



Seroprevalence of Varicella Zoster Infection at Provincial Level in Iranian Adolescents: The CASPIAN-III Study

Seyed Naseredin Mostafavi,¹ Shervin Ghaffari Hoseini,² Roya Kelishadi,¹ Behrooz Ataei,³ Omid Safari,⁴ Majid Yaran,⁵ Mohammad Esmaeil Motlagh,⁶ Ramin Heshmat,⁷ Aryan Madady,⁸ Gelayol Ardalan,¹ Rasool Mohammadi,⁹ Mohamad Hasan Tajadini,¹ and Mostafa Qorbani^{10,11,*}

¹Pediatrics Department, Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-Communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran

²Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

³Nosocomial Infection Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

⁴Pediatrics Department, Alborz University of Medical Sciences, Karaj, Iran

⁵Acquired Immunodeficiency Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

⁶Pediatrics Department, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

⁷Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

⁸Student Research Committee, Alborz University of Medical Science, Karaj, Iran

⁹Department of Epidemiology, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran

¹⁰Non-communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, Iran

¹¹Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

*Corresponding author: Mostafa Qorbani, Non-communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, Iran. E-mail: mqorbani379@yahoo.com

Received 2016 July 16; Revised 2016 December 03; Accepted 2016 December 28.

Abstract

Background: Although primary varicella zoster virus (VZV) infection (chicken pox) is a mild childhood disease, it can cause severe infection with complications in adults. As the disease is preventable by effective vaccination, it is important to determine the level of immunity to VZV in every region to implement proper vaccination strategies.

Objectives: The aim of this study was to investigate the seroprevalence of VZV infection in adolescents living in different provinces of Iran.

Methods: In a cross-sectional multicentre study, serum samples from 2315 students, aged 10 - 18 years, were examined for VZV antibodies (IgM/IgG). Students were selected by multistage cluster sampling during a national surveillance program.

Results: Prevalence of VZV antibodies was statistically different in various provinces of Iran ($P = 0.001$); it ranged from 82.4% in Isfahan, Center of Iran, to 98.5% in Mazandaran, North of the country. The VZV seroprevalence was not significantly different by gender, except for Khuzestan, South of Iran, where antibodies were much more prevalent in girls (92.7%) than in boys (78.3%, $P = 0.004$). Seroprevalence was not significantly different according to the living area (urban/rural).

Conclusions: VZV seroprevalence is different in various provinces of Iran; the susceptibility of adult population to VZV infection is suggested to be high in Ardabil, Isfahan, and Kermanshah; and low in Kerman and Mazandaran. Therefore, different strategies should be implemented in each province to protect high-risk adults from severe varicella infection.

Keywords: Chickenpox, Prevalence, Iran, Prevention

1. Background

Varicella (chickenpox) is a vaccine-preventable disease with universal distribution. The childhood illness is usually mild and self-limiting, but in some individuals including adults, health care workers, pregnant women and immune compromised patients, the disease could be severe and even life threatening (1).

The epidemiology of varicella varies considerably between countries and different regions within countries.

The most important determinant in this variability is the climate and humidity of each region, as well as socio-demographic factors and population density. Most people who live in areas with temperate climate are infected during childhood that uncommonly becomes severe or complicated; whereas in tropical areas, varicella usually occurs in adolescents and adults who usually have more severe disease and are at higher risk of complications (2). However, because of interaction of social factors with climatic

elements, there are several exceptions to this rule, accounting for the role of cultural factors in epidemiology of the varicella (3).

Iran is a vast country (the second largest in terms of land size in the Middle East) with 31 provinces that have variable climates ranging from temperate to subtropical. While Central Plateau provinces of the country experience hot, dry, and desert climates, North West provinces have cold snowy climate. Southern provinces along the Persian Gulf and Oman Sea are desert, hot, and with high humidity in some areas. A few provinces along the Caspian coast have mild semi-humid climate (4). Considering the variation of the climate in Iran, and also the diversity of other risk factors of varicella infection such as socio-demographic factors, it is expected that the epidemiology of the infection is different across the provinces.

Several sero-epidemiological studies on varicella have been performed in Iran, but neither was representative of the population in the community. These studies mainly were restricted to a city in a province or performed in specific sub-populations of the society, like healthcare workers, pregnant or premarital women, hemodialysis patients, referees to hospitals, medical students, and children of a small number of schools (5).

2. Objectives

As severe VZV infections occur more commonly in adults than in children (6), understanding the seroprevalence of varicella in adolescents of each region is important in order to determine local health priorities and implement proper preventive policies. Hence, this study was conducted to compare the seroprevalence of varicella in a representative sample of adolescents in 15 out of 31 provinces of Iran.

3. Methods

The current study was conducted on serum samples of the third survey of a national school-based surveillance system in Iran, entitled "childhood and adolescence surveillance and prevention of adult non-communicable disease" (CASPIAN) study (2009 - 2010). Participation in the study was voluntary. The participants entered the survey after explaining the study objectives and protocols and obtaining written consent from their parents. The information bank of ministry of education was used as the base of stratification of selected schools. Residence (urban/rural) and school grade (elementary/intermediate/high school) were considered for stratification of schools. Considering equal sex ratios, 5625 students aged 10 - 18 years were selected as study participants.

For data gathering phase, all processes of examinations with calibrated instruments and recording of information in validated checklists were designed and conducted under the standard protocol by trained health care professional teams (7). The questionnaires were filled out by one of the parents. Blood samples were obtained by trained experts and tested at selected provincial laboratories and residual serum samples were stored at -70 °C. Details of the study methodology have been published before (7).

We assessed seroprevalence of varicella zoster infection at provincial level in Iranian adolescents who were selected via multistage random cluster sampling method from urban and rural areas of 15 provinces in Iran. The ethics committees of Alborz University of Medical Sciences and Isfahan University of Medical Sciences approved the project and all protocols (projects number: 2015.65.786 and 294255-7).

In the current study, through quality assessment, blood samples that could not receive the required standard quality were excluded. Minimum sample size for estimation of VZV prevalence in each province was calculated as 90, by considering an expected prevalence of 60%, level of confidence of 95%, and a precision of 10%. Provinces with a lower sample size were excluded from the study. Appropriate samples from 15 provinces were sent to the laboratory of infectious diseases and tropical medicine research center, Isfahan University of Medical Sciences. Total antibodies for VZV (IgM/IgG) were assessed by a commercial enzyme linked immunosorbent kit (Viracell, Granada, Spain) with a sensitivity of 98% and specificity of 97%, based on the instruction of the kit.

Data were analysed using survey data analysis methods in the STATA Corp. 2011 (Stata statistical software: release 12. College station, TX: Stata corp LP. package). We reported the prevalence of positive varicella zoster antibody at provincial level by sex, age groups, and living areas [number (percentage)]. $P < 0.05$ was considered statistically significant.

4. Results

The study participants consisted of 2315 students (boys = 1168, girls = 1144) with a mean age of $14.38 (\pm 2.5)$ years. The prevalence of varicella zoster antibody at provincial level is shown in Table 1. Seroprevalence of VZV was statistically different in various provinces ($P = 0.001$).

Overall, VZV seroprevalence in different provinces ranged from 82.4% in Isfahan, center of Iran, to 98.5% in Mazandaran, north of Iran. Prevalence of the antibodies in boys and girls of various provinces was not statistically different except for Khuzestan, South of Iran, where antibodies were significantly more prevalent in girls (92.7%) than

in boys (78.3%, $P = 0.004$). Living area (urban/rural) was not associated with the VZV prevalence in any of the provinces.

In all of the provinces except for Isfahan, Kerman, and Gilan, the prevalence was higher in 15-18-year-old students than in 10-14-year-old group. The difference between the two age groups was statistically significant in Khorasan Razavi (74.6% vs. 91.9%, $P = 0.011$), Khuzestan (80.6% vs. 90.5%, $P = 0.019$), and Lorestan (82.2% vs. 94.7%, $P = 0.007$).

5. Discussion

Our study revealed considerable variation in the prevalence of VZV infection in various provinces in Iran, varying from 82% to 98%. The overall prevalence of VZV in Iranian adolescents has been previously reported as 87.5% (8). Minimizing the burden of VZV infection can be achieved by vaccination; however, it is necessary to select an accurate and cost-effective vaccination strategy in each area. Our results suggest that mass vaccination is not required in none of the surveyed provinces, as more than 80% of the adolescents in all provinces are immune to the infection. However, examination and vaccination of high-risk groups such as women of childbearing age, health care providers, day-care personnel, military personnel, teachers, and college students, might be necessary.

VZV prevalence in some provinces such as Kerman and Mazandaran was greater than 95%. The risk of severe or complicated primary varicella infections in these states appears to be low, and VZV vaccination in these areas seems unnecessary. In contrast, in provinces such as Ardabil, Isfahan, and Kermanshah, more than 15% of adult populations are considered susceptible to VZV infection. Local health authorities in these areas should plan strategies to minimize VZV burden in adult population especially in pregnant and immunodeficient individuals. In other provinces, VZV seroprevalence is at intermediate level.

In previous studies in adolescents of various parts of Iran, VZV seropositivity in 11-15-year age group was reported as 63.9% and 39.6% in Tehran city in Tehran province and Kashan city in Isfahan province, respectively (9, 10). Our study showed the prevalence of 88.2% and 82.9% in 10-14-year-old participants in Tehran and Isfahan provinces, respectively. The VZV prevalence in women aged 16-20 years was 77.8% in Tehran city in Tehran province (11) and 85.1% in Babol city in Gilan province (12). The VZV prevalence in our study in 15-18 years was 88.3% in Tehran and 88.4% in Gilan provinces, respectively. The difference in the results could be related to sampling method and the population under study in different surveys. We selected samples with multi stage cluster random method, which provided a representative sample of the adolescent population, while the above-mentioned studies selected their

samples from those referring to hospitals or public health centres in their study area. Moreover, different prevalence rates in various cities of each province could be another explanation for the differences in the study findings.

We did not find any difference in the rate of immunity to VZV between boys and girls except for Khuzestan province, where girls had higher immunity than boys did. This finding could be accidental or might be due to the cultural context of that province. There is no previous study in this province to compare VZV prevalence in two sexes. However, no difference was found in the VZV seropositivity in other studies in Iran (5) and some other parts of the world (13-15).

Our study is a multi-center epidemiological study with representative samples from adolescents in several provinces of Iran that provides the possibility of comparing seroprevalence of VZV in adolescents of those provinces. One limitation of the study was depletion of some serum samples from a number of provinces in previous laboratory procedures and exclusion of other provinces from the study. Another limitation was not including other age groups especially 6-9-year-old individuals in the study. Inclusion of these populations would give a more comprehensive picture of the epidemiology of VZV in different provinces of Iran.

5.1. Conclusion

VZV prevalence is different in various parts of Iran. The susceptibility of adolescent population to VZV infection in Ardabil, Isfahan, and Kermanshah is high, especially in 10-14-year old children who are in the beginning age of symptomatic VZV infection; however, this rate is low in Kerman and Mazandaran. Thus, it is suggested to implement different strategies in each area to protect high-risk adults from severe varicella infection.

Acknowledgments

The authors gratefully acknowledge the large team of CASPIAN study for providing samples and demographic data of the participants.

Footnote

Authors' Contribution: Study concept and design: Mostafa Qorbani, Seyed Naseredin Mostafavi, Roya Kelishadi, Shervin Ghaffari Hoseini. Acquisition of data: Majid Yaran, Mohammad Esmaeil Motlagh, Ramin Heshmat, Gelayol Ardalan, Omid Safari, Mohamad Hasan Tajadini, Aryan Madady, Rasool Mohammadi. Analysis and interpretation of data: Mostafa Qorbani, Shervin Ghaffari Hoseini.

Table 1. Seroprevalence of Varicella Zoster at Provincial Level by Sex, Living Place, and Age Groups: The CASPIAN III Study^a

Province	Sex		P Value	Living Place		P Value	Age Group, y		P Value	Total	Total
	Boy	Girls		Urban	Rural		10 - 14	15 - 18			
West Azerbaijan	65 (84.4)	61 (91)	0.23	91 (89.2)	35 (83.3)	0.33	51 (83.6)	75 (90.4)	0.22	126 (87.5)	144
Ardabil	78 (79.6)	90 (88.2)	0.09	110 (82.7)	58 (86.6)	0.48	58 (79.5)	110 (86.6)	0.18	168 (84.0)	200
Isfahan	63 (86.3)	49 (77.8)	0.19	82 (83.7)	30 (78.9)	0.51	63 (82.9)	49 (81.7)	0.85	112 (82.4)	136
Tehran	113 (90.4)	98 (86)	0.28	160 (87.9)	51 (89.5)	0.74	75 (88.2)	136 (88.3)	0.98	211 (88.3)	237
Khorasan Razavi	69 (87.3)	66 (83.5)	0.49	102 (88.7)	33 (76.7)	0.06	44 (74.6)	91 (91.9)	0.011	135 (85.4)	158
North Khorasan	54 (91.5)	47 (82.5)	0.14	35 (81.4)	66 (90.4)	0.16	38 (82.5)	63 (91.5)	0.119	101 (87.1)	116
South Khorasan	52 (92.9)	44 (84.6)	0.17	69 (88.5)	27 (90)	0.82	42 (85.5)	54 (91.5)	0.33	96 (88.9)	108
Khuzestan	72 (78.3)	89 (92.7)	0.004	113 (83.1)	48 (92.3)	0.10	75 (80.6)	86 (90.5)	0.019	161 (85.6)	188
Kurdistan	68 (88.3)	56 (86.2)	0.7	59 (84.3)	65 (90.3)	0.28	64 (86.5)	60 (88.2)	0.75	124 (87.3)	142
Kerman	60 (96.8)	46 (97.9)	0.72	64 (97)	42 (97.7)	0.82	37 (100)	69 (95.8)	0.20	106 (97.2)	109
Kermanshah	97 (85.8)	99 (81.8)	0.40	110 (84.6)	86 (82.7)	0.69	64 (82.1)	132 (84.6)	0.61	196 (83.8)	234
Gilan	55 (91.7)	60 (87)	0.39	71 (91)	44 (86.3)	0.39	54 (90)	61 (88.4)	0.77	115 (89.1)	129
Lorestan	58 (86.6)	70 (89.7)	0.55	123 (87.9)	5 (100)	0.40	56 (82.2)	72 (94.7)	0.007	128 (88.3)	144
Mazandaran	67 (97.1)	65 (100)	0.16	106 (98.1)	26 (100)	0.48	50 (96.2)	82 (100)	0.07	132 (98.5)	134
Yazd	57 (89.1)	61 (84.7)	0.45	67 (88.2)	51 (85)	0.58	57 (86.4)	61 (87.1)	0.89	118 (86.8)	136

^aValues are expressed as seropositive (%) unless otherwise indicated.

Drafting of the manuscript: Seyed Naseredin Mostafavi, Mostafa Qorbani, Shervin Ghaffari Hoseini. Critical revision of the manuscript for important intellectual content: Seyed Naseredin Mostafavi, Roya Kelishadi, Behrooz Ataei, Majid Yaran, Mohammad Esmaeil Motlagh, Ramin Heshmat, Ardalan, Omid Safari, Mohamad Hasan Tajadini, Aryan Madady, Rasool Mohammadi. Statistical analysis: Mostafa Qorbani, Shervin Ghaffari Hoseini. Study supervision: Roya Kelishadi, Behrooz Ataei

References

- Gould D. Varicella zoster virus: chickenpox and shingles. *Nurs Stand*. 2014;**28**(33):52–8. doi: [10.7748/ns2014.04.28.33.52.e8249](https://doi.org/10.7748/ns2014.04.28.33.52.e8249). [PubMed: [24734838](https://pubmed.ncbi.nlm.nih.gov/24734838/)] quiz 60.
- Varicella and herpes zoster vaccines: WHO position paper, June 2014. *Wkly Epidemiol Rec*. 2014;**89**(25):265–87. [PubMed: [24983077](https://pubmed.ncbi.nlm.nih.gov/24983077/)].
- Nichols RA, Averbek KT, Poulsen AG, al Bassam MM, Cabral F, Aaby P, et al. Household size is critical to varicella-zoster virus transmission in the tropics despite lower viral infectivity. *Epidemics*. 2011;**3**(1):12–8. doi: [10.1016/j.epidem.2010.11.003](https://doi.org/10.1016/j.epidem.2010.11.003). [PubMed: [21420656](https://pubmed.ncbi.nlm.nih.gov/21420656/)].
- Amiri MJ, Eslamian SS. Investigation of climate change in Iran. *J Environ Sci Technol*. 2010;**3**(4):208–16.
- Allami A, Mohammadi N. Varicella immunity in Iran: an age-stratified systematic review and meta-analysis. *Iran J Microbiol*. 2014;**6**(6):372–81. [PubMed: [25926953](https://pubmed.ncbi.nlm.nih.gov/25926953/)].
- Cherry J, Demmler-Harrison GJ, Kaplan SL, Steinbach WJ, Peter J Hotez PJ. In: Feigin and Cherry's textbook of pediatric infectious diseases. Anne AG, editor. 7th. Philadelphia: Saunders; 2014. Varicella zoster virus.
- Kelishadi R, Heshmat R, Motlagh ME, Majdzadeh R, Keramatian K, Qorbani M, et al. Methodology and Early Findings of the Third Survey of CASPIAN Study: A National School-based Surveillance of Students' High Risk Behaviors. *Int J Prev Med*. 2012;**3**(6):394–401. [PubMed: [22783465](https://pubmed.ncbi.nlm.nih.gov/22783465/)].
- 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. doi: [10.1371/journal.pone.0158398](https://doi.org/10.1371/journal.pone.0158398). [PubMed: [27355931](https://pubmed.ncbi.nlm.nih.gov/27355931/)].
- Pourakbari B, Shahbaznezhad L, Parvaneh N, Nikkha S, Mahmoudi S, Teymuri M, et al. Seroepidemiology of Varicella Zoster Virus among children, adolescents and medical students in a referral children medical center, Tehran, Iran. *Iran J Microbiol*. 2012;**4**(3):136–8. [PubMed: [23066488](https://pubmed.ncbi.nlm.nih.gov/23066488/)].
- Taghavi Ardakani A, Soltani B, Sehat M, Namjoo S. Seroprevalence and risk factors of varicella-zoster among children of Kashan-center of Iran. *Jundishapur J Microbiol*. 2013;**6**(5).
- Talebi-Taher M, Kashanian M, Khalili K. Seroprevalence of varicella-zoster virus among pregnant women in two teaching hospitals, Tehran, Iran. *Iran J Microbiol*. 2014;**6**(1):37–40. [PubMed: [25954490](https://pubmed.ncbi.nlm.nih.gov/25954490/)].
- Bayani M, Siadati S, Esmaeilzadeh S, Asgari S, Salmani S. Seroprevalence of varicella zoster antibodies among pregnant women in babol, northern Iran. *Iran J Pathol*. 2013;**8**(3):171–7.
- Alp H, Altinkaynak S, Ertekin V, Kilicaslan B, Gıiraksin A. Seroepidemiology of varicella-zoster virus infection in a cosmopolitan city (Erzurum) in the eastern Turkey. *Health Policy*. 2005;**72**(1):119–24. doi: [10.1016/j.healthpol.2004.03.008](https://doi.org/10.1016/j.healthpol.2004.03.008). [PubMed: [15760704](https://pubmed.ncbi.nlm.nih.gov/15760704/)].
- Lolekha S, Tanthiphabha W, Sornchai P, Kosuwan P, Sutra S, Warachit B, et al. Effect of climatic factors and population density on varicella zoster virus epidemiology within a tropical country. *Am J Trop Med Hyg*. 2001;**64**(3-4):131–6. [PubMed: [11442207](https://pubmed.ncbi.nlm.nih.gov/11442207/)].
- Vergara-Castaneda A, Escobar-Gutierrez A, Ruiz-Tovar K, Sotelo J, Ordonez G, Cruz-Rivera MY, et al. Epidemiology of varicella in Mexico. *J Clin Virol*. 2012;**55**(1):51–7. doi: [10.1016/j.jcv.2012.06.004](https://doi.org/10.1016/j.jcv.2012.06.004). [PubMed: [22750018](https://pubmed.ncbi.nlm.nih.gov/22750018/)].