VZV vaccination program, which is likely to have a huge impact on the incidence of chickenpox and its associated morbidity and mortality.*

Key words: *Colombo, seroprevalence, Varicella Zoster virus*

Varicella Zoster virus (VZV) causes chickenpox during primary infection and herpes zoster during reactivation. Chickenpox is usually a benign childhood illness, characterized by fever and a pruritic vesicular rash of a generalized distribution. However, it can give rise to serious complications such as *Staphylococcus aureus* skin infections, otitis media, pneumonia and central nervous system involvement in the form of cerebellar ataxia and encephalitis.[1] Complications due to chickenpox are more common in adults than in children,[2,3] with adults 25 times more likely to get pneumonia than children.[4]

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Although VZV infections occur worldwide, the epidemiology is remarkably different in tropical and temperate climates. In temperate climates, chickenpox is a common childhood illness and seropositivity ranges from 53 to 100% in 5 year olds.[5-7] However, the VZV infection seroprevalence patterns in tropical countries are markedly different, with chickenpox mainly affecting young adults.[8-10] For instance in India, only 29% of children were seropositive for VZV at 5 years of age,[10] and in Singapore less than 20% of those under 15 years[11] had detectable anti-VZV antibodies. Although the reasons for the difference in the epidemiology in tropical and temperate climates are incompletely understood, some have suggested that the differences in temperature and humidity could affect virus transmission.[8,12]

To date, published data on the epidemiology of VZV in Sri Lanka is very scarce as chickenpox was not a notifiable disease in the country till 2005. Currently, VZV infections are the commonest cause of admission to the infectious disease hospital in Sri Lanka, which is a specialized hospital designated to treat adult patients with a communicable disease. Approximately, 1,000 patients with VZV infections are admitted to this hospital each year.[13] Many patients develop complications such as secondary bacterial infections (62.1%), neurological complications (3.4%), pneumonia (9.1%) and carditis (1.01%) - with an overall mortality rate of 4.2%.[13] The availability of a safe and effective vaccine has renewed interest in the epidemiology of VZV infections worldwide. Vaccination against varicella is now routinely carried out in children aged between 12 and 18 months in some developed countries.[14] However, the vaccination of children in Sri Lanka is not routinely carried out. Data on the seroprevalence of antibodies protective against VZV in Sri Lanka are needed to develop strategies to prevent VZV infections and also for health economic evaluations of VZV vaccination strategies. Therefore, we conducted a study to determine the age-specific seroprevalence rate of VZV antibodies in Sri Lanka.

MATERIALS AND METHODS

The study was carried out in both urban and rural areas of Colombo district during 1999 to 2000. Urban and rural areas were defined according to the Department of Census and Statistics, Sri Lanka. The Colombo district is divided into several areas which are designated to a primary care medical officer along with a community health care team (MOH area). The Nugegoda MOH area (urban) and Kaduwela MOH area (rural) were selected from the Colombo district by simple random sampling. A multi-stage cluster sampling technique was used, and a total of 913 samples were collected. Informed written consent was obtained from all study participants, and parental consent was obtained for children less than 16 years. Pre-study publicity was arranged in all locations by the community health care staff. The study was approved by the Ethical Review Committee of the Faculty of Medical Sciences, University of Sri Jayawardanapura, Sri Lanka. Demographic data and past history of chickenpox infection were obtained by means of a self-administered questionnaire. A coding system was used to link patient information with experimental data so as to further ensure a high level of confidentiality.

Ten milliliters of venous blood was drawn from adults (1-5 ml from children). The blood samples were centrifuged, serum separated and stored at -20ºC until tested. The serum was tested for the presence of VZV IgG antibodies using a commercialized IgG enzyme-linked immunosorbent assay (ELISA) Kit (Human Gesellschaft fuer Biochemica und Diagnostica, Wiesbaden, Germany).[15] This ELISA uses cell-culture-derived VZV antigens for the detection of anti-VZV IgG antibodies in serum. The absorbance was read at 450 nm using an ELISA microtiter plate reader. The presence or absence of anti-VZV-specific IgG antibodies in the test samples was calculated according to the manufacturer's instructions. Results were obtained by comparing the antibody titers with the cut off values of the positive and negative controls.

Statistical analysis was carried out using SPSS (version 13). The chi-square test was used to determine differences in the seroprevalence rates in urban and rural populations, and the Spearmans correlation coefficient was used to determine the rise in VZV IgG seroprevalence with age.

RESULTS

Of the 913 individuals included in our study, 387 were from the urban area while 526 were from the rural area. Four hundred twenty-eight (47%) were males while 485 (53%) were females. A total of 331 individuals (36%) were seropositive for VZV infections [Table 1]. The seroprevalence rates to VZV were significantly different between the urban and rural populations ($P < 0.001$), with 184 (47.5%) of those from the urban population and 147 (27.9%) of those from the rural population being immune to the VZV. The seroprevalence rates were higher in females, with 179 (54%) being seropositive whereas only 152 (45.1%) males were seropositive. However, this difference was not statistically significant.

Age-specific seroprevalence to VZV

The seroprevalence of VZV-specific IgG antibodies increased with age in both the rural and urban populations [Figure 1]. However, the overall seroprevalence of VZV-specific IgG antibodies was lower in all age groups in the rural population when compared to the urban population. For instance at 60 years, 30/38 (78.9%) of those in the urban areas were seropositive for VZV, whereas only 20/40 (50%) were seropositive in the rural population. Furthermore, none of the children less than 5 years of age in the rural area had detectable anti-VZV IgG in their serum. One hundred thirty-one (56.2%)

Table 1: Varicella Zoster virus specific IgG antibody prevalence in the urban and rural populations according to age groups

Age (in years)	*Urban*		*Rural*	
	Number tested	*Positives (%)*	*Number tested*	*Positives (%)*
<1	2	0 (0)	1	0 (0)
1 to 4	10	1 (10)	14	0 (0)
5 to 9	61	23 (37.7)	94	15 (15.9)
10 to 14	69	17 (24.6)	149	24 (16.1)
15 to 19	49	15 (30.6)	74	17 (22.9)
20 to 29	47	22 (46.8)	34	7 (20.5)
30 to 39	55	36 (65.4)	65	32 (49.2)
40 to 49	31	23 (74.1)	38	23 (60.5)
50 to 59	25	17 (68)	17	9 (52.9)

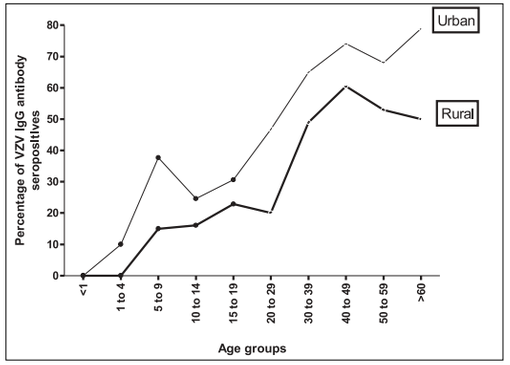

Figure 1: Age-specific VZV IgG antibody seroprevalence rates in the urban and rural populations in the Colombo district

females in both rural and urban populations of childbearing age (15-45 years) were nonimmune to chickenpox.

The association between a positive history of chickenpox and immunity to VZV

When 913 study participants were asked if they recalled an attack of chickenpox in the past, 350 (38.3%) gave a past history of chickenpox while 563 (61.7%) could not recall an attack of chickenpox in the past. Only 252 (76.1%) of those who were seropositive gave a history of exposure to chickenpox [Table 2]. Interestingly, out of the 350 individuals who claimed to have had chicken pox, 98 (28%) did not have detectable VZV-specific IgG levels in their serum. These individuals did not have any immunosuppressive illness, and they represented all age groups. Therefore, the positive predictive value of the recalled history of chickenpox with actual disease was 76.1%, and the negative predictive value of the negative past history of chickenpox was 83.1%. Furthermore, of the 252 individuals who were seropositive, 207 (82.1%) could recall the age at which they had chickenpox. Of these, 38.2% individuals said that they had chickenpox between the ages of 10 and 15 years.

Table 2: Varicella Zoster virus-specific IgG antibody status of individuals who gave a positive or negative history of chickenpox

	Positive history of chickenpox	*Negative history of chickenpox*
VZV IgG positive	252	79
VZV IgG negative	98	484
Total	350	563

VZV - Varicella Zoster virus

DISCUSSION

We report age-specific seroprevalence of VZV in an urban and a rural population in the Colombo district, Sri Lanka. The seroprevalence rates in all age groups were markedly lower in our study population than those seen in other tropical countries.[10,12] For instance, the seroprevalence rates for those aged 5 years were 29% in India,[10] 15.5% in Thailand[12] and 28.4% in Pakistan,[16] whereas in this study, the seroprevalence rates were 0% in the rural population and 8.3% in the urban population. Significant differences in seroprevalence rates were observed between the urban and rural populations. Similar findings have been observed by others, which has been attributed to higher population densities in urban areas, which facilitates transmission.[12]

The epidemiology of VZV in temperate and tropical countries is markedly different. In temperate climates, chickenpox is a common childhood illness, while chickenpox in adults is rare. In contrast, in tropical countries the incidence of chickenpox is highest among

young adults, with seroprevalence rates among children being significantly lower when compared to temperate climates.[10,12] However, the seroprevalence rates in Sri Lanka appear to be even lower than other tropical countries in South Asia. Although the reasons for these differences are not clear, it could be due to different climatic factors and cultural practices. In India the highest VZV-associated mortality is reported in the early part of the year, which is the coldest.[10,17] However, as Sri Lanka is an island lying closer to the equator, there are hardly any seasonal variations in temperature. Therefore, as previously suggested, the high temperatures seen throughout the year and the high humidity could adversely affect virus transmission.[12,17] Furthermore, in Sri Lanka chickenpox is regarded as a serious illness, probably due to the higher mortality and morbidity associated with infection in adults. Therefore, patients with chickenpox are often isolated to reduce transmission even to children. This is strikingly different to what was practiced in many Western countries before the live attenuated VZV vaccine was available. For instance, 'chickenpox parties' were considered as a way to get a child protected from more severe disease later in life, as the disease is usually less severe during childhood.

A large proportion of adults in our study were found to be seronegative for VZV-specific antibodies. For instance, at 60 years, 78.9% of those in the urban areas were seropositive for VZV, whereas only 50% were seropositive in the rural population. As VZV-specific antibody titers are not known to diminish with age,[18,19] the absence of VZV-specific antibodies in these individuals would indicate absence of exposure. This trend is particularly worrying as VZV infections are known to cause more severe disease and complications in older individuals. It is well established that cell-mediated immunity plays a crucial role in the protection against VZV infections and also against subsequent reactivation.[20,21] However, it is more laborious and expensive to screen communities for the presence of VZV-specific cell-mediated immunity and therefore precludes routine use. In addition, VZV-specific cell-mediated immunity has been shown to wane with increasing age, whereas the presence of VZV-specific antibodies does not.[22] Therefore, measuring VZV-specific IgG antibody levels could be a better indicator of past VZV exposure.

A significant proportion (56.2%) of women of childbearing age was nonimmune to VZV. VZV infections in pregnancy may have adverse effects on both the mother and the fetus, with the potential to cause congenital varicella syndrome in fetuses infected in the first trimester.[23-25] In addition, chickenpox infections in the mother may result in neonatal VZV infections which are associated with a very high morbidity and mortality.[26] Therefore, considering these facts, a VZV vaccination program in Sri Lanka is likely to have a huge impact on the incidence of chickenpox and its associated morbidity and mortality.

The predictive value of a positive history of chickenpox with actual immunity to VZV infections has been debatable. While many

studies have shown a good correlation with a positive history of chickenpox and the presence of protective antibodies in serum,[27,28] some have shown there is less correlation.[29,30] We also found the positive predictive value of a past history of chickenpox with actual immunity to be 76.1%. Furthermore, 98 (28%) individuals among those who claimed to have had chickenpox did not have any evidence of protective antibodies in their serum. Therefore, in the event of the introduction of the VZV live vaccine to Sri Lanka, these factors would have to be taken into consideration.

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