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Herpes zoster awareness: a pilot centre analysis

Herpes zoster farkındalığı: bir pilot merkez analizi

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Abstract

Purpose: Herpes zoster (HZ), or shingles, is caused by the reactivation of the varicella-zoster virus (VZV), typically occurring years after a primary VZV infection (chickenpox). This study aims to assess the awareness of HZ and its vaccine among adults in Izmir, Türkiye, to inform future public health strategies and improve vaccination rates.

Materials and methods: A survey was conducted in April 2024 among adults aged 18-69 years in Izmir, Türkiye, using a random sampling method in urban and suburban communities. The survey, administered by healthcare professionals in public, consisted of dichotomous questions to determine demographic characteristics and measure knowledge about HZ and its vaccine.

Results: A total of 71 participants were included, with a mean age of 42.28±15.83 years. The gender distribution was nearly equal (50.3% male, 49.7% female). Overall, 59.2% of respondents were aware of HZ, but only 18.3% knew about the HZ vaccine. Women were significantly more likely to be aware of HZ than men (OR=2.79, 95% CI:1.02-4.19, p=0.04). Age did not significantly correlate with disease or vaccine awareness. There were no significant differences in disease awareness (χ^2=0.58, p=0.75) or vaccine awareness (χ^2=0.21, p=0.90) between different age groups.

Conclusion: The study highlights a moderate level of awareness about HZ but a low awareness of the HZ vaccine among adults in Izmir, Türkiye. Women were more likely to be aware of HZ, suggesting a gender disparity in disease awareness. Public health initiatives should focus on increasing awareness of the HZ vaccine, particularly older adults. Further research is needed to explore the reasons behind low vaccine awareness and develop strategies to improve vaccination rates.

Keywords: Herpes zoster, shingles vaccine, herpes zoster awareness.

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Öz

Amaç: Herpes zoster (HZ) veya zona, varisella-zoster virüsünün (VZV) reaktivasyonundan kaynaklanır ve tipik olarak birincil VZV enfeksiyonundan (suçiçeği) yıllar sonra ortaya çıkar. Çalışma, gelecekteki halk sağlığı stratejilerini oluşturmak ve aşılama konusunda nosyon kazandırmak amacıyla İzmir, Türkiye'deki yetişkinler arasında HZ ve aşısı hakkındaki farkındalığı değerlendirmek üzerine yürütülmüştür.

Gereç ve yöntem: Nisan 2024'te İzmir, Türkiye'de 18-69 yaş arası yetişkinler arasında, kentsel ve banliyö topluluklarında rastgele örnekleme yöntemi kullanılarak bir anket yapılmıştır. Sağlık çalışanları tarafından halka açık olarak uygulanan anket, demografik özellikleri belirlemek ve HZ ve aşısı hakkındaki bilgileri ölçmek için dikotomik sorulardan oluşmuştur.

Bulgular: Yaş ortalaması 42,28±15,83 yıl olan toplam 71 katılımcı çalışmaya dahil edilmiştir. Cinsiyet dağılımı neredeyse eşitti (%50,3 erkek, %49,7 kadın). Genel olarak, katılımcıların %59,2'si HZ'den haberdardı, ancak sadece %18,3'ü HZ aşısını biliyordu. Kadınların HZ'den haberdar olma olasılığı erkeklere göre anlamlı derecede daha yüksekti (OR=2,79, %95 GA:1,02-4,19, p=0,04). Yaş ile hastalık veya aşı farkındalığı arasında anlamlı bir ilişki bulunmamıştır. Farklı yaş grupları arasında hastalık farkındalığı (χ^2=0,58, p=0,75) veya aşı farkındalığı (χ^2=0,21, p=0,90) açısından anlamlı bir fark saptanmamıştır.

Sonuç: Çalışma, İzmir, Türkiye'deki yetişkinler arasında HZ hakkında orta düzeyde bir farkındalık olduğunu ancak HZ aşısı konusunda farkındalığın düşük olduğunu vurgulamaktadır. Kadınların HZ'den haberdar olma olasılığının daha yüksek olması, hastalık farkındalığında cinsiyet farklılığı olduğunu düşündürmektedir. Halk sağlığı girişimleri, özellikle yaşlı yetişkinler olmak üzere HZ aşısı konusunda farkındalığı artırmaya odaklanmalıdır. Düşük aşı farkındalığının arkasındaki nedenleri araştırmak ve aşılama oranlarını iyileştirmek için stratejiler geliştirmek için daha fazla araştırmaya ihtiyaç vardır.

Anahtar kelimeler: Zona, zona aşısı, zona farkındalığı.

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Introduction

Herpes zoster (HZ) is a clinical syndrome associated with reactivation of latent varicella zoster virus (VZV), typically occurring years after VZV infection. HZ is characterized by a painful, unilateral, vesicular skin rash that usually occurs in a single dermatome (sometimes in adjacent dermatomes).

Commonly involved sites include the thoracic, lumbar, cervical and trigeminal dermatomes. Skin rashes usually begin with a prodrome of pain or paresthesia that occurs 1-5 days before rash onset [1]. HZ usually lasts for 2-4 weeks and can have a very morbid course in the elderly and immuncompromised patients, where the risk of disease development is high [2]. It usually remains latent after VZV infection in childhood and manifests itself in adulthood. Although it can cause permanent neurological disorders such as cranial nerve palsy, hearing and visual deficits; post herpathic neuralgia (PHN) is the most common complication. PHN is severe pain that can last up to 3 months after the spontaneous remission phase of the disease. The incidence can reach 30%, especially in patients over 65 years of age and immunocompromised patients [3]. Moreover, the age-related increase in incidence rates is higher in complicated HZ than in uncomplicated HZ. After experiencing a first relapse, patients have higher risk for a second relapse [4].

With the aging of the population, it is thought that herpes zoster infection will be encountered more frequently, especially in developing countries in the future. According to the US Centers for Disease Prevention (CDC), 30% of people are expected to get Herpes Zoster at some point in their lives. Reactivation of the Varicella zoster virus occurs in 1 in 5 people worldwide [2]. The overall incidence of herpes zoster in Europe is about 3 per 1000 people per year and more than 10 per 1000 people per year in people over 80 years of age. The trend of increasing incidence continues in the world: The incidence of HZ has increased 4-fold in the last 6 decades [2, 5, 6]. Although there is no general epidemiological data for our country, prevalence data based on single clinic admissions show that one out of every 100 people has had shingles at some point in their lives; an Istanbul-based event-time cross-sectional study showed that the incidence of HZ increased from 182 per 100,000 people in 2011 to 285 per 100,000 people in 2019 [5-7].

Acyclovir and Brivudine are commonly used systemic antiviral therapies that may shorten the healing process of acute herpes zoster, but only if started within the first 48 hours of rash development. Indeed, there is no convincing evidence that acyclovir affects the incidence or duration of PHN, however, early treatment with acyclovir reduces the incidence of serious eye disorders in ophthalmic HZ patients. Nevertheless acyclovir-related serious adverse effects such as acute kidney injury caused by crystalopathy needs to be taken into account. Corticosteroids generally relieve acute pain but therapeutic benefit is limited [8]. The gold standard for laboratory diagnosis is PCR and direct identification of VZV in cell cultures. Detection of IgM- and IgG-anti-VZV antibodies is less sensitive and may be helpful in immunocompromised individuals.

Association with VZV

In childhood usually VZV-infected T cells circulate during Varizella Zoster infection. It evades the host response through down-regulation of major histocompatibility complex (MHC) class I expression and inhibition of interferon response genes. After the eruptive period, it may migrate retrogradely to the nerve ganglia via sensory neuron endings and remain latent. The primary factor determining the latency of the virus here is the T cell-mediated immune response, as protection against reinfection has been demonstrated in agammaglobulinemic individuals who do not produce VZV-specific antibodies but develop T cell-specific immunity after varicella infection [9, 10].

Varicella Zoster vaccination is part of routine in 36 countries, including Türkiye, the USA and Australia, and was added to the childhood vaccination schedule in Türkiye in 2013. Although the two-dose vaccination strategy, especially the booster dose, reduces VZV complications and hospitalizations in childhood, its population-based effectiveness on Herpes Zoster is debated. 50-year modeling predicts that the incidence of HZ can be reduced [10].

The Hope Simpson [11] hypothesis, first proposed in 1965, suggested that immunity acquired through VZV vaccination or

transmission would protect against Herpes Zoster infection in adulthood VZV vaccination has not been introduced in the UK, for example, due to the disappearance of herd immunity and lack of evidence of cost-effectiveness. In addition, although the incidence of HZ has continued to increase over the 20-year period since the introduction of VZV vaccination, similar incidence is found in countries and regions where the vaccine is and is not widely practiced, making this approach controversial [12]. A controlled prospective study published in 2019 also demonstrated the inability of VZV vaccine to provide protection against Herpes Zoster infection in immunosuppressed groups (hematologic malignancy) [13].

HZV vaccine and its features

The increasing average population and age of HZ infection and the severe course of complications suggest that especially elderly patients may benefit from HZ vaccination [14, 15].

Two types of herpes zoster vaccine are currently available. One is a single-dose vaccine (LZV) containing the same live attenuated virus used in the varicella vaccine; it has 14 times more attenuated virus plaque-forming units per dose. The other is recombinant zoster vaccine (RZV), which instead of live attenuated virus contains a small fraction of the virus that does not replicate but can increase immunogenicity. In a meta-analysis of 12 prospective studies in 2018, the recombinant form (RZV) was found to have higher protection compared to live attenuated vaccine, although local side effects at the vaccination site were found to be higher in patients over 50 years of age [16].

Further clinical trials and research to assess RZV are ongoing. The randomized controlled trial of 1736 healthy people over 60 years of age found that both vaccines had similar results to the placebo arm in terms of serious adverse events and mortality, but not in terms of efficacy; it showed that 50 healthy older adults needed to be vaccinated with LVZ to prevent one shingles attack, while 33 healthy older adults needed to be vaccinated with RZV to prevent one shingles attack.

In immunocompromised patients, where live vaccine (LZV) contrandicated, RZV found effective. A study based on model simulation groups shows that to prevent one case of HZ, the number needed to vaccinate was 9, 8 and 10, for hematopoietic stem cell transplantation, breast cancer and Hodgkin's lymphoma [17, 18]. However, given the heterogeneity of the immunocompromised population and the fact that timing and conditions of vaccine administration are important in this group, more studies and real-world data are needed over time.

Awareness

Adult immunization as a topic had been introduced to medical community and society almost three decades ago but despite clear benefits for reducing morbidity and mortality vaccine coverage is low even in developed countries and evolving slower [19]. While it depends on health service offers and resources, reimbursement or physicians attitude; SARS-CoV-2 has its effect on paradigms as well.

In terms of awareness of HZ as a disease and its vaccine in Türkiye, there is little data which varies widely [20, 21]. Overall, these analyses showed that very few Turkish individuals were aware of the vaccine and that the Turkish population had inadequate knowledge about the symptoms, causes and risks of HZ [7].

In a study, which included 200-300 people based on face-to-face and telephone communication and generally based on the urban population, Türkiye, together with Chile and India, was included in the group where disease awareness was in the 15-20% band, at the lowest level. It can be argued that the grammatical and cultural expressions related to the disease in the method of preparation of the questionnaire will differ from country to country. But in general, it shows that a successful vaccine initiative will require a community-wide effort to raise global awareness of HZ [22]. In general, although the awareness of Herpes Zoster infection is over 50% in the world, the awareness is quite low in terms of the same virus causing it as varicella, its complications and the presence-effects of the vaccine [23, 24].

Despite the fact that, new recombinant HZ vaccine on its way to be introduced, we hypotesized if there is a knowledge gap, that should be highlighted. We aim to determine

the perception of HZ and its vaccines in a city, where its senior and old community relatively big and continuing to grow.

Materials and methods

We designed a survey in adults aged 18–69 years in Izmir, Türkiye, in april 2024. A convenience sampling strategy was applied to recruit respondents in a total of 3 urban and suburban communities. Survey has been conducted face-to-face by three healthcare professionals mostly in bus and subway stations. They were held in two different time interval which includes one weekday (tuesday), weekend(sunday) and over the course of day to make out a heterogeneous group.

After the literature review, the questionnaire was prepared and applied by the researchers. The purpose of the questionnaire is to determine demographic characteristic and to measure their knowledge on existence of HZ and its vaccines. To be more direct and objective, the questionnaire consists of dichotomous questions except for demographics.

According to the results obtained from the preliminary study to calculate the sample size, 50-75 participants were needed for the study based on β=80 power, α=0.05 margin of error and d=0.2 effect size (G*Power version 3.1). People aged 18 years and older were randomly selected and included in the study. Patients who were too clinically demented to participate in a face-to-face survey and patients who refused to participate in the study were excluded.

Statistical analysis

The statistical analysis was carried out using the program SPSS version 24.0. The descriptive data were given as number, percentage, mean and standard deviation. Frequency distributions were given for categorical variables. Normality distribution of continuous variables is tested with Shapiro wilk. Continuous variables are assessed and compared with Mann whitney U, if not normal distributed. The chi-square test was used for group comparisons. Logistic regression analysis was employed to determine the factors associated with awareness of disease and vaccine. A *p*-value of <0.05 was considered statistically significant.

The study was approved by the Dokuz Eylul University Medical Faculty Ethics Committee.

Results

A total of 71 participants were enrolled in the study, with a mean age of 42.28±15.83 years (range: 19 to 72 years). The gender distribution was nearly equal, with 50.3% male and 49.7% female participants. The sociodemographic characteristics and response distributions are summarized in Tables 1 and 2.

Table 1 and 2 show the sociodemographic breakdown and the levels of awareness of HZ and its vaccine. The significant findings (*p*<0.05) are highlighted to emphasize key differences .

Awareness of herpes zoster and its vaccine

Overall, 59.2% of respondents were aware of Herpes Zoster (HZ) as a disease, but only 18.3% knew about the existence of the HZ vaccine.

Table 1. Responders according disease knowledge

	Number answered	Responders know the disease	Responders do not know the disease	*p* value	Test value
Female	35	25 (71.4%)	10 (28.6%)	0.038*	χ^2:4.304
Male	36	17 (46.3%)	19 (53.7%)		
Age (Mean±S.D**)**		41.24 (15.1)	43.79 (16.8)	0.8	z:-0.503

*p<0.05 statistically significant, S.D: Standard Deviation, z: Mann Whitney U test; χ^2: Chi Square test

Table 2. Responders according vaccine knowledge

	Number answered	Responders know the vaccine	Responders do not know the vaccine	*p* value	Test value
Female	35	8 (23%)	27 (77%)	0.329	χ^2:4.304
Male	36	5 (13%)	31 (87%)		
Age (Mean±S.D)		38.31 (16.3)	43.17 (15.6)	0.330	z:-0.975

S.D: Standard Deviation, z: Mann Whitney U test, χ^2: Chi Square test

The data presented in Table 1 and 2 includes number, percentage, mean, and standard deviation for various sociodemographic variables. Figure 1 displays the awareness levels of HZ and its vaccine across different age groups, providing a visual representation of how awareness varies among age demographics.

There was no significant difference in disease awareness (χ^2=0.58, *p*=0.75) or vaccine awareness between age groups (χ^2=0.21, *p*=0.90).

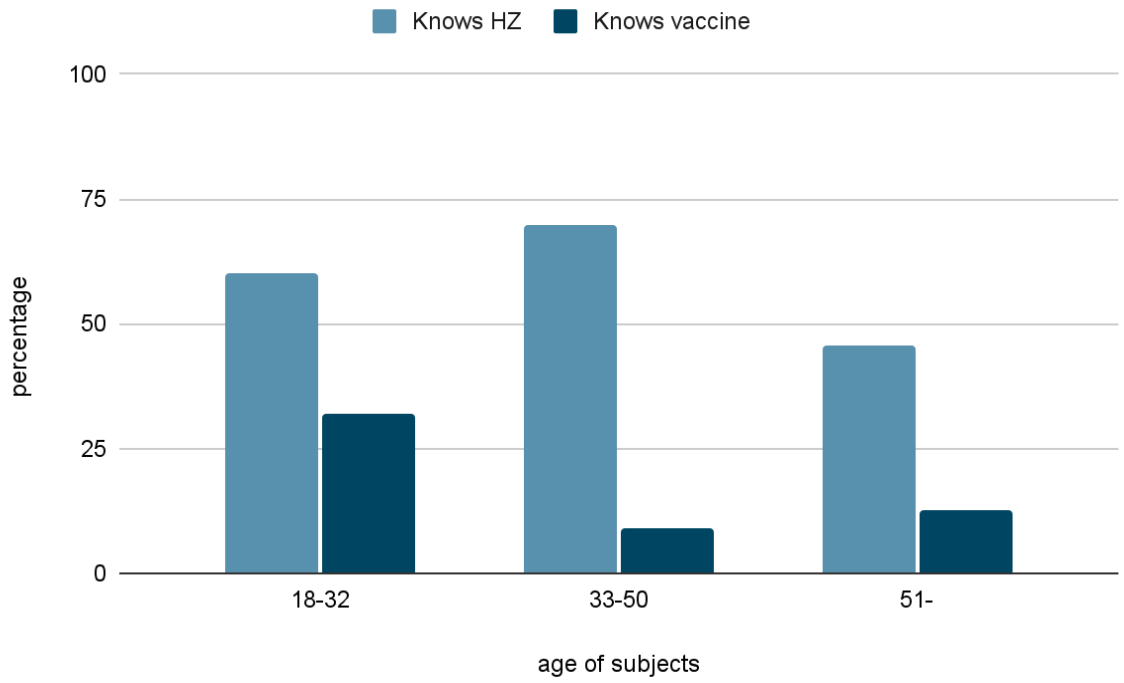

Figure 1. Age of subjects

Age and gender correlation

In the logistic regression analysis, women were significantly more likely to be aware of HZ than men, with an odds ratio (OR) of 2.79 (95% CI: 1.02-4.19, *p*=0.04). However, age did not show a significant correlation with disease awareness (*p*=0.87). Neither age nor gender showed a significant correlation with awareness of the HZ vaccine (Table 3).

Table 3. Logistic regressions

	Disease knowledge		Vaccine Knowledge	
	OR (CI 95%)	***p* value**	**OR (CI 95%)**	***p* value**
Female	2.79 (1.9-3.2)	0.04*	1.90 (1.24-2.5)	0.31
Age	1.010 (0.97-1.032)	0.87	1.023 (0.98-1.103)	0.29

*$p<0.05$ statistically significant, OR: Odds Ratio, CI: Confidence Interval

Discussion

Determination requirement of awareness of HZ as disease and vaccine in Türkiye has been adressed in the field [7]. The aging of the population will be associated with the morbidity of HZ and its complications over time. In addition, given that the risk of developing HZ is increased not only by malignancies but also by chronic conditions or comorbidities such as asthma, chronic heart disease, chronic obstructive pulmonary disorder, depression and rheumatoid arthritis, it will be necessary to raise awareness among a large population and the health professionals who treat them [4].

Although Türkiye currently has a relatively young demographic structure (median age of citizens is 34 years), in the last 15 years, the percentage of the population over the age of 65 has increased from 7.1 to 10.2. And the number of people over 65, currently 10.2 million, is estimated to be 16.3 in 2040 [25].

Most data, including a meta analysis of 8-countries reflecting younger age, female gender, higher income and education level were associated with increased willingness to vaccinate [26, 27]. This is another indicator of the importance of raising awareness of the HZ vaccine, especially among older, at-risk populations. Our data do not show any age discrepancy but show a knowledge dominance of women over men, which is consistent with previous data [26, 28]. Regarding the direct relationship between disease knowledge and vaccination willingness is debatable and this existence of disease awareness difference could convey itself in the vaccination rate is argumentative, but this is gender gap reflected in the HZ vaccination rate, as shown by a Canadian study [29]. In the awareness analysis study with the questionnaire applied in the United Arab Emirates, the awareness of the disease was 64.3% and the awareness of the presence of vaccine was 15%, which is similar to our data and most of those who had information about vaccination were women and those with chronic diseases [27].

Insufficient knowledge of HZ of the Turkish population may be attributable to insufficient information from vaccination clinics or other health care providers. While reliability and validity of studies in Türkiye regarding HZ is limited since most of them conducted in or outpatient clinics; we were able to measure information of public awareness by conducting it in public [7].

In a Chinese study, greater knowledge and awareness in participants did not contribute to higher willingness, but regarding difference, it can be hypothesized due to lack of HZ vaccine reimbursement [30]. And also physician attitudes play a large role, this needs to be hypothesised in further studies. Although vaccine orientation and its implementation in risk groups are also subject to factors such as reimbursement and health chain/system, studies have shown that one of the most determinant factors is physician-patient information flow and recommendation [31]. It is thought that healthy and sick individuals who are undecided or reluctant about vaccination and who are in risk groups will tend to be vaccinated with the recommendation of health professionals [27]. As with the HPV vaccine, acceptance by doctors and the public is at least as influential as the level of scientific evidence in real life, and to some extent determines reimbursement and inclusion in the routine vaccination schedule. As a vaccine topic, HZ has a newly introduced recombinant vaccine and it can be foreseen that knowledge will increase as it is administered over time.

Patient demand had a profound impact on physicians' decisions; 84.9% (73/86) of physicians who said they did not recommend HZ

vaccination reported that they would vaccinate upon patient request. This points to the health awareness of not only physicians but also individuals [31]. The study's strength include the fact that the opinion can be clearly assessed thanks to the small number of sequential questions and that it is not-time consuming, which has eliminated selection and survey bias to some extent. It is also considered to reflect the general population base in terms of public realisation.

There are a few limitations. The study is conducted in a single city with a different average age and education level than the country as a whole. And although some of the participants had heard of HZ or vaccine, this did not reflect how knowledgeable they were about them, so the measure of awareness did not assess the depth of knowledge about HZ and its vaccine.

The lack of knowledge about HZ in Türkiye must be taken seriously and steps must be taken to address it. The role of healthcare providers is crucial. Physicians and other healthcare professionals should actively engage in educating their patients about the benefits of the HZ vaccine, especially for high-risk groups. There is a need for comprehensive public health campaigns to raise awareness about the HZ vaccine, particularly focusing on older adults and men who demonstrated lower levels of awareness.

The study suggests the necessity of further research to explore the reasons behind the low awareness of the HZ vaccine and to develop strategies to improve vaccination rates.

Conflict of interest: The authors have declared no conflict of interest in relation to this article.

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Authors' contributions to the article

H.O.S. constructed the main idea and hypothesis of the study. H.O.S and S.K. developed the theory and arranged/edited the material and method section. H.O.S and S.K have done the evaluation of the data in the Results section. Discussion section of the article was written by H.O.S, S.K. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.