

Seroprevalence of Antibodies Against Varicella-Zoster Virus Among Prevalent Hemodialysis Patients

Mahshid Talebi-Taher,¹ Tina Hassanzadeh,² Shahrzad Ossareh³

¹Antimicrobial Resistance Research Center, Department of Infectious Diseases, Rasoul-e-Akram Hospital, Iran University of Medical Sciences, Tehran, Iran

²Department of Internal Medicine, Iran University of Medical Sciences, Tehran, Iran

³Division of Nephrology, Hasheminejad Kidney Center, Iran University of Medical Sciences, Tehran, Iran

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Introduction. Varicella-zoster virus (VZV) can cause life-threatening disease in immunosuppressed patients, including kidney allograft recipients. This study was designed to evaluate the immune status of the cohort of hemodialysis patients, who could potentially be candidates for kidney transplantation, against VZV, and to determine the correlation between the self-reported history of chickenpox infection and the VZV antibody status in this population.

Materials and Methods. Serologic testing for VZV was performed for 187 patients at different age groups receiving hemodialysis treatment at Hasheminejad Hospital, Tehran. The enzyme immunoassay method was used for determining immunoglobulin G antibodies against VZV.

Results. A total of 187 patients, aged 18 to 88 years (mean, 57.5 ± 16.2 years), were examined. Ninety-five patients (50.8%) were men. Overall, 183 patients (97.9%) were found to be seropositive for VZV. No significant correlation was observed between patients' history of chickenpox disease and seropositivity of VZV. The sensitivity, specificity, and positive and negative predictive values of patients' self-reported history was 39.3%, 50%, 97.2%, and 1.7%, respectively. **Conclusions.** Serologic screening for VZV in patients who are candidates for transplantation is essential to determine their immune status prior to transplant surgery. We suggest that this population be considered as the target group for future immunization programs in Iran.

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INTRODUCTION

The varicella-zoster virus (VZV) causes 2 forms of clinical diseases: chickenpox and herpes zoster.¹ Chickenpox is a benign disease among healthy children; however, severe illness may occur with visceral involvements, such as interstitial or necrotizing pneumonia, hepatitis, coagulopathies, and bacterial super infections.^{2,3}

In most temperate countries, more than 90% of adults are immune against VZV infection,⁴⁻⁷ but VZV seroprevalence rates are lower in tropical areas. Liyanage and colleagues showed that only 50% of people aged 60 years in the rural population

and 78.9% of those in the urban population of Sri Lanka were immune against VZV.⁸ Considering the variety of climate in Iran, studies in tropical areas such as Fars province showed that the overall seropositivity rate in elementary school children, aged between 6 and 10 years, was 35.2%, and in temperate areas, the seropositivity was 90% in individuals at the age of 30 years.^{9,10}

In kidney transplant recipients, delayed diagnosis of chickenpox may occur, due to atypical symptoms such as acute abdomen or low back pain, which can be life-threatening and fatal. Immunosuppressive therapy following transplantation may lead to an

increase in the number of severe illness in case of contacting VZV.¹¹ Mustapic and colleagues showed that 40 of 1139 patients who received kidney allografts developed VZV infection and 2 patients who were previously VZV immunoglobulin G (IgG)-negative developed chickenpox afterward. These findings guided them to recommend active immunization for all seronegative patients prior to organ transplantation.¹²

Some authors have recommended that all patients on waiting lists for the transplants should be screened for VZV seropositivity, irrespective of their previous history of infection, and live vaccine should be administered in seronegative patients.¹³

We need more data about seropositivity rate in patients awaiting kidney transplant in Iran to suggest immunization against VZV infection. The objectives of this study were to assess the seroprevalence of VZV antibodies among hemodialysis patients in a main referral hemodialysis center in Iran, who could be assumed as potential kidney transplant candidates and to evaluate the predictive value of self-reported history of chickenpox disease. The latter is a possible proxy for seroprevalence and may be used to provide efficient identification of candidates for vaccination.

MATERIALS AND METHODS

This cross-sectional study was designed to assess the seroprevalence of VZV among 187 patients from the hemodialysis unit of Hasheminejad Kidney Center, who were potential transplant candidates, between March and July 2010. A checklist including demographic data and the history of VZV infection was completed for each patient. Blood samples were collected and the separated serum was stored at -20°C prior to testing. Enzyme immunoassay for varicella-specific IgG was performed using a commercial virus-specific IgG. Enzyme immunoassay kit's optical density values (Varicella-IgG enzyme immunoassay well, RADIM, Rome, Italy; sensitivity, 100% and specificity, 88%) were indexed according to the manufacturer's instructions. Sera were classified as negative if the optical density was less than 0.20 and as positive if it was higher than 0.70. Sera with optical density between 0.20 and 0.70 were considered equivocal, which were assumed negative.

Statistical analysis was performed using the SPSS software (Statistical Package for the Social

Sciences, version 15.0, SPSS Inc, Chicago, Ill, USA). After conducting descriptive statistical analyses, we used the chi-square test to study the differences in the proportions of the categorical variables between the study groups. We compared the history of VZV infection with the results of testing for antibody against VZV to assess the reliability of the patient's self-reported history of the infection. Sensitivity, specificity, and positive and negative predictive values of patients' self-reported history were calculated considering the serum antibody prevalence as the gold-standard. A *P* value of less than .05 was considered significant.

RESULTS

A total of 187 patients were tested for anti-varicella IgG. They had a mean age of 57.5 ± 16.2 years (range, 18 to 88 years). Ninety-five patients (50.8%) were men. One-hundred and eighty-three patients (97.9%) were seropositive for VZV. The mean ages of the patients with seropositive and seronegative results were 58.1 ± 15.7 years and 29.5 ± 10.4 years, respectively (*P* = .001). There was a significant relationship between age and seropositivity of our patients (*P* = .001; Table 1). All of the seronegative patients were under 55 years of age.

There was no correlation between the patients' self-reported history of VZV infection and their seroprevalence status (*P* = .60; Table 2). The

Table 1. Characteristics of Patients in the Kidney Transplant Waiting List*

Characteristics	Total	Seropositivity	Seronegativity	<i>P</i>
Sex				
Female	92 (49.2)	89 (96.7)	3 (3.3)	
Male	95 (50.8)	94 (98.9)	1 (1.1)	.05
Age, y				
≤ 40	27 (14.4)	24 (88.8)	3 (11.2)	
41 to 55	58 (31.0)	57 (98.2)	1 (1.8)	
56 to 70	53 (28.3)	53 (100)	0	
≥ 71	48 (25.6)	48 (100)	0	.001

*Values are absolute frequencies (percentages).

Table 2. Varicella Antibodies in Two Groups With and Without a History of Varicella-Zoster Infection*

History of Varicella Infection	Total	Seropositivity	Seronegativity	<i>P</i>
Positive	74	72 (97.3)	2 (2.7)	
Negative†	113	111 (98.2)	2 (1.8)	.60

*Values are absolute frequencies (percentages).

†Including uncertain diagnoses

sensitivity, specificity, and positive and negative predictive values of patients' self-reported history were 39.3%, 50%, 97.2%, and 1.7%, respectively.

DISCUSSION

Primary VZV infection in kidney transplant recipients is a rare, but lethal illness.^{14,15} In 2007, Shahbazian and colleagues reported an outbreak of chickenpox in adult kidney transplant recipients in Ahwaz, Iran¹³; therefore, we were interested in the number of our adult patients in a main referral hemodialysis unit of the country, who were potential transplant candidates, were at risk for VZV infection. Reactivation of VZV occurs at all ages, but mainly in the elderly and immunocompromised patients. The severity of symptoms increase with age and with immunosuppressive therapy, including glucocorticoids, which also increases the risk of dissemination and the complication of reactivation.¹⁶

One-hundred and eighty-seven hemodialysis patients were tested to determine their immunity status against VZV. The results revealed that 97.9% of them were seropositive. In fact, a significant proportion of patients were immune to VZV infection. These rates were 96.8% and 98.8% in the Netherlands and Scotland, respectively, which guided the authors to vaccinate the patients susceptible to VZV; however, vaccination resulted in a moderate efficiency of 64%.^{17,18}

There are assumptions of more frequent occurrence of VZV amongst adults in tropical countries.¹¹ In contrast, it has been shown that in countries with temperate climate and among the age group of patients older than 40 years old, only few individuals were susceptible for VZV infection.^{19,20} Reports from Iran, with various types of climates, revealed a nearly 90% seropositivity in individuals at the age of 30 years old.¹⁰ Our study findings are consistent with these findings, as the mean age of seronegative patients was lower than the seropositive ones.

We compared the history of VZV infection with the results of antibody testing to assess the reliability of the self-reported history of VZV infection. The analysis revealed that the history of varicella was not a reliable predictor of the VZV antibody status in patients. In the populations of Iran, Singapore, and Brazil the positive predictive value of a clinical history of VZV ranged from 85% to 98%.²¹⁻²⁴ On the other hand, the low negative

predictive value of 1.7%, which is consistent with a study from Turkey, may reflect the correlation between the lower negative predictive value and older age.²⁵ Some authors reported that about 50% of patients with a negative history of varicella were seropositive, so they concluded that serologic testing is more cost-benefit than routinely immunizing patients with unknown history.²⁶ Other studies recommended the prevention of VZV infection by vaccinating all seronegative kidney transplant candidates before surgery in order to decrease the morbidity and mortality rates.^{15,27,28}

CONCLUSIONS

The findings of our study showed no correlation between the patients' self-reported history of chickenpox and seroprevalence of antibodies, emphasizing the importance of serological screening of all patients on waiting list of kidney transplantation, especially for those under the age of 55 years. We believe that before making any decision to start a vaccination program against VZV, it is crucial to conduct large-scale studies to determine the seroepidemiology of VZV in different population groups in Iran.

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CONFLICT OF INTEREST

None declared.

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Correspondence to:

Mahshid Talebi-Taher, MD, MPH
 Antimicrobial Resistance Research Center, Department of
 Infectious Diseases, Rasoul-e-Akram Hospital, Sattarkhan St,
 Niayesh, Tehran, Iran
 Tel: +98 21 6650 7056
 Fax: +98 21 6650 6864
 E-mail: mtalebitaher2000@yahoo.com

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