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# Retrospective evaluation of clinical features in hospitalized herpes zoster patients

## *Hastanede yatırılarak izlenen herpes zoster hastalarının retrospektif olarak değerlendirilmesi*

Ayda Acar, Ayşe Hande Yoldaş, Işıl Karaarslan, İlgen Ertam Sağduyu, Can Ceylan, İdil Unal, Günseli Öztürk

Ege University Faculty of Medicine, Department of Dermatology and Venereal Diseases, İzmir, Turkiye

**ABSTRACT**

**Aim:** Herpes zoster is a dermatomal vesicular eruption caused by the reactivation of varicella-zoster virus (VZV) that remains latent in the dorsal root ganglia. Due to the impairment of cellular immune capacity with aging, it is commonly seen in advanced age. Approximately 3-10% of the cases need to be hospitalized. We aimed to determine the frequency of dissemination and the demographic and clinical characteristics in hospitalized herpes zoster patients in a dermatology clinic of a tertiary hospital.

**Materials and Methods:** The records of 19 herpes zoster patients hospitalized in our clinic between June 2019 and November 2020 were retrospectively reviewed. Patients' age, gender, dermatome involved, presence of dissemination, concomitant diseases, and development of post-herpetic neuralgia were noted.

**Results:** Disseminated herpes zoster was seen in 36.8% (no:7) of the patients. Of patients 63.2% (no:12) had ophthalmic herpes zoster. The relationship between dissemination and age, gender, presence of immunosuppression and development of post-herpetic neuralgia was not statistically significant. While no death was observed in the non-disseminated group, one patient died in the disseminated herpes zoster group.

**Conclusion:** In this study, the mean age of the patients, the accompanying immunosuppressive state, and the rate of post-herpetic neuralgia were found to be higher in the disseminated herpes zoster group than the non-disseminated group. But it was not significant. Studies on disseminated herpes zoster which have a higher mortality are limited due to the low frequency of the disease. Studies involving larger numbers of patients are needed in order to report the clinical features and mortality rates more clearly in these patients.

**Keywords:** Herpes zoster, disseminated herpes zoster, immunosuppression.

***ÖZ***

***Amaç:*** *Herpes zoster dorsal kök gangliyonlarında latent kalan varisella zoster virüsün reaktive olmasıyla gelişen dermatomal veziküler erüpsiyondur. Yaş alma ile birlikte görülen hücresel bağışıklık kapasitesindeki azalma nedeniyle çoğunlukla ileri yaşta görülmektedir. Olgularının yaklaşık %3-10'unun hastaneye yatarak tedavi alması gerekir. Bu çalışmada kliniğimizde yatırılarak izlenen herpes zoster olgularının retrospektif olarak değerlendirilerek disseminasyon sıklığının ve bu hastalardaki demografik ve klinik özelliklerin saptanması amaçlanmıştır.*

***Gereç ve Yöntem:*** *Haziran 2019 ile Kasım 2020 tarihleri arasında kliniğimizde yatarak izlenen 19 herpes zoster olgusunun dosyası retrospektif olarak gözden geçirildi. Hasta dosyalarından hastaların yaşı, cinsiyeti, tutulan dermatom, disseminasyon varlığı, eşlik eden hastalıklar, postherpetik nevralji gelişimi olup olmadığı not edildi.*

Corresponding author: Ayda Acar
Ege University Faculty of Medicine, Department of Dermatology and Venereal Diseases, İzmir, Turkey
E-mail: *aydaerbas@yahoo.com*
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***Bulgular:*** *Dissemine herpes zoster %36,8 (no:7) oranında görüldü. Hastaların %63,2'sinde (no:12) oftalmik herpes zoster mevcuttu. Disseminasyon ile yaş, cinsiyet, immunsupresyon varlığı ve PNH gelişimi arasındaki ilişki istatiksel olarak anlamlı değildi (p:0,051, p:0,216, p: 0,865, p:0,419). Dissemine olmayan hasta grubunda ölüm gözlenmezken dissemine herpes zoster grubunda bir hasta hayatını kaybetti.*

***Sonuç:*** *Bu çalışmada dissemine herpes zoster olan grupta hastaların yaş ortalaması, eşlik eden immunsupresif durum, post herpetik nevralji gelişim oranı dissemine olmayan gruba göre daha yüksek saptanmıştır fakat bu yükseklik anlamlı bulunmamıştır. Mortalitesi klasik zonaya göre daha yüksek olan dissemine zona ile ilgili çalışmalar hastalığın sık görülmemesi nedeniyle kısıtlıdır. Bu hastalardaki klinik özellikleri ve mortalite oranlarını daha net bildirebilmek için daha fazla sayıda hasta içeren çalışmalara ihtiyaç vardır.*

***Anahtar Sözcükler:*** *Herpes zoster, dissemine zoster, immünsupresyon.*

## INTRODUCTION

Varicella-zoster virus (VZV), a double-stranded DNA virus, remains latent in the sensory dorsal root and cranial nerve ganglia in patients after primary infection. Dermatomal vesicular eruption, which develops spontaneously or in the presence of triggers such as immunosuppression, malignancy, and infection, caused by the reactivation of latent VZV virus is called herpes zoster (HZ) (1). The virus multiplies in the reactivated ganglion and reaches the skin by infecting the afferent sensory nerve retrograde from the related ganglion. Thus, it causes unilateral dermatomal rash and pain matching the dermatome of the affected nerve (2).

Up to the age of 50, the incidence of HZ is 4 in 1000 people per year, while the incidence increases with age, and at the age of 75 it rises to 14 in 1000 people per year. The reason for the increase in the incidence of HZ after the age of 50 is the impairment of cellular immune capacity with aging. Half of the immunosuppressed individuals and 15% of the immunocompetent individuals have HZ in their lifetime (3).

Classical clinical presentation is painful grouped vesicular eruption on an erythematous background with unilateral dermatomal involvement that develops 3 to 5 days after reactivation. Atypical clinics may also be observed (1). Usually, the lesions heal within 7-10 days (2). Transmission from virions in vesicular lesions to individuals who do not have varicella is possible but the transmission risk is much lower compared to varicella (1, 4).

The involvement of most common dermatomes are; thoracic (55%), trigeminal (20%), cervical (11%), lumbar (13%) and sacral (2%). Sometimes, more than one dermatome involvement can be seen (1, 4). Ophthalmic complications may develop in ophthalmic HZ (OHZ) that can cause permanent visual impairment. Seventh and 8th cranial nerves are involved in HZ oticus. Ramsay Hunt syndrome, in which facial paralysis and partial loss in sense of taste, may be seen in the involvement of 7th cranial nerve since the sensory and motor fibers converge in the seventh cranial nerve (4, 5). HZ can be seen atypically as verrucous, lichenoid, follicular and granulomatous lesions. Disseminated herpes zoster (DHZ) is compatible with more severe disease in which visceral involvement can be observed (4).

Complications may develop in approximately 14% of patients with HZ (6). Post-herpetic neuralgia (PHN), which is the most common complication of HZ, is dermatomal pain that lasts for more than 3 months (1, 4). PHN develops in 10% of HZ patients older than 60 years (2) and in 30% of patients older than 80 years (7). Other complications are; development of secondary bacterial infection, uveitis in OHZ, motor paresis, encephalitis, other neurological complications, vasculopathy, other vascular complications such as stroke, transient ischemic attack and myocardial infarction and DHZ (2,4,7). Ocular damage is observed in 4% of all HZ patients (2).

## MATERIALS and METHODS

The records of HZ patients who were hospitalized in our clinic between June 2019 and November 2020 were retrospectively reviewed. Patients' age, gender, dermatome involved, presence of dissemination and accompanying diseases were noted from the patient files. Descriptive statistics of the data; are given as mean, standard deviation, frequency and percentage values. Normality assumption of quantitative data was checked by Shapiro-Wilk test. Independent sample t-test was used for variables with normal distribution. Relationships between categorical variables were analyzed using the Pearson Chi-

square test. Statistical analyzes were performed using IBM SPSS Statistics 25.0 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) package program. The level of significance was set at 0.05 in all analyzes.

## RESULTS

There were 19 HZ patients in our study. The demographic data of the patients are grouped according to the dissemination status and shown in Table-1. Primary dermatome involvement was present in all patients. Twelve patients (63.2%) had facial involvement (Figure-1). The other involved dermatomes were; C5-6, T2-3, T3-4, T4-5, T5-6, L2-3, L4-5 (Figure-2). DHZ was seen in 36.8% (7 patients). Concomitant pre-septal and periorbital cellulitis were observed in 50% (6 patients) and 8.3% (1 patient) respectively in patients with OHZ. No visual complications occurred in OHZ patients.

**Table-1.** Demographic and clinical features of HZ patients. (HZ: herpes zoster, DHZ: disseminated herpes zoster, PNH: post-herpetic neuralgia)

| Features | All patients | Non-DHZ group | DHZ group |
|---|---|---|---|
| **Number** | 19 | 12 | 7 |
| **Percent** | 100 | 63.2 | 36.8 |
| **Male gender** | 13 (68.4%) | 7 (58%) | 6 (85%) |
| **Age range** | 29-90 | 29-85 | 61-90 |
| **Mean age** | 68.5±15.2 | 63.4±15.5 | 77.2±10.4 |
| **Immunosuppression** | 7 (36.8%) | 4 (33.3%) | 3 (42.8%) |
| **PNH** | 6 (31.6%) | 3 (25%) | 3 (42.3%) |
| **Parenteral acyclovir** | 14 (73.7%) | 7 (58.3%) | 7 (100%) |
| **Mortality** | 1 (5.2%) | 0 | 1 (14.3%) |

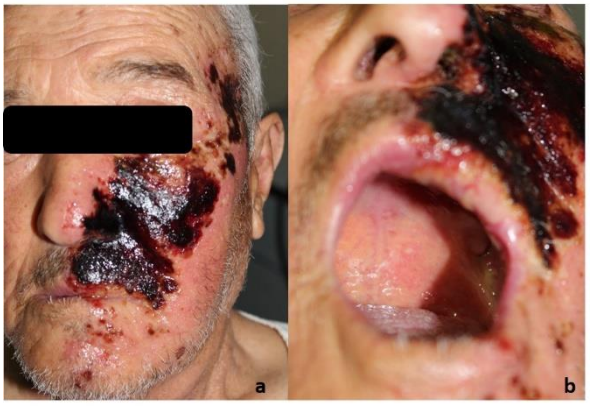


**Figure-1 (a, b):** A necrotic ulcerated lesion in the V2 (maxillary nerve) dermatome (a). Ulcerated lesions in the oral mucosa that do not exceed the midline on the left soft palate (b).

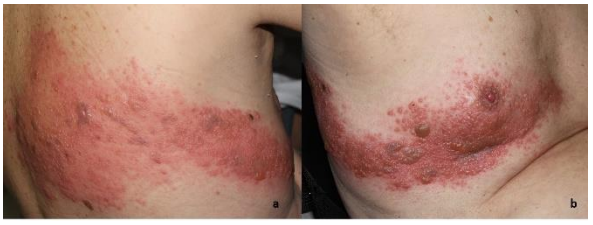


**Figure-2 (a, b):** Grouped vesicles and bullae on erythematous background in the right T4-T5 dermatome (a, b).

In patients with DHZ, no visceral organ involvement was seen. Three patients (42.8%) had immunosuppression (use of methotrexate for psoriatic arthritis, bladder cancer and anaplastic cell lymphoma,). The dermatomes involved were; 71.4% ophthalmic dermatome (5 patients), 14.3% T3-4 dermatome (1 patient) and 14.3% T4-5 dermatome (1 patient), respectively. The relationship between the presence of dissemination and age, gender, the presence of immunosuppression and the development of PNH was not statistically significant (p: 0.051, p: 0.216, p: 0.865, p: 0.419).

In patients with non-DHZ, four patients (33.3%) had immunosuppression (operated renal cell carcinoma, prostate cancer, breast cancer, previous kidney transplant). PHN was observed in 25% (3 patients). The dermatomes involved were; 58.3% (7 patients) ophthalmic dermatome, and C5-6, T2-3, T5-6, L2-3, L4-5 dermatomes in the remaining patients.

The mean time between the onset of symptoms and admission to our center was 4.5 days in the non-DHZ group, while it was 5 days in the DHZ group. Antibacterial therapy was required in addition to antiviral treatment due to secondary bacterial infections in 58.3% (7 patients) of non-

DHZ group, and 57.1% (4 patients) of DHZ group.

C reactive protein (CRP) value was high in 75% of the non-DHZ group and was 24.04 mg/L on average. CRP value was high in 71% of the DHZ group and the mean value was 28.04 mg/L. Leukopenia was detected in 25% (3 patients) of non-DHZ group and in 14.3% (1 patient) of DHZ group. Thrombocytopenia was present of 8.33% (1 patient) in the non-DHZ group and 14.3% (1 patient) in the DHZ group. Leukopenia and thrombocytopenia were observed in the same patient in the DHZ group, this patient was the only patient who died during follow-up.

All patients with DHZ received intravenous acyclovir as antiviral therapy. In non-DHZ group 58% (7 patients) had intravenous acyclovir, 33% (4 patients) had valaciclovir, and 8.33% (1 patient) had brivudine treatment. Acyclovir was discontinued in two patients due to creatinine progression during the treatment.

While all of the patients in the non-DHZ group were discharged, one patient in the DHZ group died on the second day of treatment. The deceased patient had a history of hypertension and epilepsy, and had no known immunosuppressive disease or use of immunosuppressive drugs.

## DISCUSSION

Observation of more than 20 vesicular lesions or involvement of more than two dermatomes other than the primary dermatome is defined as DHZ (3, 8). DHZ develops as hematogenous dissemination of VZV from the dorsal root ganglia. It is especially seen in patients with cellular immune disorders (9). Although dissemination is more common in immunosuppressive patients, it can also be seen in immunocompetent patients. It occurs at an older age in immunocompetent individuals compared to immunosuppressed patients. Generally, it starts with a dermatomal involvement and dissemination is observed subsequently, but more rarely, it can also occur with widespread lesions without dermatomal involvement (3). Risk factors for DHZ are; being older than 50 years of age, accompanying or prodromal moderate or severe pain and presence of immunosuppression (4). Sometimes it may be the first sign of immunosuppression. The presence of DHZ indicates a higher risk of complications (10). There are quite a few studies in the literature about DHZ because of its low prevalence, and the reports are mostly in the form of case reports. In a study of 32 patients in which HZ development was evaluated in patients with Systemic Lupus Erythematosus (SLE), the incidence of DHZ was reported to be approximately 22% (11). In the study of Vukelic et al. evaluating 1755 HZ patients hospitalized during 20 years, generalized HZ was detected in 22% of the patients. In the study, the authors stated that drug-induced immunosuppression and advanced age were associated with generalized HZ (6). In our study, the rate of DHZ was found to be 36.8%.

OHZ constitutes 10-20% of HZ cases (4). In our study, the rate of OHZ was 63.2% and the incidence of OHZ was higher in the DHZ group (71.4%). Approximately 3-10% of HZ cases need to be hospitalized (4, 12). Hospitalization indications are; having severe infection, DHZ, OHZ, and CNS or visceral involvement (13). In our study, the rates of DHZ and OHZ are thought to be high due to the fact that hospitalized HZ cases were evaluated.

The average age of HZ patients is approximately 64 (5). It has been reported that the risk of developing HZ is higher in women than in men (14, 15). In a study in which 811.541 HZ patients were evaluated, the male sex ratio was found to be 48.3% (15). Özkol et al. from our country evaluated the pediatric and adult HZ cases who applied to the dermatology outpatient clinic and they reported that 59.1% of the patients were male and the mean age was 42.21 ± 23.88 (2-93) (16). In the study by Köse et al. evaluating 23 HZ patients who were hospitalized, the mean age was 64.08 (22-90) and male gender predominance was reported with a rate of 74% (17). In the study of Vukelic et al. in which 1755 hospitalized HZ patients during 20 years were evaluated, the mean age was found to be 70 (17-97) and 42.3% of the patients were male (6). In the present study, the mean age of the patients was found to be 68.4, similar to the literature. Contrary to the female gender predominance reported in the literature, we found male gender predominance with a rate of 68.4% in our study.

In the study by Bollea-Garlatti et al. evaluating 41 DHZ cases, 51% of the patients were male, with a mean age of 70 (52-82) (3). In our study, male gender predominance was also observed in the DHZ group with a rate of 85%. While the mean age of the patients was 77.2 years in the DHZ

group, it was 63.4 years in the non-DHZ group. The relationship between age and dissemination was not statistically significant (p: 0.051).

In the study by Buchan et al. evaluated 135.206 HZ cases admitted to the hospital during 14 years, it was found that 13% of the HZ cases were immunocompromised (3% of the population was immunocompromised). They hospitalized 8% of HZ cases admitted to the hospital. Hospitalization rate was reported as 6% and 24% in immunocompetent and in immunocompromised patients respectively. They observed that the development of PNH, intensive care admission and death were more common in immunocompromised patients compared to immunocompetent patients (18). In the present study, 36.8% of the hospitalized HZ patients had an immunosuppressive condition. This rate was higher in the group with DHZ.

In the study of Bollea-Garlatti et al., in which they evaluated 41 DHZ cases, they detected immunosuppressive condition in 58.5% of the patients. In the laboratory tests, thrombocytopenia was observed in 56% of the cases, and leucopenia in 31% (3). Immunosuppression was detected in 42.8% of the DHZ cases in our study. Leukopenia and thrombocytopenia were observed in 1 patient (14.3%) and this patient was the only patient who died during follow-up. The relationship between dissemination and the presence of immunosuppression was not statistically significant (p: 0.865).

PHN was observed in 42% of DHZ cases in our study. This rate was reported as 24% by Bollea-Garlatti (3). While 1 patient (14.3%) died in our study, the rate of patients lost in Borlea-Garlatti's study was 14.6% (6 patients) (3). Borlea-Garlatti et al. stated that the frequency of DHZ was similar in immunosuppressive and immunocompetent individuals, and it was significant that the mean age of immunocompetent individuals was higher than immunosuppressive individuals. They found no significant difference in clinical and mortality between the two different groups (3).

## CONCLUSION

In the present study, in the group with DHZ, the mean age of the patients, the accompanying immunosuppressive state, and the rate of PHN development were found to be higher than the non-DHZ group, but this highness was not statistically significant. Studies on DHZ, which has a higher mortality compared to classical HZ, are limited due to the low frequency of the disease. Studies involving larger numbers of patients are needed in order to report more clearly the clinical features and mortality rates in these patients.

**Conflict of Interest:** None.

**References**

1. Kennedy PGE, Gershon AA. Clinical Features of Varicella-Zoster Virus Infection. Viruses. 2018; 10 (11): 609.
2. Johnson RW, Levin MJ. Herpes Zoster and Its Prevention by Vaccination. Interdiscip Top Gerontol Geriatr. 2020; 43: 131-45.
3. Bollea-Garlatti ML, Bollea-Garlatti LA, Vacas AS et al. Clinical Characteristics and Outcomes in a Population with Disseminated Herpes Zoster: A Retrospective Cohort Study. Actas Dermosifiliogr. 2017; 108 (2): 145-52.
4. Gross GE, Eisert L, Doerr HW et al. S2k guidelines for the diagnosis and treatment of herpes zoster and postherpetic neuralgia. J Dtsch Dermatol Ges. 2020; 18 (1): 55-78.
5. Dworkin RH, Johnson RW, Breuer J et al. Recommendations for the management of herpes zoster. Clin Infect Dis. 2007; 44 Suppl 1:S1-26.
6. Vukelić D, Oroši Končić D, Prepolec J et al. Clinical characteristics of hospitalized adults and adolescents with herpes zoster in Croatia: more than 20 years of a single-center experience. Croat Med J. 2020; 61 (5): 401-9.
7. Yin D, Van Oorschot D, Jiang N et al. A systematic literature review to assess the burden of herpes zoster disease in China. Expert Rev Anti Infect Ther. 2020:1-15.
8. Nair PA, Patel BC. Herpes Zoster. 2021 Nov 2. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–.
9. Pitton Rissardo J, Fornari Caprara AL. Herpes Zoster Oticus, Ophthalmicus, and Cutaneous Disseminated: Case Report and Literature Review. Neuroophthalmology. 2018; 43 (6):407-10.
10. Chen LK, Arai H, Chen LY et al. Looking back to move forward: a twenty-year audit of herpes zoster in Asia-Pacific. BMC Infect Dis. 2017; 17(1): 213.

11. Sayeeda A, Al Arfaj H, Khalil N, Al Arfaj AS. Herpes Zoster Infections in SLE in a University Hospital in Saudi Arabia: Risk Factors and Outcomes. Autoimmune Dis. 2010; 2011: 174891.
12. Ahronowitz I, Fox LP. Herpes zoster in hospitalized adults: Practice gaps, new evidence, and remaining questions. J Am Acad Dermatol. 2018; 78 (1): 223-30.e3.
13. Bader MS. Herpes zoster: diagnostic, therapeutic, and preventive approaches. Postgrad Med. 2013; 125 (5): 78-91.
14. Le P, Rothberg M. Herpes zoster infection. BMJ. 2019; 364: k5095.
15. Esteban-Vasallo MD, Domínguez-Berjón MF, Gil-Prieto R, Astray-Mochales J, Gil de Miguel A. Sociodemographic characteristics and chronic medical conditions as risk factors for herpes zoster: a population-based study from primary care in Madrid (Spain). Hum Vaccin Immunother. 2014; 10 (6): 1650-60.
16. Özkol HU, Bilgili SG, Karadag AS, Altun F, Calka O. The Evaluation Clinical and Demographic Characteristics of 115 Patients Diagnosed with Herpes Zoster in Eeastern Turkey. Turk J Dermatol 2013; 7: 201-5.
17. Köse Ş, Atalay S, Gül S, Sönmez U, Ödemiş İ. Tepecik Eğit Hast Derg 2013; 23 (2): 89-92.
18. Buchan SA, Daneman N, Wang J et al. Incidence of Hospitalizations and Emergency Department Visits for Herpes Zoster in Immunocompromised and Immunocompetent Adults in Ontario, Canada, 2002-2016. Clin Infect Dis. 2020; 71 (1): 22-9.