ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

DOI: 10.5336/ophthal.2025-111681

Demographic and Clinical Characteristics of Herpes Zoster Ophthalmicus: Retrospective Descriptive Research

Herpes Zoster Oftalmikus Hastalarının Demografik ve Klinik Özellikleri: Retrospektif Tanımlayıcı Araştırma

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This study was presented as an oral presentation at 2024 TOD National congress, November 21st-24th, 2024, Antalya, Türkiye.

ABSTRACT Objective: To evaluate the demographic characteristics, systemic comorbidities, and ocular manifestations of herpes zoster ophthalmicus (HZO) patients in a tertiary referral center, and to analyze associations between Hutchinson's sign and ocular involvement. **Material and Methods:** In this retrospective descriptive study, the medical records of patients diagnosed with HZO between January 2022-March 2025 were reviewed. Data on demographics, systemic diseases, ocular findings, and treatments were collected. Comprehensive ophthalmological examinations included best-corrected visual acuity, intraocular pressure, and detailed assessment of anterior and posterior segment involvement. The relationship between Hutchinson's sign and ocular complications was statistically analyzed. **Results:** A total of 115 patients (115 eyes) were included, with a mean age of 57.9±20.3 years; 53.9% were female. Systemic comorbidities were present in 64.3%, with hypertension (40.9%), immunosuppression (28.7%), and diabetes (27.0%) being the most common. Unilateral involvement was predominant (87.8%), while bilateral disease was observed in 12.2%. Ocular findings included vesicular eyelid lesions (87.0%), blepharoconjunctivitis (73.9%), periorbital edema (68.7%), ptosis (55.7%), and corneal involvement (51.3%), with pseudodendritic (23.5%) and stromal keratitis (14.8%) being the most common corneal pathologies. Anterior uveitis was detected in 13%. Hutchinson's sign was significantly associated with iris involvement (p=0.023), anterior uveitis (p=0.020), disciform keratitis (p=0.002), and skin involvement (p=0.007). **Conclusion:** HZO remains a significant cause of ocular morbidity, especially in older adults and those with systemic comorbidities. Hutchinson's sign is a critical predictor of severe ocular involvement. Early diagnosis and antiviral therapy are essential for preventing vision-threatening complications.

Keywords: Herpes zoster ophthalmicus; corneal diseases; anterior uveitis; keratitis

ÖZET Amaç: Bu çalışmanın amacı, 3. basamak bir sevk merkezinde herpes zoster oftalmikus (HZO) hastalarının demografik özelliklerini, sistemik komorbiditelerini ve oküler bulgularını değerlendirmek ve Hutchinson belirtisi ile oküler tutulum arasındaki ilişkileri analiz etmektir. **Gereç ve Yöntemler:** Bu retrospektif tanımlayıcı çalışmada, Ocak 2022-Mart 2025 tarihleri arasında HZO tanısı alan hastaların tıbbi kayıtları incelendi. Demografik bilgiler, sistemik hastalıklar, oküler bulgular ve tedaviler ile ilgili veriler toplandı. Hastaların en iyi düzeltilmiş görme keskinliği, göz içi basıncı ve ön ile arka segment tutulumları ayrıntılı değerlendirildi. Hutchinson belirtisi ile oküler komplikasyonlar arasındaki ilişki istatistiksel olarak analiz edildi. **Bulgular:** Çalışmaya, toplam 115 hasta (115 göz) dâhil edildi. Ortalama yaş, 57,9±20,3 yıl olup hastaların %53,9'u kadındı. Hastaların %64,3'ünde sistemik eşlik eden hastalıklar mevcuttu; en sık hipertansiyon (%40,9), immünsüpresyon (%28,7) ve diyabet (%27,0) görüldü. Olguların %87,8'inde tek taraflı tutulum izlenirken, %12,2'sinde bilateral tutulum mevcuttu. Oküler bulgular arasında veziküler göz kapağı lezyonları (%87,0), blefarokonjunktivit (%73,9), periorbital ödem (%68,7), pitozis (%55,7) ve kornea tutulumu (%51,3) saptandı. En sık gözlenen kornea patolojileri psödodendritik keratit (%23,5) ve stromal keratit (%14,8) idi. Ön üveit %13 oranında tespit edildi. Hutchinson belirtisi; iris tutulumu (p=0,023), ön üveit (p=0,020), diskiform keratit (p=0,002) ve kutanöz tutulum (p=0,007) ile anlamlı şekilde ilişkili bulundu. **Sonuç:** HZO, özellikle ileri yaş grubunda ve sistemik eşlik eden hastalıkları bulunan bireylerde önemli bir oküler morbidite nedenidir. Hutchinson belirtisi, ciddi oküler tutulumunun önemli bir göstergesidir. Görme kaybına yol açabilecek komplikasyonların önlenmesinde erken tanı ve antiviral tedavi büyük önem taşımaktadır.

Anahtar Kelimeler: Herpes zoster oftalmikus; kornea hastalıkları; ön üveit; keratit

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Peer review under responsibility of Turkiye Klinikleri Journal of Ophthalmology.

Received: 08 May 2025 ***Received in revised form:*** 10 Jul 2025 ***Accepted:*** 24 Jul 2025 ***Available online:*** 03 Sep 2025

Herpes zoster (HZ) is a disease caused by the reactivation of the varicella-zoster virus (VZV), characterized by dermatomal rash and neuropathic pain. *After the initial varicella (chickenpox) infection, the VZV can stay dormant in sensory ganglia and may reactivate later when the immune system becomes compromised*.[1] HZ ophthalmicus (HZO) represents an advanced form of HZ characterized by involvement of the ophthalmic branch (V1) of the trigeminal nerve, leading to periocular and ocular tissue involvement.[2] It develops in approximately 10-20% of HZ cases.[3] HZO is considered a significant public health concern due to the risk of ocular complications and permanent vision loss.[4]

The clinical course of HZO typically begins with a prodromal phase, during which patients may experience nonspecific symptoms such as fever, malaise, headache, and periocular pain.[5] As the disease progresses, vesicular eruptions, ocular inflammation, and various ocular findings appear in the dermatomal distribution of the V1 branch of the trigeminal nerve. Involvement of the nasociliary branch, indicated by herpetic lesions on the tip of the nose (known as Hutchinson's sign), is associated with a high risk of ocular involvement.[6] The most common ocular manifestations of HZO include conjunctivitis, keratitis, iridocyclitis, secondary glaucoma, and retinal involvement. If left untreated, these complications can lead to permanent vision loss.[7]

Risk factors for HZO include advanced age, immunosuppression, hematologic malignancies, transplantation, immunosuppressive medication use, and various comorbidities (such as diabetes mellitus, rheumatoid arthritis, and cardiovascular diseases).[8] Immunocompromised individuals are particularly prone to a more severe clinical course and increased risk of complications. However, it is important to note that HZO can also cause significant morbidity in immunocompetent individuals.[9]

The diagnosis of HZO is primarily based on clinical findings. However, in cases of atypical presentation or when differentiation from herpes simplex virus infection is necessary, molecular diagnostic methods such as polymerase chain reaction may be employed.[10] Early diagnosis and treatment are critical for preventing ocular complications and improving visual prognosis. The effectiveness of antiviral medications is maximized when treatment begins within the first 72 hours of the initial symptoms.[11] In addition to antiviral agents, treatment strategies may include topical corticosteroids, antibiotics, and supportive therapies, which play a significant role in disease management.[4]

The aim of this study is to comprehensively evaluate the demographic and clinical characteristics of patients diagnosed with HZO at a tertiary referral center. A better understanding of the epidemiological patterns, clinical course, and potential complications of HZO will contribute to optimizing early diagnosis and treatment strategies. Furthermore, this study aims to provide in-depth data on the impact of HZO on the population, its risk factors, and visual prognosis. The findings will offer valuable insights to improve the clinical management of HZO and guide future research in this field.

MATERIAL AND METHODS

This retrospective descriptive study was approved by the Ethics Committee of Çam and Sakura City Hospital Scientific Research Ethics Committee No. 1 (date: January 6, 2025; no: 25) and conducted in accordance with the principles of the Helsinki Declaration. The medical records of patients who presented to our clinic or were referred by the dermatology department with a diagnosis of HZ or HZO between January 2022-March 2025 were retrospectively reviewed.

Patients diagnosed with HZ by dermatology specialists and referred to our department due to suspected ocular involvement or those identified with ocular involvement in the emergency department were examined at ophthalmology department and HZO diagnosis was based on clinical findings of ophthalmology specialists. All patients underwent biomicroscopic examination and detailed ophthalmologic evaluation, and their clinical findings and medical histories were recorded. Patients with incomplete examination notes were excluded from the study.

During the examinations, the best-corrected visual acuity (BCVA), intraocular pressure, corneal and eyelid involvement, Hutchinson sign, periorbital

edema, ptosis, conjunctivitis, keratitis, corneal ulcer or scarring, neurotrophic keratitis, anterior uveitis, and optic neuritis were thoroughly evaluated. The relationship between Hutchinson sign and other ocular involvements was evaluated. Additionally, patients' systemic diseases, immunosuppression status, and medication use were recorded. Treatment methods were planned based on clinical findings and individual patient characteristics, and this information was included in the study data.

SPSS for Windows (Version 25.0, IBM Corp, NY, USA) was utilized for statistical analysis. Descriptive statistics included mean and standard deviation. Statistical significance was determined by x2 test, or Fisher's exact test. A p value of <0.05 was considered statistically significant.

RESULTS

The study included 115 eyes of 115 patients. The mean age of the participants was 57.90±20.32 years. The mean BCVA of the affected eyes was 0.32±0.42 logMAR, while the mean BCVA of the fellow eyes was 0.22±0.34 logMAR. Of the patients, 62 (53.9%) were female, and 53 (46.1%) were male. Unilateral disease was observed in 101 (87.8%) patients, whereas bilateral disease was present in 14 (12.2%) patients.

Systemic comorbidities were identified in 74 (64.3%) patients. A comprehensive overview of these systemic conditions is provided in Table 1. Skin involvement was observed in 113 (98.3%) patients. When the relationship between Hutchinson's sign and clinical findings was analyzed; iris involvement (p=0.023), anterior uveitis (p=0.020), disciform keratitis (p=0.002), and skin involvement (p=0.007) were significantly associated (Figure 1).

Ocular symptoms and clinical findings are summarized in Table 2. Notably, hypopyon, posterior uveitis, retinitis, scleritis, corneal perforation, and optic neuritis were not observed in any of the cases.

Regarding treatment, 98 (85.2%) patients received topical antiviral therapy, while all patients

TABLE 1: Systemic conditions of patients

Systemic condition	n (%)
Hypertension	47 (40.9)
Immunosuppression	33 (28.7)
Immunosuppressive drug use	22 (19.1)
Pancytopenia (secondary to chronic renal failure or malignancy)	8 (7.8)
HIV-positive	3 (2.6)
Diabetes mellitus	31 (27)
Cardiovascular disease	21 (18.3)
Chronic renal failure	20 (17.4)
Others (interstitial lung disease, atopic dermatitis, asthma)	13 (11.3)
Malignancy	11 (9.6)
Rheumatologic diseases	8 (7.0)

HIV: Human immunodeficiency virus

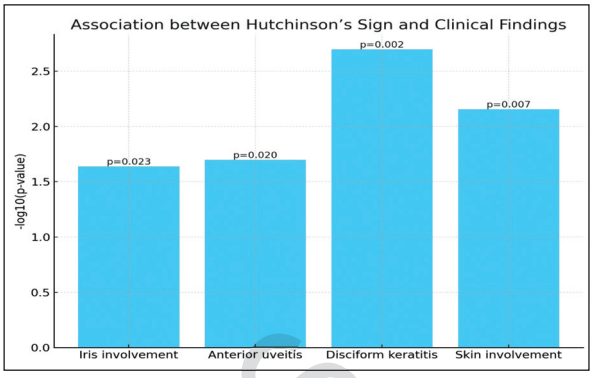

FIGURE 1: Association between Hutchinson's sign and selected clinical findings Statistical analysis was performed using the chi-square test. The y-axis represents the negative base-10 logarithm of the p values [$-\log_{10}$(p-value)] for each finding, indicating the statistical significance of the association with Hutchinson's sign. Lower p values correspond to higher bars, representing stronger significance.

TABLE 2: Frequency of clinical signs and symptoms

Clinical signs and symptoms	n (%)
Vesicular lesion on eyelid	100 (87.0)
Blepharoconjunctivitis	85 (73.9)
Periorbital edema	79 (68.7)
Pitosis	64 (55.7)
Corneal involvement	59 (51.3)
Pseudodendrite	27 (23.5)
Stromal keratitis	17 (14.8)
Disciform keratitis	14 (12.2)
Neurotrophic corneal ulcer	5 (4.3)
Corneal Scar	9 (7.8)
Postherpetic neuralgia	55 (47.8)
Hutchinson sign	25 (21.7)
Hypoesthesia	16 (13.9)
Anterior uveitis	15 (13)
Iris involvement	9 (7.8)
IOP increase	7 (6.1)

IOP: Intraocular pressure

were administered systemic (oral) antiviral treatment. Additionally, 28 patients were treated with topical steroids.

DISCUSSION

This retrospective descriptive study provides a comprehensive overview of the demographic and clinical characteristics of patients diagnosed with HZO at a tertiary care center. Our findings contribute valuable insights into the epidemiological distribution, risk factors, and spectrum of ocular involvement in HZO, underlining its significance as a potentially sight-threatening condition that requires timely diagnosis and intervention.

Consistent with previous studies, the mean age of the patients in our cohort was approximately 58 years, reaffirming the age-related increase in HZO incidence due to the progressive decline in VZV-specific cell-mediated immunity.[3,12,13]

A number of studies around the world have shown that the incidence of HZO is increasing.[6,14,15] The most extensive of these studies observed that the incidence rate of HZO exhibited an annual increase of 3.6% from 1994 to 2018.[13,16] This rising trend has been attributed to several factors, including the increased use of immunosuppressive therapies, the increased prevalence of immunocompromising conditions, and potential viral genetic recombination.[17-19]

Patients with underlying diseases such as malignancy, autoimmune diseases, metabolic diseases, diabetes mellitus, hypertension, renal failure, and even depression have been shown to have a higher risk for HZ than patients with any other diagnosis.[8,19-22] This has been attributed to the significantly lower VZV-specific cell-mediated immunity that occurs in conditions that compromise immune function compared to healthy individuals.[9,23] In our study population, the most frequent systemic comorbidities included hypertension (40.9%), immunosuppression (either disease- or medication-induced, 28.7%), and diabetes mellitus (27.0%). These findings corroborate existing epidemiological data demonstrating the significant association between HZO and underlying immunosuppressive states.

HZO has been found to be more prevalent in the female population.[4,6,24] The present study's demographic revealed a 53.9% female participation rate, which is in line with the literature. In our study, 87.8% of patients presented with unilateral disease, aligning with the typical clinical manifestation of HZO. However, the detection of bilateral involvement in 12.2% of cases is higher than reported in previous literature, where bilateral HZO is rare and often associated with significant immunosuppression.[6,25,26] This discrepancy may reflect a referral bias to our tertiary center, where more complex or severe cases are evaluated.

Keratitis, conjunctivitis and anterior uveitis are among the most commonly reported ocular manifestations of HZO. During the course of the studies, conjunctivitis was observed with a frequency ranging from 8% to 76%, keratitis with a frequency ranging from 5% to 76%, and anterior uveitis with a frequency ranging from 11% to 48%.[6,14,26-32] In the present study, the most prevalent ocular findings were vesicular eyelid lesions (87.0%), blepharoconjunctivitis (73.9%), periorbital oedema (68.7%) and ptosis (55.7%), followed by corneal involvement (51.3%). Pseudodendrites (23.5%) and stromal keratitis (14.8%) were more prevalent as corneal involvement, while disciform keratitis was observed in 12.2% of patients. Neurotrophic corneal ulcers and corneal scarring, although less prevalent, underscore the potential for protracted visual morbidity. The present findings are consistent with those of previous studies that emphasized the multifaceted nature of corneal involvement in HZO. This involvement can develop over time from epithelial changes to stromal changes and neurotrophic changes.[4]

The prevalence of postherpetic neuralgia in our study population (47.8%) was notably higher than the rates reported in other studies, which ranged from 13.3% to 20.9%.[27,29-31]

The observed discrepancies in the incidence of these symptoms between the present study and those documented in the literature may be attributable to disparities in sample size and selection criteria.

This study has several limitations. Its retrospective design and reliance on medical records may have

introduced documentation and selection biases. As a tertiary referral center, the inclusion of more severe cases could have influenced complication rates. The lack of standardized follow-up limited the evaluation of long-term outcomes, and psychological factors such as stress and anxiety, which may affect disease progression, were not assessed. Prospective multicenter studies are needed to validate these findings.

Although this study does not introduce a novel diagnostic or therapeutic method, it addresses a notable gap in the current literature by presenting comprehensive data from a large patient cohort managed in a high-volume tertiary referral center. Given the scarcity of large-scale, region-specific studies on HZO, especially from Middle Eastern-European settings, our findings provide valuable epidemiologic and clinical insights that can inform future research, contribute to international comparative analyses, and support the development of regionally relevant management strategies.

CONCLUSION

HZO represents a major cause of ocular morbidity, particularly among older adults and immunocompromised populations. This study underscores the critical importance of early diagnosis, comprehensive ophthalmologic assessment, and prompt initiation of antiviral therapy to mitigate the risk of severe ocular complications. A deeper understanding of associated systemic risk factors and clinical presentations is essential for optimizing patient management. Further prospective, multicenter studies are warranted to better characterize the long-term outcomes and to refine therapeutic strategies for HZO.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Ali Ceylan, Burçin Kepez Yıldız, Yusuf Berk Akbaş;* ***Design:*** *Ali Ceylan, Burçin Kepez Yıldız;* ***Control/Supervision:*** *Burçin Kepez Yıldız, Yusuf Yıldırım;* ***Data Collection and/or Processing:*** *Gülçiçek Cayhan, Fahri Onur Aydın, Yusuf Berk Akbaş;* ***Analysis and/or Interpretation:*** *Ali Ceylan, Fahri Onur Aydın;* ***Literature Review:*** *Ali Ceylan;* ***Writing the Article:*** *Ali Ceylan;* ***Critical Review:*** *Burçin Kepez Yıldız, Yusuf Yıldırım.*

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