



SEROPREVALENCE OF VARICELLA ZOSTER VIRUS IMMUNOGLOBULIN G ANTIBODY AMONG PREGNANT WOMEN IN THE PLEVEN REGION, BULGARIA

Anton G. Petrov¹, Milena D. Karcheva², Alexander B. Blazhev³, Elitsa H. Gyokova¹, Yoana Ivanova-Yoncheva¹, Iordan D. Popov¹, Rositsa V. Petrova⁴

1) Department of Obstetrics and gynecology, Medical University - Pleven, Bulgaria

2) Department of Epidemiology, Medical University - Pleven, Bulgaria

3) Department of Anatomy and biology, Medical University - Pleven, Bulgaria

4) Department of Hygiene, medical ecology, occupational diseases and disaster medicine, Medical University - Pleven, Bulgaria.

SUMMARY

The purpose of this study was to assess the immunity against *Varicella Zoster Virus* (VZV) among pregnant women in the Plevan Region, Bulgaria.

Material/Methods Cross-sectional study was carried out. After informed consent, 251 women were hospitalized in a Clinic of obstetrics and gynecology at the University hospital in Plevan, Bulgaria. From every participant 5 ml blood was obtained, and all serum samples were tested by Enzyme-linked immunosorbent assay (ELISA). NovaLisa Varicella-Zoster Virus (VZV), ELISA Kit (NovaTec Immunodiagnostica GmsH) for detection of VZV Immunoglobulin G (IgG) antibody and UVmax kinetic microplate reader were used. Demographic characteristics of participants were collected by interview. Data were managed in Microsoft Excel 2007 and analyzed using Statgraphics software.

Results VZV IgG antibodies positive were detected in 178/251 (70.92%) of the women. Forty-four (17.53%) of all women were VZV IgG antibodies negative, and 29/251 (11.55%) were considered as equivocal. In women up to 20 years of age (n=33), 19(57.57%) samples were positive. In women aged between 20 and 30 years of age (n=138), 99 (71.74%) positive samples were found. In women aged more than over 30 years (n=80), 59 (73.75%) were positive. In all three age groups sero-negative women were found, but the highest relative share was in the age group up to 20 years - 21.21%

Conclusions Seroprevalence of VZV serum IgG antibodies is comparatively high among pregnant women. Established seronegative women have a potential risk of natural infection and its transmission to the fetus.

Keywords: Varicella-Zoster Virus, seroepidemiology, pregnant women

INTRODUCTION

Varicella is the most common infection in Bulgaria. The etiological agent, *Varicella-zoster virus* (VZV), is transmitted by air-borne route or direct contact with infectious lesions. In the absence of vaccination, the annual number of varicella cases is high. In 2017, in the public databases of the National Centre of Infectious and Parasitic Diseases were registered 25007 new cases in the country (incidence rate 352.12/100,000) [1]. Varicella represents 47.73% of all infectious diseases. It is a highly contagious disease, with a secondary attack rate of 90% in close contacts. In the countries with temperate climate most of the people become infected before adulthood, but about 10% of young adults remain susceptible. The most useful indicator for past infection is the presence of specific serum antibodies. In the European countries, which have not included the vaccine in their immunization program, antibodies to VZV are generally acquired before 10-15 years of age [2, 3, 4].

After primary infection, VZV has the capacity to persist as a latent infection and reactivation of virus may to cause herpes zoster. The illness usually had a good outcome, but complications are also observed - secondary bacterial infections of skin lesions, pneumonia, aseptic meningitis or encephalitis, cerebral ataxia and other.

Pregnant women and those with a suppressed immune system are at highest risk of serious complications. Women who are immune to varicella cannot become infected and do not need to be concerned about it for themselves or their infant during pregnancy. The acquisition of maternal antibodies protects the infant during the first few months of life. Varicella infection in pregnant women could lead to viral transmission via the placenta and infection of the fetus. If infection occurs during the first 28 weeks of gestation, this can lead to fetal varicella syndrome which may occur in nearly 2% [5]. Possible problems include: damage of the brain (encephalitis, microcephaly, hydrocephaly, aplasia of brain), damage of the eye (optic stalk, optic cap, and lens vesicles), microphthalmia, cataracts, chorioretinitis, optic

atrophy), other neurological disorders (damage of the cervical and lumbosacral spinal cords, motor/sensory deficits, absent deep tendon reflexes, anisocoria/Horner's syndrome), damage of the body - hypoplasia of upper/lower extremities, anal and bladder sphincter dysfunction, skin disorders (cicatrical skin lesions, hypopigmentation).

In most European countries varicella is a rare disease during pregnancy, as more than 90% of women of childbearing age have virus-specific immunoglobulin G. However, little is known about the seroprevalence of anti-varicella-zoster virus (VZV) serum antibodies in pregnant women. In some studies, less than 3-5% [3,6] of pregnant women were seronegative to VZV antibodies. Other studies found that 10-12% of pregnant women were seronegative. [6, 7].

The purpose of this study was to assess the immunity against VZV among pregnant women in the Plevan Region, Bulgaria.

MATERIAL AND METHODS

A cross-sectional study was carried out for a period of one year (2018). After informed consent, 251 women were hospitalized in a Clinic of Obstetrics and Gynecology at the University Hospital in Plevan, Bulgaria. The women were divided into two groups: women with a normal pregnancy who has entered the clinic for birth and women with miscarriage who has entered the clinic for treatment. From every participant 5 ml blood was obtained, and all serum samples were tested by *enzyme-linked immunosorbent assay (ELISA)*. NovaLisa Varicella-Zoster Virus (VZV) IgG, ELISA Kit (NovaTec Immunodiagnostica GmsH) for detection of VZV IgG antibody and UVmax kinetic microplate reader were used. According to supplier instruction antibody levels, greater than 11 NTU (NovaTec Units) considered as positive, 9-11 – equivocal and lower than 9 NTU as negative. Demographic characteristics of participants (age, education, occupation, an location of residency) were collected by interview. Data were managed in Microsoft Excel 2007 and analyzed using Statgraphics software in order to investigate the statistically significant association between the IgG antibodies against VZV and participants' characteristics in the study. Correlations with $p < 0.05$ were considered statistically significant.

RESULTS

Demographic characteristics of the study population

We examined a total of 251 women aged 14 to 45 years (average age was 27 years, $sd=6.404$). Women were separated in three groups depending of age (in years): less than 20 years - 33 (13.15%), between 20 and 30 years - 138 (54.98%) and greater than 30 years - 80 (31.87%).

Most of the women - 145 (57.77%) lived in cities in the Plevan Region, and the rest lived in the villages - 106 (42.23%). One hundred and one (40.24%) of the women had high school education, followed by women with higher education - 62 (24.70%), women with primary education - 43 (17.13%) and women without education - 45 (17.93%). Among the hospitalized women

there were unemployed - 100 (39.84%), employees - 88 (35.06%), work-people - 42 (16.73%), working in risk places (child day care, hospital) - 21 (8.37%). The comparison of seroprevalence between women living in urban area and these living in rural areas, did not show any significant difference (F-ratio = 0.51, P-value = 2.32). No statistically significant association between the level of immunity against VZV and participants' occupation (F-ratio = 2.26, P-value = 1.92) and education (F-ratio = 2.23, P-value = 3.65) was found. The reasons for hospitalization of the women from the studied group were different (Table 1). The data showed that women diagnosed with premature labor were predominant - 71 (28.29%).

Table 1. Reasons for hospitalization of the study population

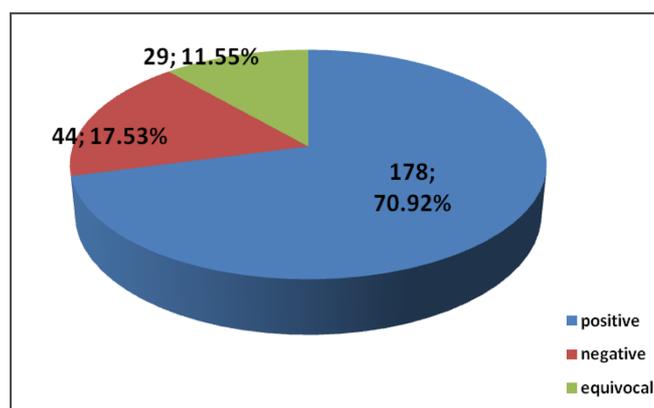
Reasons for hospitalization	N	%
Women with normal delivery	63	25.10
Women with premature birth	71	28.29
Women with prolonged pregnancies	29	11.55
Women with threatened abortion	39	15.54
Women with complete abortion	18	7.17
Women with other reasons*	31	12.35

* urinary tract infections, vomiting, anemia

Serological study

All 251 women hospitalized in the Clinic of obstetrics and gynecology were tested for IgG antibodies against VZV. They were with an unknown varicella history. The seroprevalence of VZV IgG antibodies in the studied population was 70.92 % (Figure 1).

Fig. 1. Seroprevalence of VZV IgG antibodies of the studied population



Depending on the separated age groups, the seroprevalence was as follows (table 2). The results showed that the seroprevalence was higher in the bigger age groups.

Table 2. Seroprevalence of VZV IgG antibodies in the studied population depending on the age groups

Age (in years)	Total N, %	VZV IgG positive N, %	VZV IgG Negative N, %	VZV IgG Equivocal N, %
less than 20	33 (13.15)	20 (60.61)	7 (21.21)	6 (18.18)
between 20 and 30	138 (54.98)	99 (71.74)	20 (14.50)	19 (13.76)
greater than 30	80 (57.97)	59 (73.75)	16 (20.0)	5 (6.25)
total	251 (100.0)	178 (70.92)	44 (17.53)	29 (11.55)

By the one-way ANOVA analysis of variance of age groups for the seroprevalence of VZV IgG antibodies of the studied group was established no significant differences between both factors (F-Ratio = 1.85, P-Value = 0.15).

DISCUSSION

Based on the literature in different European countries, it was found that by the age of 15 years more than 90% of the population has been infected by varicella in all countries except for Greece (86.6%) and Italy (85.3%) [1, 8, 9]. Little is known about the seroprevalence of anti-varicella-zoster virus serum antibodies in adolescents and adults in Bulgaria. Ivanova L. (2007) in a randomly chosen population of North/Eastern Bulgaria by a different method determined antibody prevalence against VZV and indicated seropositivity between 50% - 62% [10]. In some studies, age differences in seroprevalence were established, and in others, there were no [9, 11].

For the purposes of our study, we chose pregnant women for a serological study to assess the risk of varicella. The study group was presented from 251 women of age between 14 and 45, mean age $27 \pm \text{sd } 6.404$. In recent years there has been a tendency to increase the number of pregnancies among girls who have not reached the age of majority. Most women lived in cities and less - in the villages. No statistically significant association between the level of immunity and education and occupation of participants has been found.

This study demonstrated that the mean seropositive rate in pregnant women to VZV was 70.92%. We found age depending dynamic in seropositivity rate - seroprevalence rates increased from 60.61% among pregnant women younger than 20 years old to 73.75% in women older than 30 years which confirmed immunity against VZV in the older age group of pregnant women. A similar trend is compatible with others studies [6,10].

This trend is explained with the fact that under the conditions of the naturally acquired primary VZV infection and the memory immune response that characterizes the persistence of VZV IgG antibodies guarantee lifelong immunity. In some studies have been reported a difference in immunity against VZV among pregnant women from tropical and temperate countries. An increased risk of varicella infection during pregnancy have for women who live in a tropical area [6, 12, 13].

We found that the percentage of young women who were susceptible to VZV was high. They are at risk of getting infected during pregnancy which, in turn, may result in fetal abnormalities. Some authors determine as a risk group individuals who grow up without siblings and have a significant risk of evading natural VZV infection in childhood [14, 15]. It has also been established that seronegative women working in child day care and healthcare workers were more susceptible to the infection [16, 17]. Close contact in the family may result in infecting a seronegative mother from her child [18].

Vaccination against varicella is recommended as part of routine childhood vaccination schedules in several countries. In Bulgaria, vaccination against varicella during childhood is not generally recommended.

CONCLUSION

Our results indicate that part of the young pregnant women were susceptible to varicella. We consider that women with a negative or unknown disease history are appropriate for performing a serological test, if they are negative - to recommend them to be immunized against varicella before pregnancy.

Acknowledgments:

This study was carried out on a research project No. 1/2018 funded by the Medical University of Plevna, Bulgaria.

REFERENCES:

1. National Centre for Infectious and Parasitic Diseases. Annual analyses. [Accessed at: 01 January 2019]. [in Bulgarian].
2. Gabutti G, Penna C, Rossi M, Salmaso S, Rota MC, Bella A, et al. The seroepidemiology of varicella in Italy. *Epidemiol Infect.* 2001 Jun; 126(3):433-40. [PubMed]
3. Alanen A, Kahala K, Vahlberg T, Koskela P, Vainionpää 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 Jan;112(1):50-6. [PubMed] [Crossref]
4. Riera-Montes M, Bollaerts K, Heininger U, Hens N, Gabutti G, Gil A, et al. Estimation of the burden of varicella in Europe before the introduction of universal childhood immunization. *BMC Infectious Diseases.* 2017 May 18;17(1):353. [PubMed] [Crossref]
5. Sauerbrei A.. Review of varicella-zoster virus infections in pregnant women and neonates. *Health.* 2010; 2(2): 143-152. [Crossref]
6. 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 Nov;135(8):1344-53. [PubMed] [Crossref]
7. Suarez Gonzalez A, Otero Guerra L, De La Guerra GV, La Iglesia Martinez Pd Pd, Solis Sanchez G, Rodriguez Fernandez A. [Varicella and parvovirus B19 immunity among pregnant women in Gijón, Spain]. [in Spanish] *Med Clin (Barc).* 2002 Jul 6;119(5):171-3. [PubMed]
8. Todorova TT. Varicella infection in a non-universally vaccinated population: Actual epidemiology in Bulgaria (2013–2015). *Journal of Infection and Public Health.* 2018; 11; 326-330.
9. Bollaerts K, Riera-Montes M, Heininger U, Hens N, Souverain A, T. Verstraeten and Hartwig S. A systematic review of varicella seroprevalence in European countries before universal childhood immunization: deriving incidence from seroprevalence data. *Epidemiol Infect.* 2017, 145, 2666–2677.
10. Ivanova L. Herpes virus infections in human population in north / eastern Bulgaria. *Scripta Scientifica Medica.* 2007; 39(2):125-128.
11. Wutzler P, Färber I, Wagenpfeil S, Bisanz H and Tischer A. Seroprevalence of varicella-zoster virus in the German population. *Vaccine.* 2001 Oct 12;20(1-2):121-4. [PubMed]
12. Talebi-Taher M, Kashanian M, Khalili K. Seroprevalence of varicella-zoster virus among pregnant women in two teaching hospitals, Tehran, Iran. *Iranian Journal of Microbiology.* 2014 Feb;6(1):37-40.
13. Majidy P, Khodabandehloo M, Azadi NA. Seroprevalence of Varicella zoster virus antibody among young women before marriage in Sanandaj, Iran. *Iran J Microbiol.* 2016 Apr; 8(2):147–152.
14. Heininger U, Braun-Fahrlander C, Desgrandchamps D, Glaus J, Grize L, Wutzler P, et al. Seroprevalence of varicella-zoster virus immunoglobulin G antibodies in Swiss adolescents and risk factor analysis for seronegativity. *The Pediatric Infectious Disease Journal.* 2001 Aug;20(8):775-8. [PubMed]
15. Freuler M, De Cromas S, Hatza C, Bühler S. Varicella seroprevalence in individuals with a negative or unknown varicella history - results from a large travel clinic in Switzerland between 2008 and 2015. *Swiss Med Weekly.* 2016;146:w14342.
16. van Rijckevorsel GC, Bovée LP, Damen M, Sonder GJ, Schim van der Loeff MF and van den Hoek A. Increased seroprevalence of IgG-class antibodies against cytomegalovirus, parvovirus B19, and varicella-zoster virus in women working in child day care. *BMC Public Health.* 2012; 12:475.
17. Shady I. Seroprevalence of antibodies against varicella zoster virus and rubella virus among newly recruited expatriate healthcare workers: a cross-sectional study. *BMJ Open* 2018; 8:e019339.
18. Pembrey L, Raynor P, Griffiths P, Chaytor S, Wright J, Hall AJ. Seroprevalence of Cytomegalovirus, Epstein Barr Virus and Varicella Zoster Virus among Pregnant Women in Bradford: A Cohort Study. *PLoS ONE.* 2013; 8(11):e81881.

Please cite this article as: Petrov AG, Karcheva MD, Blazhev AB, Gyokova EH, Ivanova-Yoncheva Y, Popov YD, Petrova RV. Seroprevalence of *Varicella Zoster Virus* Immunoglobulin G antibody among Pregnant Women in the Pleven Region, Bulgaria. *J of IMAB.* 2019 Apr-Jun;25(2):2549-2552. DOI: <https://doi.org/10.5272/jimab.2019252.2549>

Received: 05/12/2018; Published online: 16/05/2019



Address for correspondence:

Assoc. Prof. Dr Milena Karcheva, MD, PhD
Department of Epidemiology, Parasitology and Tropical Medicine”, Medical University-Pleven, Bulgaria
E-mail: milena_karcheva@abv.bg