Original Article

Seroepidemiology of varicella zoster virus in healthcare workers in Babol, Northern Iran

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Abstract

Background: Varicella zoster virus (VZV) infection is one of the nosocomial infections and healthcare workers (HCWs) are at high risk group who work in the hospital with likelihood of varicella acquisition or transmission. This study evaluated the VZV seroprevalence in this high risk population in Babol, Iran.

Methods: Serological testing for VZV using enzyme linked immunosorbent assay (ELISA) was performed on 459 HCWs in Ayatollah Rouhani Hospital, Babol, Northern Iran from 2011 to 2012. A questionnaire was completed including age, gender, place of residence, marital status, history of chickenpox, educational level, working experience and risk of exposure. The data were collected and analyzed.

Results: The mean age of these subjects was 32.2±1.1 years. Four hundred-sixteen (90.6%) cases were females and 43 (9.4%) were males. The overall positive seroprevalence of VZV was 94.6%. No statistically significant differences were observed between age, gender, place of residence, risk of exposure, marital status, educational level, working experience and seropositivity. The seropositivity of varicella was seen in 278 (95.5%) of 297 cases with positive history and in 30 (81.1%) of 37 cases who did not (p=0.005).

Conclusion: The results show that a positive history of VZV is associated with positive seroprevalence but can not be a reliable indicator of the immunity, therefore, serological screening should be considered for all the HCWs.

Keywords: Seroprevalence, VZV, Healthcare workers, Iran

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Varicella zoster virus (VZV) is easily transmitted through respiratory droplets, saliva or vesicle fluid in chicken pox or shingles. It is usually self -limited in children. However, in nonimmune adults, it can cause more severe diseases. Immunocompromised patients, neonates and pregnant women are at higher risk for morbidity and mortality (1-4). In temperate climate countries, most of the cases occur before adolescence (5). In Iran, seropositivity was 83.2% by the age of 16-20 years old which is lower than most reports from the USA and European countries (6-9).

The transmission of VZV is a well – known nosocomial infection and considered as an occupational hazard for susceptible healthcare workers (HCWs), which can spread to other susceptible coworkers and patients. The center for disease control and prevention (CDC) recommended VZV vaccination for varicella susceptible HCWs (1, 4, 7-9). Based on CDC guidelines, the documentation of the appropriate vaccination is the reliable indicator of immunity to varicella (10). Different studies showed a different approach to the prevention of varicella outbreaks in hospital setting. These recommendations based on various VZV seroprevalence in different geographic regions of the world (1-4, 7-9).

With regard to these epidemiologic differences, we must adopt our prevention policy based on reliable epidemiologic data on VZV in Iran. Thus, the knowledge of these data is essential in making the best decision against varicella. Limited studies were conducted in Iran. Hence, the purpose of the present study was to determine the prevalence of VZV- IgG level among the HCWs in Ayatollah Rouhani Hospital, Babol, Northern Iran.

Methods

Between March 2011 and March 2012, a total of 459 hospital staff volunteers including nurse, aid-nurse and paramedical technician of Ayatollah Rouhani Hospital, Babol, Northern Iran participated in this study. All of these HCWs were indirect contact with the patients.

Written informed consent was obtained from all subjects and approved by the Ethics Committee of Babol University of Medical Sciences. A questionnaire was completed by all the subjects including age, gender, place of residence (urban and rural), educational level, marital status, history of chicken pox, working experience (number of years) and risk of exposure. Blood samples were obtained and sera were separated and kept at -20^{o} C until the time of examination, the enzyme linked immunosorbent assay (ELISA) using commercial kit (IBL, Hamburg, Germany) were used. Specificity and sensitivity of the test was > 95%.

According to the manufacturer´s recommendation, antibody values more the 12 Uml^{-1} were considered as seropositive, values less than 8 Uml^{-1} as seronegative and values between those two as equivocal.

The analysis was performed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA). The mean±SD values for continuous and frequencies (%) for categorical variables are expressed for healthcare workers characteristics. VZV antibody prevalence and history of varicella infection were calculated for the different variables. A $p<0.05$ was considered as the level of statistical significance level. Chi-square and Fisher exact test were used to assess the differences in proportions. Sensitivity, specificity, positive and negative predictive values of the varicella a history of previous varicella for the presence of VZV-IgG were determined.

Results

Out of the four hundred fifty-one HCWs, 43 (9.4%) were males and 416 (90.6%) were females with the mean age of 32.22±1.024 years were assessed. Generally 88.9% of the applicants were aged less than 40 years and 17.5% were classified being at higher risk of varicella infection exposure. Table 1 shows the demographic characteristics of all 459 HCWs. The prevalence of positive VZV serology was 94.6%. Twenty – two (4.7%) and 3(0.7%) serum samples were seronegative and sero-equivocal, respectively.

No significant difference was found between VZV positive seroprevalence among the different age groups. Also, there was no significant difference between the HCWs who were VZV seronegative, seropositive or sero-equivocl and gender (table 1).

A total of 328 (71.5%) participants reported about their varicella infection history, 291 (63.4%) cases with positive history, 37 (8.6%) cases with negative history and 13 (28.54%) unaware cases (table 2). Among the 291 participants who reported positive history of varicella infection, 278 (95.5%) were seropositive and 12 (4.1%) were seronegative.

From the 37 HCWs who were reported with negative history of varicella infection, 30 (81.1%) cases were seropositive and 6 (16.2%) cases were seronegative (table 1). The positive history of varicella infection was statistically associated with a higher prevalence of varicella seropositivity (95.5%vs 81.1%, p=0.005).

In the HCWs population, sensitivity of a positive history of varicella infection to identify seropositivity for VZV was 81.08% (95% CI, 0.64-0.91) while specificity was 44.67% (95% CI, 0.025-0.077). The positive predictive value (PPV) was 97% (95% CI, 0.068-0.137) whereas, negative predictive value (NPV) was 65% (95% CI, 0.41-0.84). No significant difference was seen in terms of prevalence between rural and urban residence (p=0.115). From the 459 HCWs with high risk of exposure, VZV seropositivity was reported in 96.8%.

However, there was no statistically significant difference in the seroprevalence between the HCWs who were with high risk exposure and those with normal risk exposure (94.2 vs 96.8, p=0.632). Also marital status, educational level and working experience did not have any effect on seroprevalence. (p=0.14, p=0.86 and p=0.73, respectively) (table 1).

The younger HCWs (aged <40 years), female staffs, and married HCWs more likely to informed a positive history of varicella infection (table 3).

Table 1. Baseline characteristics of study population by age groups

		N	Positive (%)	Equivocal (%)	Negative (%)
Gender	Male	26 (16.2)	14 (5.6)	3 (5.9)	43 (9.4)
	Female	134 (83.8)	234 (94.4)	48 (94.1)	416 (90.4)
Working Experience (year)	<5	156 (97.5)	183 (73.8)	12 (23.5)	351 (76.5)
	5-10	4 (2.5)	43 (17.3)	5 (9.8)	52 (11.3)
	>5	0	22 (8.9)	34 (66.7)	56 (12.2)
Marital status	Married	107 (66.9)	204 (82.3)	47 (92.8)	358 (78)
	Single	53 (33.1)	44 (17.7)	4 (7.8)	101 (2.2)
Education	<Diploma	15 (9.4)	18 (7.3)	4 (7.8)	37 (8.1)
	≥Diploma	145 (90.6)	220 (82.7)	47 (92.2)	422 (91.9)
Residental area	Rural	123 (769)	183 (73.8)	37 (72.5)	343 (74.7)
	Urban	37 (23.1)	65 (26.2)	14 (27.5)	116 (25.3)
History of VZV	Yes	91 (56.9)	162 (65.3)	38 (74.5)	291 (63.4)
	No	21 (13.1)	14 (5.6)	2 (3.9)	131 (28.5)
	Unknown	48 (30.0)	72 (29.0)	11 (21.6)	131 (28.5)
Risk of exposure	Normal	132 (82.5)	214 (86.3)	50 (98.0)	396 (86.3)
	High	28 (17.5)	34 (13.7)	1 (2.0)	63 (13.7)

Table 2. Serum result of varicella antibody by different characteristics

		N	Positive (%)	Equivocal (%)	Negative (%)	p-value
Age (year)	20-29	160	146 (91.2)	3 (1.9)	11 (9.6)	0.067
	30-39	248	240 (96.8)	0	8 (3.2)	
	>40	51	48 (94.1)	0	3 (5.9)	
Gender	Male	43	40 (93.0)	0	3 (7.0)	0.672
	Female	416	394 (94.7)	3 (0.7)		
Education	<Diploma	37	35 (94.6)	0	2 (5.4)	0.86
	≥Diploma	422	399 (94.5)	3 (0.7)	20 (90.9)	
Marital status	Married	358	341	1 (0.7)	6 (4.7)	0.14
	Single	101	93 (92.1)	2 (2.0)	6 (5.9)	
Working Experience(year)	<5	351	330 (94.0)	3 (0.9)	18 (5.1)	0.73
	5-10	52	51 (98.1)	0 (0.0)	1 (1.9)	
	>5	56	53 (12.2)	0 (0.0)	3 (5.4)	
Risk of exposure	Normal	396	373 (94.2)	3 (0.8)	20 (5.1)	0.632
	High	63	61 (96.8)	0	2 (3.2)	
History of VZV	Yes	291	278 (95.5)	1 (0.3)	12 (4.1)	0.005
	No	37	30 (81.1)		1 (2.7)	
	Unknown	131	126 (96.2)	1 (0.8)	4 (3.1)	
Residental area	Rural	343	323 (94.2)	1 (0.3)	19 (5.5)	0.115
	Urban	116	111 (95.7)	2 (1.7)	3 (2.6)	

Table 3. Distribution of selective variables in relation to history of varicella

		Yes (%)	No (%)	Unknown (%)	p-value
Age (year)	20-29	91 (56.9)	21 (13.1)	48 (30.0)	0.025
	30-39	162 (65.3)	14 (5.6)	72 (29.0)	
	>40	38 (74.5)	2 (3.9)	11 (8.4)	
Gender	Male	20 (46.5)	8 (18.6)	15 (34.9)	0.009
	Female	271 (65.1)	29 (7.0)	116 (27.9)	
Risk of exposure	Normal	37 (58.7)	4 (6.3)	22 (34.9)	0.46
	High	254 (64.1)	33 (8.3)	109 (27.5)	
Residental area	Rural	79 (36.1)	5 (4.3)	32 (27.6)	0.192
	Urban	212 (61.8)	32 (9.3)	99 (28.9)	
Marital status	Married	232 (64.8)	22 (601)	104 (29.1)	0.018
	Single	59 (58.4)	151 (14.9)	27 (26.1)	
Education	<Diploma	17 (45.9)	7 (18.9)	13 (35.1)	0.015
	≥Diploma	274 (64.9)	30 (7.1)	1178 (28.0)	
Working Experience(year)	<5	214 (61.0)	34 (9.7)	103 (29.3)	0.143
	5-10	36 (69.2)	2 (5.4)	14 (26.9)	
	>5	41 (73.2)	1 (2.7)	14 (25.0)	

Discussion

This study demonstrated the 94.6% seropositivity among the 459 HCWs and 5.4% seronegative subjects that were susceptible to VZV infection. To our knowledge, another varicella seroprevalence study among the HCWs was performed in Tehran, Iran. This study revealed 71.4% seropositivity that was lower from our results (11). Similar studies from different countries revealed various results. Lerman et al. studied VZV – antibody level among 335 HCWs with 94.4% seroprevalence which was unexpectedly high for a tropical country (3). Although, this finding is quantitavely similar to the result of our study, with regard to temperate climate of northern Iran, seropositivity should be higher in our region. The VZV seropositivity rate of 94.6% was lower than the studies carried out among the HCWs in temperate climate countries (ranging from 96% to 98.5%) (12-16).

On the other hand, in comparision to most reports from tropical countries, our result was higher (4, 17). This might be because northern Iran has a climate most likely to temperate regions. In our study, seropositivity was higher among the HCWs who were reported with positive history of VZV infection (95.5%) in comparison to those with negative history of VZV infection (81.1%). It has been accepted that 94% ≤ seropositivity is needed to protect against viral transmission in the hospital setting (18). Thus, 94.6% seropositivity among HCWs in this hospital seems sufficient to prevent varicella outbreaks. In the current study, 63.4% of HCWs recalled a history of varicella which was in the range of other studies (1, 17).

Several studies were carried out in order to assess the predictive value of a history of varicella infection. Some authors believed that a positive history of varicella infection is an excellent predictor of seropositivity. This idea was based on high seroprevalence and high PPV (1, 2, 16, 19). However, the authors insisted on a particular risk of varicella infection among the high- risk groups such as HCWs. They recommended that considering the level of risk of exposure was so critical. On the other hand, for the HCWs lifetime immunity after primary varicella infection may not be true, because of decreasing antibody levels along with repeated exposure to virus in the hospital setting. They recommended routine serological testing of VZV- IgG for high-risk groups, such as the HCWs regardless of positive varicella history (4, 11, 17, 20-22).

Although the seroprevalence rate in this study was 94.6%, but PPV was 97%, which was lower compared with some other studies (1, 12, 13). This means that the positive history of VZV infection may not guarantee protection

against varicella infection. On the other hand, 4.1% of those HCWs who recalled varicella infection were seronegative, leading to put them susceptible to hospital acquired varicella infection. Therefore, positive history alone may be unreliable and measuring VZV – IgG level must be considered for the HCWs. In the current study, 81.1% of individuals with negative VZV history were seropositive with 65% NPV. A negative history of VZV did not rule out the presence of VZV- IgG. Most previous studies recommended serology screening test for those HCWs with negative or uncertain history of VZV (1, 2, 4). In our study, no significant difference was seen between seroprevalence and the other parameters (place of residence, work experience, risk of exposure, marital status, educational level, age, gender). According to the population based study in Iran, nearly 90% of all varicella infection cases occured up to 20 years of age and this can be considered as the main reason. The limitations of our study were marked female preponderance (416 women vs. 43 men) and the small sample size. Also, we did not include the physicians in this survey. Large scale studies including all the HCWs are required.

In conclusion, the present study reveals 94.6% of our HCWS have protective antibodies against varicella. Considering the cost of VZV vaccination for all the HCWs, routine VZV IgG measuring is recommended and vaccination is reserved for the susceptible persons. The cost effectiveness of this policy needs more investigations.

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Conflict of interests: No conflicts of interest to declare.

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