

Clinical features of hospitalized herpes zoster patients and comparison of elderly patients with younger patients: tertiary care clinical experience.**Hastanede yatan herpes zoster hastalarının klinik özellikleri ve yaşlı hastaların genç hastalarla karşılaştırılması: Üçüncü basamak klinik deneyimi**Berkay TEMEL¹, Ozge Mine ORENAY¹, Nermin KARAOSMANOGLU¹**ABSTRACT**

AIM: Several studies were conducted to determine the characteristics of hospitalized patients with Herpes Zoster. This study aimed to evaluate the characteristics of hospitalized especially elderly patients with Herpes Zoster and compare them with young adult patients in tertiary clinic in Türkiye.

MATERIAL AND METHOD: Hospitalized HZ patients were enrolled 2008 and 2020. Age, gender, length of hospitalization, affected dermatomes, treatment agents, comorbidities, complications were recorded from the electronic medical files retrospectively.

RESULTS: Totally 82 patients were evaluated. 62.2% (n=51) of the patients were over 65 years old. In the group over 65 years of age, the proportion of female patients were 54.9% (n=28), cervical dermatome involvement was 49% (n=25), the most common comorbidity is hypertension, the proportion of comorbid patients was 92.2% (n=47), the proportion of immunosuppressive patients were 39.2% (n=20), the most common complication was acute neuralgia, the proportion of complicated patients was 68.6% (n=35), the most commonly used treatment agents were valacyclovir and NSAID. The mean length of hospital stay was 11.9 days.

CONCLUSION: Elderly hospitalized patients with HZ tend to be more complicated and have longer hospital stays.

Keywords: zoster, zoster complication, neuralgia, valacyclovir

ÖZET

AMAÇ: Herpes Zoster (HZ) ile hastaneye yatırılan hastaların özelliklerini belirlemek için çeşitli çalışmalar yapılmıştır. Bu çalışma, Türkiye'de üçüncü basamak klinikte yatan özellikle yaşlı Herpes Zoster hastalarının özelliklerini değerlendirmeyi ve genç erişkin hastalarla karşılaştırmayı amaçlamıştır.

YÖNTEM: 2008-2020 yılları arasında hastanede yatan HZ hastaları alındı. Yaş, cinsiyet, hastanede kalış süresi, etkilenen dermatomlar, tedavi ajanları, komorbiditeler, komplikasyonlar retrospektif olarak elektronik tıbbi dosyalardan kaydedildi.

BULGULAR: Toplamda 82 hasta değerlendirildi. Hastaların %62.2'si (n=51) 65 yaşın üzerindeydi. 65 yaş üstü grupta kadın hasta oranı %54,9 (n=28), servikal dermatom tutulumu %49 (n=25), en sık eşlik eden hastalık hipertansiyon, komorbid hasta oranı %92,2 idi. (n=47), immünsüpresif hastalar %39.2 (n=20), en sık görülen komplikasyon akut nevralji, komplike hasta oranı %68.6 (n=35), en sık kullanılan tedavi ajanları valasiklovir ve NSAİİ idi. Ortalama hastanede kalış süresi 11.9 gündü.

SONUÇ: HZ ile hastaneye yatırılan yaşlı hastalar daha komplike olma ve hastanede daha uzun süre kalma eğilimindedir.

Anahtar kelime: zoster, zoster komplikasyonu, nöralji, valasiklovir

¹Department of Dermatology, Ministry of Health, Ankara Training and Research Hospital, Ankara, Türkiye

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Sorumlu Yazar / Corresponding Author:

Berkay TEMEL

Address: Department of Dermatology, Ministry of Health, Ankara Training and Research Hospital, Sakarya Mahallesi, Ulucanlar Caddesi, No: 89, 06230, Altındağ, Ankara, Türkiye

Phone: +90 505 819 0789

E-mail: berkaytemel42@gmail.com

ORCID: 0000-0001-5528-9006

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Yazar Bilgileri / Author Information:

Ozge Mine ORENAY: ORCID: 0000-0001-5848-7323, ozgeorenay@gmail.com

Nermin KARAOSMANOGLU: ORCID: 0000-0002-3462-1628, nermin_kara@yahoo.com

INTRODUCTION

Herpes zoster (HZ) is caused by the reactivation of the varicella-zoster virus (VZV). VZV can reactivate later in a person's life and cause a painful maculopapular rash called herpes zoster. People with HZ most commonly have a rash in one or two adjacent dermatomes (localized zoster). The rash is usually painful, itchy, or tingly [1].

Postherpetic neuralgia (PHN) is the most common and debilitating complication of Herpes zoster. Other complications are ophthalmic involvement, bacterial superinfection, peripheral nerve palsy, visceral involvement, and dissemination [1].

In the literature, there were some studies investigating the risk factors of herpes zoster. The best known risk factors were increasing age and a decrease in cellular immunity. Bone marrow or solid organ transplant, hematologic and solid malignancies, human immunodeficiency virus (HIV)/AIDS, and immunosuppressive drugs cause a decrease in cellular immunity. [2,3] In addition, chronic kidney disease, autoimmune diseases, inflammatory bowel disease, chronic obstructive pulmonary disease, diabetes mellitus, and depression were reported as diseases associated with increased risk in HZ. [4]

The lifetime risk of being HZ is between 20–30%, and this rate reaches 50% at the age of 85 years [5,6]. These rates indicate that HZ can be seen quite frequently in older adults. Some epidemiological studies were conducted to determine the burden of Herpes Zoster in elderly populations. Although the majority of these studies included older hospitalized adult HZ patients but these studies did not compare them with hospitalized young HZ patients [7–9]. This study aimed to evaluate both the characteristics of hospitalized elderly HZ patients and compare them with young HZ patients.

MATERIAL AND METHOD

Study design, patient selection, and variables

Patients who were hospitalized for HZ between January 2008 and December 2020 in a tertiary clinic in Türkiye were enrolled. The study was designed as a cross-sectional retrospective study. Local ethics committee approval was obtained (No:601-2021). Patients with International Classification of Disease (ICD-10) B02-Herpes Zoster and subgroups were selected from the hospital electronic medical records. Anamnesis, physical examination, and follow-up notes of HZ patients were reviewed by two different dermatologists. Age, gender, length of hospitalization, affected dermatomes, treatment agents, comorbidities and complications were recorded from the electronic medical records. The patients classified two age groups as under 65 years (U65) group and over 65 (O65) years group. Patients between the ages of 18–65 were enrolled into the U65 age group. Patients with at least one comorbidity were termed as comorbid patients. Charlson comorbidity index (CCI) of each patient was calculated. This index analyzes the risk of mortality by examining various factors such as diseases [9]. Patients with HIV, malignancy, chemotherapeutic/immunosuppressive drug use, diabetes mellitus, rheumatoid arthritis, chronic kidney, and liver disease were termed as the immunosuppressed patient. Complications were classified as acute neuralgia, ophthalmic involvement, secondary infection, peripheral nerve palsy, and dissemination. Patients with at least one complication were termed as complicated patients. Acyclovir, valacyclovir, brivudine, antiepileptics, antidepressants, nonsteroidal anti-inflammatory drugs, and opioids were the treatment agents. The number of hospitalized patients with HZ also was divided into 5-year periods between the examined dates. (2007–2011, 2012–2016, 2017–2021).

Statistical Analysis

Research data was evaluated via Statistical Package for the Social Sciences (SPSS.22, IBM SPSS Statistics for Windows, Version 22.0. Armonk, New York: IBM Corp.). Descriptive statistics were recorded as mean (\pm) standard deviation, frequency distribution, and percentage. Normality analyzes of the data were analyzed with the Shapiro Wilk test. For categorical variables, whether there is a difference in frequency between groups was compared by using Pearson chi-square. The Mann Whitney U test was used to compare the means of two independent groups in a non-normally distribution. The statistical significance value of this study was accepted as $p < 0.05$.

RESULTS

Demographic and clinical findings of hospitalized older and younger adult

patients

Totally 82 hospitalized patients with HZ were evaluated. Thirty-one (37.8%) of the patients were U65 group, and their mean age was 52.25. Fifty-one (62.2%) of the patients were O65 group and their mean age was 76.8. The mean age of 82 patients in total was 67.57. There was a statistical significance in terms of mean age between groups. ($p=0.01$) (Table-1)

The proportion of female patients was 48.4% ($n=15$) in the U65 group and 54.9% ($n=51$) in the O65 group. There was no statistically significant difference in terms of gender between age groups. ($p=0.56$) (Table-1)

Cervical dermatome was the most frequently affected dermatome in both age groups, followed by a thoracic dermatome. The proportion of patients whose cervical dermatome was affected in the U65 group was 37.8% ($n=18$) and 49% ($n=25$) in the O65 group. The list of remaining affected dermatomes and proportions were shown in Table-1. There was no statistically significant difference in terms of affected dermatomes between age groups. ($p>0.05$)

Table 1: Clinical characteristics of hospitalized herpes zoster patients

	< 65 years n=31 (37.8%)	>65 year n=51 (62.2%)	Total n=82 (100%)	P value
Age,mean \pm Std	52.25 \pm 14.6	76.8 \pm 6.13	67.57 \pm 15.73	0.01
Gender,n(%)				0.56
Male	16 (51.6)	23 (45.1)	39 (47.6)	
Female	15 (48.4)	28 (54.9)	43 (52.4)	
Affected Dermatomes, n(%)				
Cervical	18 (37.8)	25 (49)	43 (52.4)	0.42
Thoracic	9 (29)	21 (41.2)	30 (36.6)	0.26
Lumbosacral	5 (16.1)	9 (17.6)	14 (17.1)	0.85
Comorbidities, n(%)				
Diabetes Mellitus	7 (22.6)	9 (17.6)	16 (19.5)	0.58
Hypertension	9 (29)	25 (49)	34 (41.5)	0.07
Rheumatoid Arthritis	4 (12.9)	0 (0)	4 (4.9)	0.01
Chronic Pulmonary Disease	4 (12.9)	6 (11.8)	10 (12.2)	0.87
Chronic Liver Disease	2 (6.5)	1 (2)	3 (3.7)	0.29
Chronic Kidney Disease	4 (12.9)	9 (17.6)	13 (15.9)	0.56
Chronic Heart Disease	4 (12.9)	13 (25.5)	17 (20.7)	0.17
Chronic Neurological Disease	1 (3.2)	4 (7.8)	5 (6.1)	0.39
Psychiatric Disease	0 (0)	3 (5.9)	3 (3.7)	0.16
Malignancy	3 (9.7)	3 (5.9)	6 (7.3)	0.52
Concomitant Skin Disease	4 (12.9)	1 (2)	5 (6.1)	0.04
Charlson Comorbidity index, mean	2.22	4.27	3.5	0.01
Comorbid patient, n(%)	26 (83.9)	47 (%92.2)	73 (89)	0.24
Immunosuppression, n(%)	16 (51.6)	20 (39.2)	36 (43.9)	0.27
Complications, n(%)				
Acute neuralgia	11 (35.5)	24 (47.1)	35 (42.7)	0.3
Ophthalmic involvement	9 (29)	12 (23.5)	21 (25.6)	0.58
Secondary Infection	5 (16.1)	10 (19.6)	15 (18.3)	0.69
Peripheral Nerve Palsy	1 (3.2)	3 (5.9)	3 (3.7)	0.87
Dissemination	3 (9.7)	4 (7.8)	7 (8.5)	0.77
Complicated, n (%)	16 (51.6)	35 (68.6)	51 (62.2)	0.12
Treatment agents, n(%)				
Acyclovir	6 (19.4)	7 (13.7)	13 (15.9)	0.49
Valacyclovir	26 (83.9)	40 (78.4)	66 (80.5)	0.54
Brivudine	0 (0)	5 (9.8)	5 (6.1)	0.04
Antiepileptics	11 (35.5)	27 (52.9)	38 (46.3)	0.12
Antidepressant	2 (6.5)	2 (3.9)	4 (4.9)	0.6
NSAIDs	16 (51.6)	27 (52.9)	43 (52.4)	0.9
Opioids	8 (25.8)	16 (31.4)	24 (29.3)	0.59
Length of hospital stay, mean day	10.61	11.9	11.41	0.11

Comorbidity profiles of hospitalized older and younger adult patients

The proportion of comorbid patients in the O65 group was 92.2%, and this proportion was 83.9% in the U65 group. There was no statistically significant difference between the groups in terms of comorbid patients. ($p=0.24$) (Table-1)

The most common comorbidity was hypertension, followed by chronic heart disease and diabetes mellitus in both age groups. Hypertension, chronic heart diseases, chronic kidney diseases, chronic neurological disease, and psychiatric diseases tended to be more common in the O65 age group compared to the U65 group. The proportions of rheumatoid arthritis and concomitant skin disease were statistically significantly higher in the U65 group compared to the O65 group. ($p=0.01$, $p=0.04$) Concomitant skin diseases were pemphigus vulgaris ($n=4$) and psoriasis vulgaris ($n=1$). The comorbidity profiles of the patients were shown in Table-1.

The mean CCI scores of the patients were 3.5. CCI scores were statistically significantly higher in the O65 group (4.27), compared to the U65 group (2.22). ($p=0.01$) (Table-1)

The proportion of immunosuppressive patients in the U65 group was 51.6%

(n=16). This proportion was 39.2% (n=20) in the O65 group. There was no statistically significant difference between the groups in terms of immunosuppression. (p=0.27) (Table-1)

Complication profiles of hospitalized older and younger adult patients

The most common complication was acute neuralgia in both groups, followed by ophthalmic involvement and secondary infection. There was no statistically significant difference between the groups in terms of complications. (Table-1) The proportion of complicated patients was 51.6% (n=16) in the U65 group. This proportion was 68.6% (n=35) in the O65 group. There was no statistically significant difference between the groups in terms of complicated patient proportion. (p=0.12) (Table-1)

Treatment profiles of hospitalized older and younger adult patients

The most commonly used antiviral agent was valacyclovir in both groups, followed by acyclovir and brivudine. The proportion of brivudine use was statistically significantly higher in the O65 group compared to the U65 group. (p=0.04) (Table-1)

The most commonly used analgesic agent was NSAIDs in both age groups. The proportion of antiepileptic use was equal to the proportion of NSAID use in the O65 group (n=27, 52.9%) There was no statistically significant difference between the groups in terms of treatment agents except brivudine. (Table-1)

Hospitalization characteristics of older and younger adult patients

The mean length of hospitalization of the patients was 11.41 days. Meanwhile, this means was 10.61 in the U65 group, it was 11.9 in the O65 group. There was no statistical significance between the groups in terms of length of hospitalization mean.

The number of hospitalized patients was the highest between 2007 and 2011. The number of hospitalized patients tended to decrease over the years.

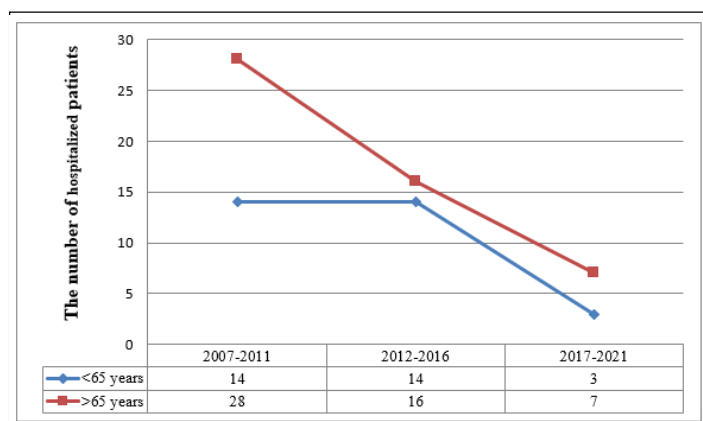


Figure1: Distribution of old and young adult hospitalized herpes zoster patients by years

DISCUSSION

This study showed that the O65 group constitutes the majority of hospitalized patients. In addition, the proportions of female patient, cervical, thoracic, lumbosacral dermatome involvement, hypertension, chronic heart diseases, chronic kidney diseases, chronic neurological disease, and psychiatric diseases, acute neuralgia, secondary infection, peripheral nerve palsy, antiepileptic usage in the O65 group tended to be higher than in the U65 group. However statistical significance was not observed. The CCI score, and the length of hospital stay in the O65 group statistically significantly higher than the U65 group.

The mean age of patients with HZ hospitalized in the literature was between 63.6-80 years and the majority of the patients were over 60 years old. [7-11] Our results were compatible with earlier researches. The mechanism that causes this is thought to be the decrease in cellular immunity associated with VZV with increasing age. [6,12]

The proportion of hospitalized female patients with HZ was between 48-57.9% in the previous studies. [7,9,10,13] Although the results of our study were consistent with this, this proportion was higher in the O65 group, unlike the U65 group. It has been suggested that the reason for this situation is related to the longevity of females. [14]

Previous studies have identified many comorbidities associated with hospitalized patients with HZ. In these studies, comorbidities were classified differently and 26.7%-61.6% of hospitalized patients had at least one comorbidity. The most common comorbidities associated with hospitalized patients with HZ were diabetes mellitus, co-infections, chronic heart diseases, chronic renal diseases, gastroesophageal reflux, and malignancies. [8-11] Most of these diseases cause secondary immunosuppression due to both the diseases themselves and the treatment agents used. Although similar comorbidities were reported in our study, previous studies did not compare these comorbidities among age groups. Some studies also evaluated the immunosuppression status in hospitalized patients with HZ. Although immunosuppression criteria were classified differently, In a study, the proportion of immunosuppressed patients in the group over 60 years of age was reported as 21%. [6] In our study, contrary to expectations, immunosuppression was less common over 65 years of age. This may have been caused by the unequal number of age groups.

Acute or chronic complications of herpes zoster adversely affect the quality of life of patients. Herpes zoster can be followed by chronic pain (postherpetic neuralgia), cranial nerve palsies, zoster paresis, meningoencephalitis, cerebellitis, myelopathy, multiple ocular disorders, and vasculopathy that can mimic giant cell arteritis. [15] Some of the patients are hospitalized due to complications and they create a burden on the health system. In previous studies, the proportion of complicated patients in hospitalized HZ ranged from 43.1% to 68%. Although similar results were obtained in our study, as expected, we also concluded that the proportion of complicated patients was higher in the O65 group. This was also expected because the incidence, severity, and duration of HZ complications generally increase with age. [16]

One of the most important criteria for evaluating the burden of a disease on the health system is the length of hospital stay. In studies evaluating patients with hospitalized HZ, the length of hospital stay ranged from 6 to 15.8 days. [7,9,10,13] In some of these studies, it showed that the length of hospital stay increases with increasing age. [7-10] Similar results were obtained in our study. Especially complications and comorbidities may prolong the length of hospital stay.

In the literature, the number of hospitalized patients has been increasing from past to present in national cohort studies with large participation. [8-10] In our study, contrary to expectations, the number of hospitalized patients in every age group tended to decrease from past to present. This may have been due to hospitalization criteria, and the difference in accessing the health system.

To the best of our knowledge, the treatment agents used in hospitalized patients and the affected dermatomes were not presented in the English literature. In our study, the most commonly used antiviral and analgesics in all age groups were valacyclovir and NSAIDs. The most frequently affected dermatome in all age groups was cervical. These data, together with the data to be added to the literature later, can help create new hospitalization criteria or treatment strategies.

Limitations of the study

This study had some limitations. This study was a cross-sectional retrospective study with a small number of participants. Hospitalized patients were selected only from the dermatology clinic. As diagnoses are based on ICD-10 codes, there may be individual coding errors.

CONCLUSION

Herpes zoster often affects the elderly patients. This study showed that elderly hospitalized patients with HZ tend to be more complicated and have longer hospital stays compared with the younger ones.

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