

Original Article

Seroprevalence of Antibodies against Varicella Zoster Virus among Women before Marriage in Yazd, Iran

Zeynali L¹, Ayatollahi J¹, Sharifi M R¹, Tayebzadeh M A¹, Ahmadi A S², Doosti M^{1*}

1. Infectious Diseases Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

2. Department of Microbiology, Golestan University of Medical Sciences, Gorgan, Iran

Abstract

Background and Aims: Varicella-zoster virus (VZV) infection among pregnant women can cause a serious threat to the health of mother and fetus. Varicella is clearly less dangerous for immunized mothers. The aim of this study was to determine the prevalence of VZV antibody among women before marriage.

Materials and Methods: This cross-sectional study was conducted on 300 women of child-bearing age who referred to Yazd clinic for premarital screening. The enzyme-linked immunosorbent assay (ELISA) technique was performed to detect antibodies against VZV. Demographic characteristics of each participant, including age, educational level, place of residence, family and self-reported history of chickenpox were collected by a questionnaire.

Results: Mean age of women under study was 23 ± 5.4 years that 223 participants (73.7%) were seropositive, and 77 cases (25.7%) were seronegative for anti-VZV antibody, while 2 (0.6%) subjects had an equivocal result. A higher immunity ratio (86.4%) was found among older women (33-44 years). Data showed no significant correlation between immunity to VZV and age, educational level, place of residence. A statistically significant association was found between the family history, self-reported history of chickenpox and immunity to VZV. The positive and negative predictive values for self-reported history of chicken pox were 97.1% and 81.1%, respectively.

Conclusions: A significant number of women before marriage had no immunity to VZV. They are in risk of getting varicella, which can cause serious complications in mother and fetus. It, therefore, seems necessary to screen women of child-bearing age for anti-VZV antibody. In addition, vaccination against VZV in Iranian women before marriage can be a good recommendation.

Keywords: Antibody, Chickenpox, seroprevalence, Varicella-Zoster Virus

Introduction

Varicella zoster virus (VZV) is a member of the Herpesviridae family that often causes chickenpox in children (1). After a period of latency in trigeminal ganglia, VZV can be reactivate and cause shingles in adults (2). The virus is very

contagious and is transmitted to people through direct contact with the mucosa of the upper respiratory tract or the eyes (3). Varicella is usually a mild and self-limiting illness, but it may be associated with severe complications or even death in patients with weakened immune system and pregnant women (1). Women who get the varicella zoster virus during pregnancy are at risk for serious life-threatening complications including pneumonia (up to 20%) and encephalitis (up to 1%) (3).

If varicella infection occurs within the first trimester of pregnancy (weeks 1 to 12), the risk of serious birth defects is 0.5-1% (4). When a

* **Corresponding author:** Masoud doosti, Infectious Diseases Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
Tel: +98353183605, Fax: +983538224100
E mail: m.doosti58@gmail.com

woman gets the infection during the first 20 weeks of pregnancy, the risk of congenital varicella syndrome (CVS) in newborn is 2% (5). The major clinical manifestations of congenital varicella syndrome include skin lesions (73%), neurological disorders (62%), visual disturbances (52%), limb abnormality (hypoplasia malformed or paralyzed limbs) (46%), and low birth weight (23%) (6). The incidence of CVS is estimated to be 1–5 cases per 10,000 pregnancies that generates a mortality rate of 30% in the first few months of infant life (5).

The immunity against the Varicella zoster virus is complex and not understood clearly (7). Following primary infection and development of rash, VZV-antibodies produce and remain for long times in blood. Antibodies are associated with a decreased risk of reinfection. Subclinical reinfection with VZV in naturally immune persons may occur despite detectable specific neutralizing antibodies in blood (3).

Vaccination against VZV has been highly effective in reducing chickenpox in childhood (8). Despite worldwide availability of VZV vaccine in, vaccination policy is not same in all countries. Routine childhood immunization against VZV is considered in developed countries, but the VZV vaccination program has not been established in developing countries such as Iran (9). Susceptible people who did not get varicella vaccine, including pregnant women are at risk of developing a serious infection (3).

Epidemiology of chickenpox is evidently different according to the climate factor. Prevalence of VZV is higher in the temperate regions than the tropical or cold area (7). Iran is a country with three types of climate, including temperate, subtropical, and cold. Seroprevalence of VZV in West region of Iran with cold climate is 85.24% while in Southeast region with subtropical climate is 94.59% (10). Overall, in countries located within the temperate climate such as Iran, chickenpox occurs during early childhood and a large population of young adults have VZV-antibody (3). In the Iranian general population, immunity level against the varicella-zoster

virus has been reported from 71.4% to 78.5% (11). Also, VZV seroprevalence among Iranian women of child-bearing age is from 76.5% to 86.9% (12).

Immunity to VZV is very important for pregnant women. Varicella zoster virus can be transmitted to non-immune pregnant women through physical contact with an infectious patient (1). Women before and during pregnancy should be screened for VZV-antibody using laboratory tests. If women do not have enough immunity against VZV, they should receive either immunoglobulin or antiviral therapy (13). Determining the immune status of women to VZV before marriage or pregnancy is useful for healthcare system to protect mother and baby from possible complications of varicella. Research on seroprevalence of varicella in Iranian women has not been enough, especially in central regions of Iran such as Yazd province. This study aimed to evaluate the seroprevalence of antibodies against the varicella zoster virus among women before marriage in Yazd.

Methods

In this descriptive cross-sectional study, 300 women who were referred to Akbari clinic in Yazd for premarital examinations were registered. All subjects sign an informed consent for participation in research. The study was approved by the Research Committee of Yazd Shahid Sadoughi University of Medical Sciences. A 5 ml blood sample was collected from each participant. Serum was separated from each blood sample and stored at -20°C. Demographic information of participants, including their age, place of residency, education, history of chickenpox, family history and vaccination status were also recorded using the questionnaire. For detecting the VZV-IgG in serum samples, enzyme immunoassay test (ELISA) performed using a commercial kit (Viracell, Granada, Spain). Sensitivity and specificity of ELISA kit were 96%. Test was performed according to manufacturer's protocols. Positive, negative and cut-off controls were used for each test.

Antibody index was calculated using the following formula: Antibody index= (sample O.D. / cut off serum mean O.D.) x 10. Samples with indexes below 9 were considered as VZV negative. Sera were classified as positive if indexes were above 11 and as equivocal for indexes between 9 and 11. Data were analyzed by the Chi-square and Fisher exact tests using SPSS software version 17 (Chicago, IL, USA). The p-value less than 0.05 was considered statistically significant. Positive predictive value (PPV) and negative predictive value (NPV) of self-reported history of varicella were calculated using the following formulas:

$$PPV = \frac{\text{number of women with positive varicella history and positive VZV - antibody}}{\text{number of women who reported positive varicella history}}$$

$$NPV = \frac{\text{number of women with negative varicella history and negative VZV - antibody}}{\text{number of women who reported negative varicella history}}$$

Results

In this study, anti-varicella antibodies were evaluated in 300 premarital young women. Participants were ranged from 14 to 44 years with the mean (\pm SE) of 23 ± 5.4 . Most participants (56%) were in the age group of 14-23 years. Positive levels of VZV-antibody were detected in 223 (73.7%) of women and 77 cases (25.7%) were negative for anti-varicella antibody, while 2 (0.6%) subjects had an equivocal result. The frequency and prevalence of varicella antibodies in the population under study according to studied variables are summarized in Table 1. Data show that with increasing age from 14 to 44 years, the proportion of the positive anti-VZV samples is increased. There was no statistically significant relationship between immunity against varicella zoster virus and variables of age and educational level ($p > 0.05$). Furthermore, comparison of VZV prevalence between women living in Yazd province with those living in out of Yazd was not shown any significant difference ($P = 0.501$).

In the present study, a total of 210 participants (out of 300) were reported the history of having chickenpox infection, whereas 90 subjects did not remember any history of infection. Of the 210 participants with self-reported positive history of varicella, 204 (97.1%) and 4 (1.9%) were seropositive and seronegative to VZV, respectively. Therefore, positive predictive value (PPV) was equal 97.1%. Also, negative predictive value (NPV) of self-reported history of varicella was calculated as 81.1%. A significant association was obtained between immunity to varicella and history of infection ($p < 0.05$). Moreover, most persons (79.3%) with a family history of chickenpox had immunity to varicella ($p = 0.001$).

Discussion

The result of the present study showed that only 73.7% of women before marriage in Yazd had anti-varicella antibody. In a similar study conducted in Iran by Pourahmal et al., 72.7% of women who intent to marry were seropositive for VZV (13). In study of Majidi et al., the prevalence of anti-VZV antibody in women before marriage in Sanandaj was 72.1% (7). Barazesh et al. reported that the level of immunity to varicella in women of Bushehr was 74.5% (14). In other researches, the higher proportions of women were seropositive for VZV.

Serologic screening for VZV in Tehran was indicated that immunity to varicella among women population was more than 90% (15) that is higher than our finding among Yazdian women. A possible reason behind this difference is higher population density in Tehran in comparison to Yazd. In other studies, the estimated proportion of seropositivity among women in Hamadan, Kerman and Babol was 78.4%, 89.3%, and 90.2%, respectively (11, 16, 17). Therefore, in Iran with different climate zones, prevalence of VZV is varied from about 70% in cold low crowded cities to 90% in the hot crowded cities.

In compatible with previous studies (18, 19), we found that varicella seroprevalence

Table 1: Prevalence of varicella antibodies in women before marriage in Yazd

variable		Number	VZV-antibody			P value
			Positive	Negative	Equivocal	
Age (years)	14-23	168	116 (69%)	51 (30.4%)	1 (0.6%)	0.198
	24-33	110	86 (78.2%)	23 (20.9%)	1 (0.9%)	
	34-44	22	19 (86.4%)	3 (13.4%)	0	
History of chicken pox	Yes	210	204 (97.1%)	4 (1.9%)	2 (1%)	<0.05
	No	90	17 (18.9%)	73 (81.1%)	0	
Family history of varicella	Yes	198	157 (79.3%)	39 (19.7%)	2 (1%)	0.001
	No	102	64 (62.7%)	38 (37.3%)	0	
Educational level	Under Diploma	103	78 (75.7%)	25 (24.3%)	0	0.339
	Diploma	126	86 (68.3%)	39 (31%)	1 (0.7%)	
	Bachelor	64	51 (79.7%)	12 (18.8%)	1 (1.6%)	
	Master of Science	7	6 (85.7%)	1 (14.3%)	0	
Place of Residence	Yazd	296	218 (73.6%)	76 (25.7%)	2 (0.7%)	0.501
	Out of Yazd	4	3 (75%)	1 (25%)	0	

increases from 69% among women 14-23 years old to 86.4% in women 34-44 years, which confirmed the more immunity against the Varicella zoster virus in the older women. Studies in some countries reported higher proportion of anti-VZV seroprevalence than that we obtained in the present study. In

Croatia, the prevalence of VZV-antibody among women of child-bearing age reported equal 84.3% (18). In Italy (19), Tunisia (20) and Korea (21), it has been reported 80.9%, 80.9% and 89.6%, respectively. In 2007, 96.1% of Spanish women during their fertility period were immune to VZV (22). In Belgium,

the prevalence of Anti-VZV IgG among young women was 100% (23). In addition to demographic, climatic, and socioeconomic factors, the performance of the varicella vaccination program in developed countries may partly explain the difference between these findings and our result.

In agreement with our results, in some studies was not significant association between prevalence of VZV antibody and place of residence or educational levels (7, 11, 14, 16, 18, 22). Many studies have indicated a statistically significant relationship between history of chickenpox and immunity to varicella (15, 17). In the present study, the validity of self-reported history of varicella was evaluated considering the result of serological tests in participants. The PPV and the NPV of self-reported history of chicken pox were 97.1% and 81%, respectively, that were strong predictors of VZV immunity. Compatible with our data, Hosseininasab et al. found that the PPV and the NPV of varicella history in women population were 94% and 85%, respectively (17). Majidi and colleagues reported a PPV of 94.5% and a NPV of 50.7% for self-reported history of chicken pox in premarital women (7). Pourahmad et al. reported that the PPV of women with positive history of chickenpox was 79.5% and the NPV of those with negative history of chickenpox was 30.5% (13). In contrast to our finding, Talebi-Taher et al. obtained a NPV of 13.8% as a poor predictor of Varicella immunity (15). Also, Linder et al. estimated that a woman with a negative chickenpox history had a NPV of 6.8% (24).

In conclusion, in the present study, the mean of marital age was 23 years. Proportion of VZV-seronegative women was 30.4% at age group 14-23 and 20.9% among 24-33 years participants. Thus, the VZV screening of women under 30 years, especially who report no varicella history is recommended. According to our findings, seroprevalence of anti-varicella antibody among Yazdian women of child-bearing age is under 80% similar to the other regions of Iran. This shows that a noticeable proportion of young women is susceptible to the varicella-zoster virus. This

makes women vulnerable to virus and increases the possibility of birth defects. VZV vaccination in developed countries is decreased the incidence of varicella infection and is declined the rate of abnormality in the fetus. Therefore, vaccination of Iranian women against chickenpox before marriage and pregnancy can be considerable.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

1. Ho DY, Arvin AM. Varicella Zoster Virus Infections. Thomas' Hematopoietic Cell Transplantation, Fifth Edition. 2016;1085-110.
2. Zerboni L, Arvin AM. The pathogenesis of varicella-zoster virus neurotropism and infection. Neurotropic viral infections: Springer; 2016. p. 135-73.
3. Fields B, Knipe D, Howley P. Fields virology. 6th.: Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2013.
4. Jassawalla VWM. Manual of Perinatal Infections: Jaypee Brothers; 2008.
5. Villota VA, Delgado J, Pachajoa H. Congenital varicella syndrome in a monochorionic diamniotic twin pregnancy. Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences. 2014;19(5):474-6.
6. Sauerbrei A, Wutzler P. Fetales varizellensyndrom. Monatsschrift Kinderheilkunde. 2003;151(2):209-13.
7. Parviz Majidy MK, Namam-Ali Azadi. Seroprevalence of Varicella zoster virus antibody among young women before marriage in Sanandaj, Iran. IRANIAN JOURNAL OF MICROBIOLOGY. 2016;8(2):147-52.
8. Lili Wang LZaHZ. Efficacy of varicella (VZV) vaccination: an update for the clinician. Therapeutic Advances in Vaccines. 2016;4(1-2):20-31.
9. Sadzot-Delvaux C, Rentier B, Wutzler P, Asano Y, Suga S, Yoshikawa T, et al. Varicella vaccination in Japan, South Korea, and Europe. The Journal of infectious diseases. 2008;197 Suppl 2:S185-90.
10. Hoseini SG, Kelishadi R, Kasaeian A, Ataei B, Yaran M, Motlagh ME, et al. Seroprevalence and Risk Factors of Varicella Zoster Infection in

Iranian Adolescents: A Multilevel Analysis; The CASPIAN-III Study. PloS one. 2016;11(6):e0158398.

11.Mamani M, Zamani M, Hashemi SH, Akhtari M, Niayesh A. Seroepidemiology of varicella-zoster virus among pregnant women in Hamedan, Iran. African Journal of Microbiology Research. 2012;6(8):1829-32.

12.Ziyaeyan M, Alborzi A, Jamalidoust M, Moieni M, Pourabbas B. Seroepidemiology of varicella zoster virus infection among 1-70 year individuals in Iran. Iranian Red Crescent Medical Journal. 2010;2010(2):176-80.

13.Pourahmad M, Davami MH, Jahromi ARS. Evaluation of anti-varicella antibody in young women before their marriage: A sero-epidemiologic study in Iran. Journal of Clinical Virology. 2010;48(4):260-3.

14.Barazesh A, Zandi K, Hadavand F, Moatamed N, Hefzollah F, Hefzollah B, et al. Seroepidemiology of Rubella, Cytomegalovirus, Herpes simplex & Varicella zoster virus in college women of Bushehr. ISMJ. 2014;16(6):459-66.

15.Mahshid Talebi-Taher1 MK, Katayoon Khalili3. Seroprevalence of varicella-zoster virus among pregnant women in two teaching hospitals, Tehran, Iran. IRANIAN JOURNAL OF MICROBIOLOGY. 2013;6(1):37-40.

16.Bayani M, Siadati S, Esmailzadeh S, Asgari S, Salmani S. Seroprevalence of Varricella Zoster Antibodies among Pregnant Women in Babol, Northern Iran. Iranian Journal of Pathology. 2013;8(3):171-7.

17.Hosseininasab A, Arabzadeh A-M, Haghdooost AA, Helmi Z. Immunity against varicella zoster virus based on history of previous chickenpox: a study in premarital Iranian women. International Journal of Infectious Diseases. 2013;17(7):e568-e9.

18.Vilibic-Cavlek T, Ljubin-Sternak S, Kolaric B, Kaic B, Sviben M, Kos L, et al. Immunity to varicella-zoster virus in Croatian women of reproductive age targeted for serology testing. Archives of gynecology and obstetrics. 2012;286(4):901-4.

19.Alfonsi V, Montomoli E, Manini I, Alberini I, Gentile C, Rota MC, et al. Susceptibility to varicella in childbearing age women, Central Italy: Is there a need for vaccinating this population group? Vaccine. 2007;25(32):6086-8.

20.Hannachi N, Marzouk M, Harrabi I, Ferjani A, Ksouri Z, Ghannem H, et al. Seroprevalence of rubella virus, varicella zoster virus, cytomegalovirus and parvovirus B19 among pregnant women in the Sousse region, Tunisia. Bulletin de la Societe de pathologie exotique (1990). 2011;104(1):62-7.

21.Lee H, Cho HK, Kim KH. Seroepidemiology of varicella-zoster virus in Korea. Journal of Korean medical science. 2013;28(2):195-9.

22.Plans P, Costa J, Espuñes J, Plasencia A, Salleras L. Prevalence of varicella-zoster antibodies in pregnant women in Catalonia (Spain). Rationale for varicella vaccination of women of childbearing age. BJOG: An International Journal of Obstetrics & Gynaecology. 2007;114(9):1122-7.

23.Thiry N BP, Shkedy Z, et al. The seroepidemiology of Primary varicella zoster virus infection in Flanders (Belgium). Europ J of Ped. 2002;161:588-93.

24.Linder N, Ferber A, Kopilov U, Smetana Z, Barzilai A, Mendelson E, et al. Reported exposure to chickenpox: a predictor of positive anti-varicella-zoster antibodies in parturient women. Fetal diagnosis and therapy. 2001;16(6):423-6.