Iranian Journal of Pathology (2013) 8 (3), 171 - 177

Original Article

Seroprevalence of *Varricella Zoster* Antibodies among Pregnant Women in Babol, Northern Iran

Masomeh Bayani[1], Sepideh Siadati[2], Seddigheh Esmaeilzadeh[3], Samaneh Asgari[2], Saeed Salmani[1]

1- Infectious Disease Research Center, Babol University of Medical Sciences, Babol, Iran
2- Dept. of Pathology, Babol University of Medical Sciences, Babol, Iran
3- Fatemeh Zahra Infertility and Reproductive Health Research Center, Babol University of Medical Sciences, Babol, Iran

ABSTRACT

Background and Objectives: **Chicken pox has potential complications during pregnancy for both the mother and her baby. The aim of this study was to determine the *Varicella-Zoster* virus (VZV) immune status in pregnant women in Babol and its surrounding neighborhoods.**

Materials and Methods: **This seroepidemiological study was carried out on 427 pregnant women referred to Rohani Hospital, Babol, northern Iran from 2010 to 2011. The immune status (IgG level) was determined using ELISA method and correlation with age, place of residence, history of VZV infection and the number of siblings were evaluated.**

Results: **The mean age of the subjects was 27.16 $\pm$ 5.7 years and their mean antibody level was 103.552 + 63.37 U/ml. Out of 427 pregnant women studied, 8.7% were seronegative, 1.2% were equivocal and 90.2% were seropositive. There was no correlation between age, the place of residence (urban or rural) and titer of antibody. However, higher antibody titer was found in women with more siblings.**

Conclusion: **Considering 90.2% of pregnant women were VZV seropositive, evaluation of VZV antibody in order to prevent complications in non-immune pregnant women and vaccination for women with age less than 25 years old and no VZV infection history, prior to pregnancy is recommended.**

Keywords: **Seroprevalence, VZ Virus, Pregnant Women, Iran**

Received : 21 November 2012
Accepted: 09 January 2013
Address Communications to : Dr. Sepideh Siadati. Department of Pathology, Babol Unversity of Medical Sciences, Babol, Iran
E-mail : Siadati_sepideh@yahoo.com

Introduction

Varicella zoster virus (VZV), a human alpha- herpes virus, is the causative agent of varicella (chicken pox) in childhood and herpes zoster (shingles) as a latent infection (1-4). Although, varicella is usually a mild and self- limited disease, it can cause serious complications or even death in healthy adults, immunocompromised patients and neonates (1-6). The primary infection of VZV in pregnant women can have consequences for both the mother (pneumonia, encephalitis) and the fetus (1,6-10). Primary infection during the first 20 weeks of pregnancy could be associated with congenital varicella syndrome (CVS), including limb hypoplasia and neurologic abnormalities. The risk of CVS in about 1-2% (3, 7, 8). Varicella infection during the third trimester or close to delivery can result in VZV infection in neonate with 20% mortality rate (3, 8, 10, 11).

Despite general use of varicella vaccine in children in many developed countries, routine immunization against VZV is not yet practiced in Iran.

In temperate climate countries, chicken pox occurring mostly during childhood and seroconversion occurred by early adolescence (1, 4, 7, 11, 12). According to the different studies in Iran, seropositivity was 83.2% in the age range of 16-20 and increasing to 86.9% in those people over 20 years old. For women in childbearing age, seroprevalence was reported 76.5% to 86.9% (1-3).

The objective of this study was to determine the seroprevalence of VZV in pregnant women in the city of Babol and its surrounding neighborhoods, northern Iran.

Material and Methods

From September 2010 to February 2011, a seroprevalence study of varicella antibodies was performed on pregnant women referred to Rohani Hospital, Babol. Informed consent was obtained from all women and approved by the Ethics Committee of Babol University of Medical Sciences. A questionnaire was completed including the age, place of residence, history of chicken pox and the number of siblings.

Five ml blood sample was obtained from each individual, and separated sera were stored at -20 ^{o}C until analysis. Serum samples were tested for anti- VZV IgG antibodies using a commercially available enzyme- linked immunosorbent assay (ELISA) kit (IBL, Hamburg, Germany).

Both sensitivity and specificity of the test was> 95%. Based on the manufacturer's guidelines, antibody level less than 8 U/ml was considered negative, antibody level more than > 12 U/ml was considered positive, indicating previous infection and immune protection against VZV, while levels ranging from 8 to 12 were considered equivocal.

Statistical analysis

Quantitative values of the data were showed as mean $\pm$ SD. Mean comparisons for continues variables were done using t-test and one way ANOVA. Comparison for categorical subjects was done using Chi-square tests. A P-value of <0.05 was considered as significant level using 2-sided comparisons.

Results

Anti- varicella antibody was evaluated in 427 pregnant women with 27.16 $\pm$ 5.7 (age range 16-50 years). The antibody titer mean value was 103.552 $\pm$ 68.37 UML, with minimum and maximum values of 0 and 327 U/ml, respectively. There was no correlation between the age of the women and their antibody titer (cor= -0.007, *P*= 0.88). From 427 subjects, 385 (90.2%) were positive, 37 (8.7%) were negative and 5 (1.2%) were equivocal for antibody titer. Table 1 demonstrated that in all age groups no relation was found between these age categories and antibody titers (*P*=0.24).

Figure 1 demonstrated the mean levels of antibody titer in each age category. The highest mean antibody titer was seen in the age group 30 – 39 years old.

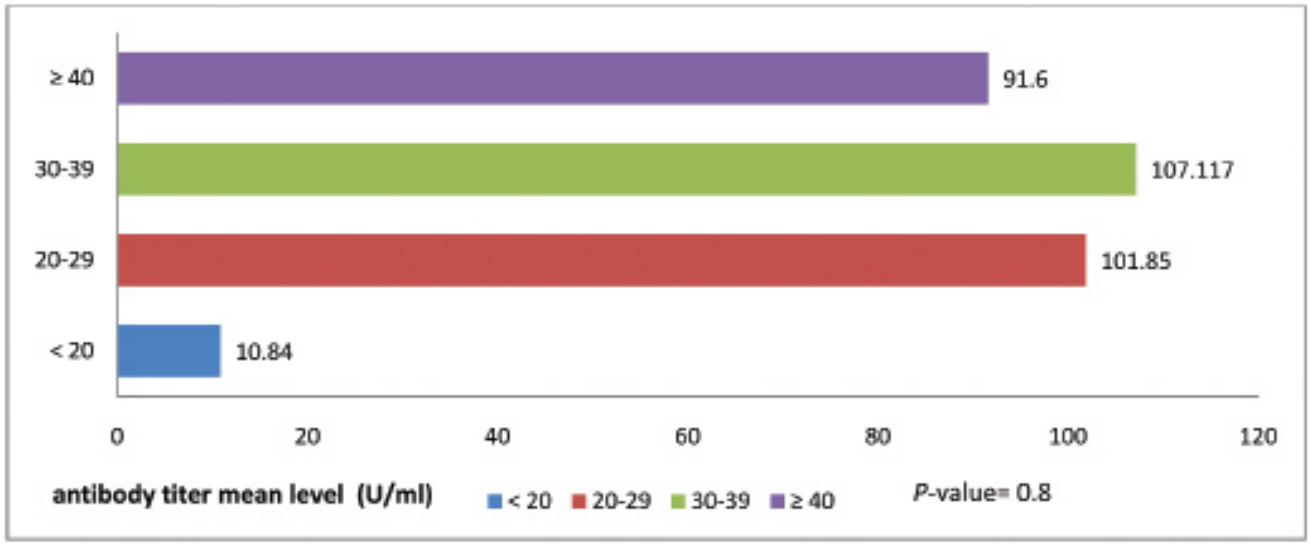

Fig. 1- Mean antibody titer in different age groups

Out of 427 participants who answered the question about the history of varicella infection, a positive history was reported in 231 (54.1%), whereas, 88 (20.6%) reported a negative history and 108 (25.3%) had an uncertain history of infection. Out of 231 subjects who reported a positive history of infection, 216 (93.5%) and 13 (5.6%) were seropositive and seronegative, respectively, and two had equivocal test (Table 1).

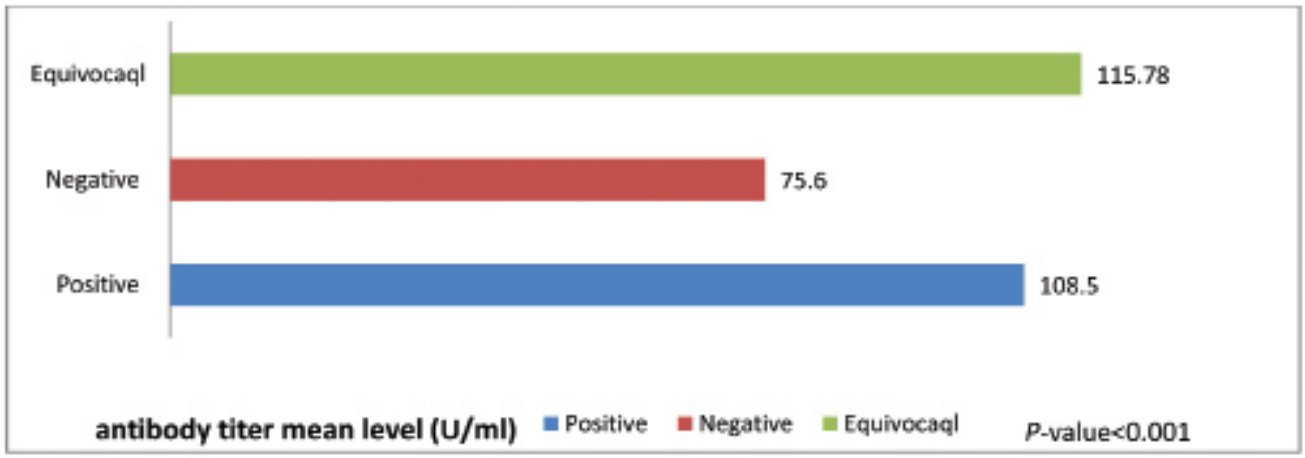

Fig. 2- Mean antibody titer in different subjects upon their history of infection

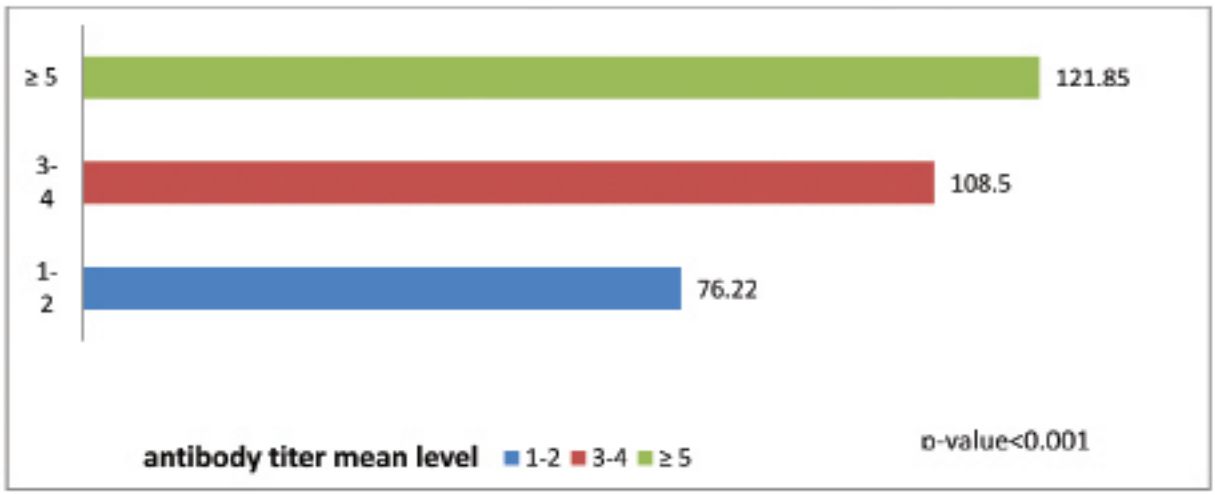

Fig. 3- Mean antibody titer upon different sibling groups

Table 1- Antibody titer in the pregnant women upon their characteristics

	Antibody				
	Negative (antibody level <8Uml-1)	**Equivocal (8<antibody level <12Uml-1)**	**Positive (antibody level >12Uml-1)**	**Total**	***P*-value**
Age groups(years)					
< 20	6(12.8%)	1(2.1%)	40(85.1%)	47	
20-29	22(8.8%)	2(0.8%)	227(90.4%)	251	
30-39	6(5.1%)	2(1.7%)	109(93.2%)	117	
≥40	3(25%)	0(0%)	9(75%)	12	0.24
Siblings					
1-2	23(21.7%)	4(3.8%)	79 (74.5%)	106	
3-4	13(5.8%)	1(0.4%)	209(93.7%)	223	
≥5	1(1%)	0(0%)	97(99%)	98	<0.001
History of chicken pox					
Negative	23(26.1%)	3(3.4%)	62 (16.1%)	88	
Equivocal	1(0.9%)	0(0%)	107(99.1%)	108	
positive	13(5.6%)	2(0.9%)	216(93.5%)	231	<0.001
location					
Urban	27(7.5%)	3(0.8%)	328 (91.6%)	328	
Rural	10(14.5%)	2(2.9%)	57(82.6%)	69	.054
Total	37(8.66%)	5(1.17%)	385(90.17%)	427	

The average antibody level in the 88 women, who reported negative history of infection, was 75.6 ± 66.93 U/ml and the mean level in the 231 subjects, who reported positive history, was 108.5 ± 68.32 U/ml. In the 108 participants with equivocal history of infection, the mean antibody level was 115.78 ± 63.95 U/ml (*P*-value < 0.001) (Fig. 2).

With respect to the number of siblings, we categorized the women into three groups:

participants in the first group had one or two sibling(s), the second group had three or four siblings and subjects in third group had five or more siblings. The probability for antibody titer positively increased when the number of siblings was greater, also the differences were statistically significant (*P*-value < 0.001) (Table 1).

The mean antibody level in the first group was 76.22 ± 70.78 U/ml; in the second group 108.5 ± 67.25 U/ml and in the third group 121.85 ± 60 (*P*-value < 0.001) (Fig. 3).

Of 358 and 69 participants who live in urban and rural areas, respectively, the mean antibody titers were 105.62 and 92.84 U/ml, respectively, showing the possibility of antibody titer positively increased in urban residents, although the variations were not statistically significant (*P*=0.054)(Table 1).

Discussion

The present study was conducted on 427 pregnant women of which 90.2% were VZV seropositive and 8.7% were susceptible to VZV infection. Similar studies from different regions of Iran reported various results.

A study from Hamadan, west of Iran showed that 78.4% of pregnant women were immune to chicken pox. A study from Jahrom, southern Iran revealed 72.7% seroprevalence among the young women prior to their marriage (2, 8). Considering the different regions of our country with the different climates, as well as north of Iran as part of Mediterranean climate, might be the reason of these different results.

A study was carried out in pregnant women in Lyon, France reported 98.8% seroprevalence, that was higher in comparison with those reported from Iran, as well as in our study (9). Also, studies from other developed countries such as Spain, UK, US, Canada, Germany and Finland reported higher rate of seroprevalence among the pregnant women than those observed in our study (6, 7, 10, 13-15). As mentioned earlier, the use of vaccination against VZV in developed countries could be explained this discrepancy.

Studies from Asia and Africa showed 80.3% seroprevalence in pregnant women (16). Low rate of VZV transmission among children and adolescents could be the reason of this low level of antibody titer in these countries in comparison to western countries.

The prevalence of VZV antibody in women in childbearing age reported from Bolivia and Argentina were 88.4% and 98.5%, respectively, that are higher than those reported from Tehran, Iran (80.9%) and Shiraz, southern Iran (86.9%) (1, 3, 17, 18).

On the other hand, in Iran the mean age of pregnancy is 27.5 years (8). Taking all together, it seems that VZV vaccination must be incorporated to routine immunization program of our country, at least for women under 25 years old prior to pregnancy.

In the present study, no correlation was found between age and antibody level. Contrary to this result, a study from Catalonia, Spain and another study from central Italy showed the significant trend by age in antibody level (6, 15). This discrepancy is due to high transmission in young age in these countries.

In our study, 93.5% of women with positive VZV disease history were seropositive. Although the mean level of antibody of these women was higher than those with negative history of infection, was lower than the antibody titer in those women with equivocal history of VZV disease. This showed that positive VZV history could be a good predictor of seropositivity, however, negative or equivocal history continued to be a poor predictor of immunity and serological analysis should be performed before pregnancy.

In the present study, there was increasing in antibody level with increasing in number of

siblings and differences were statistically significant. This is similar to the results reported from Turkey and Iran (8, 19). The increasing of seroprevalence could be due to the increasing of transmission in family with increased number of siblings.

In our study, there was no significant difference in antibody level among the women living in urban areas and those in rural areas. This was similar to another study from Iran and also a study from Spain (2, 6). In our study, no difference between the number of siblings in families live in urban and rural areas could be the reason.

Conclusion

Considering that in Iran, the mean age of pregnancy is 27.5 year and also the noticeable rate of seronegative pregnant women and women in childbearing age in our country as well as high cost of VZV vaccination, we recommend the evaluation of VZV antibody for women under 25 years old with no VZV infection history prior to pregnancy. For women who are seronegative, vaccination is recommended.

Acknowledgment

We would like to thank the Vice Chancellery for Research of Babol University of Medical Sciences for the financial support. The authors declare no conflict of interests.

References

1. Sharifi Z, Emadi Ghanjin S. The seroepidemiology of *varicella zoster* (VZV) in different age groups in Tehran, Iran. IJAAI 2005;4(2):95-8.

2. Mamani M, Zamani M, Hashemi SH, Akhtari M, Niayesh A. Seroepidemiology of *varicella – zoster* virus among pregnant women in Hamedan, Iran. Afr J Microbiol Res 2012;6(8):1829 –32.

3. Ziyaeyan M, Alborzi A, Jamalidoust M, Moieni M, Pourabbas B. Seroepidemiology of *varicella zoster* virus infection among 1-70 year individuals in Iran. IRCMJ 2012;12(2):176-80.

4. Motamedifar M, Handjani F, Hadi N, Shahkarami MK, Mehrabani D. Seroprevalence of *varicella – zoster* virus in children from Shiraz-Iran. Iran J Immunol 2006;3(1):43–6.

5. lafer MM, De Moraes-Pinto MI, Weckx LY. Prevalence of IgG *varicella zoster* virus antibodies in the kuikuro and kaiabi indigenous communities in xingu national park, Brazil, before varicella vaccination. Rev Inst Med Trop S Paulo 2005;47(3):139 –42.

6. Plans P, Costa J, Espunes 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 2007;114(9):1122-7.

7. Talukder YS, Kafatos G, Pinot De Moira A, Aquilina J, Parker SP, Crowcroft NS, *et al*. The seroepidemiology of *varicella zoster* virus among pregnant Bangladeshi and white British women in the London Borough of Tower Hamlets, UK. Epidemiol Infect 2007;135:1344–53.

8. Pourahmad M, Davami MH, Sotoodeh Jahromi AR. Evaluation of anti-varicella antibody in young women before their marriage : a sero-epidemiologic study in Iran. J Clin Virol 2010;48(4):260-3.

9. Saadatian –Elahi M, Mekki Y, Del Signore C, Lina B, Derrough T, Caulin E, *et al*. Seroprevalence of varicella antibodies among pregnant women in Lyon- France. Eur J Epidemiol 2007;22:405–9.

10. Watson B, Civen R, Reynolds M, Heath K, Perella D, Carbajal T, *et al*. Validity of self-reported varicella disease history in pregnant women attending prenatal clinics. Public Health Rep 2007;122(4):499–506.

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

12. Alp H, Altinkaynak S, Ertekin V, Kilicaslan B, Giiraksin A. Seroepidemiology of varicella-zoster virus

infection in a cosmopolitan city (Erzurum) in the eastern Turkey. Health Policy 2005; 2:119–24.

13. Ratnam S. Varicella susceptibility in a Canadian population. Can J Infect Dis 2000;11: 249 -53.

14. Sauerbrei A, Prager J, Bischoff A, Wutzler P. Antibodies against vaccine-preventable diseases in pregnant women and their offspring. Measles, mumps, rubella, poliomyelitis, and varicella. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2007;47:10-15.

15. Alanen A, Kahala K, Vahlberg T, Koskela P, Vainionpaa R. Seroprevalence, incidence of prenatal infections and reliability of maternal history of *varicella zoster* virus, cytomegalovirus, herpes simplex virus and parvovirus B19 infection in South- Western Finland. BJOG 2005;112:50-6.

16. Knowles SJ, Grindy K, cahill I, Cafferkey MT. Susceptibility to infection rash illness in pregnant women from diverse geographical regions. Common Dis Public Health 2004;7:344-8.

17. Bartoloni A, Bartalesi F, Roselli M, Manteilla A, Dini F, Carballo ES, *et al*. Seroprevalence of *varicella zoster* and rubella antibodies among rural populations of the Chaco region, south –eastern Bolivia. Trop Med In the alth 2002;7:512–7.

18. Dayan GH, Panero MS, Debbag R, Urquiza A, Molina M, Prieto S,*et al*. Varicella seroprevalence and molecular epidemiology of *varicella-zoster* virus in Argentina, 2002. J Clin Microbiol 2004;42:5698–704.

19. Savas S, Dallar Y, Arikan I, Onde U. Varicella – zoster virus seroprevalence in children between 0-15 years old. Mikrobiyol Bull 2004;38(1-2):69-75.