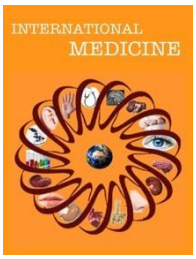

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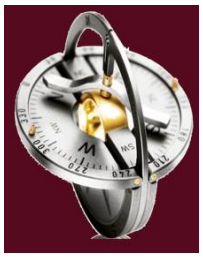

Original Research

A Study of The Clinical Presentations and Ocular Complications of Herpes Zoster Ophthalmicus in A Tertiary Care Centre

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Received: 15 Jun 2025 / Accepted: 16 Jul 2025

Abstract

Background Herpes zoster ophthalmicus (HZO) presents unique challenges due to its potential for significant ocular involvement. Understanding its clinical manifestations and associated complications is crucial for effective management. ***Methods***: This observational, retrospective study was conducted at a tertiary care center, analyzing clinical records of patients diagnosed with HZO. Demographic details like age and gender prevalance, ocular manifestations, complications, and associated systemic comorbidities were evaluated. ***Results***: A total of 72 patients (74 eyes) were included in the study. Males accounted for 58.3% and females 41.7% of cases. The most affected age group was 50-60 years (44.4%), followed by 60-70 years (34.8%). Unilateral eye involvement was seen in 97.2% of cases, with bilateral involvement in 2.8%. Common ocular findings included lid edema (56.7%), blepharoconjunctivitis (37.8%), keratoconjunctivitis (32.4%), anterior uveitis only and elevated intraocular pressure (24.3% each), and keratouveitis (20.2%). Neurological complications included oculomotor nerve palsy (4.1%) and optic neuritis (2.7%). Postherpetic neuralgia (39%) and paresthesia (34.7%) were the most frequent systemic complications. Corneal scarring (2.7%) and neurotrophic keratitis (1.35%) were also observed. Diabetes mellitus (41.6%) and HIV (13.8%) were the most common comorbid conditions. Only 5.4% of affected eyes had a best-corrected visual acuity (BCVA) of ≤6/60 at final follow up visit. ***Conclusion***: This study highlights the diverse clinical spectrum and ocular complications associated with HZO. Early diagnosis, vigilant follow-up, and a multidisciplinary treatment approach are essential for reducing long-term visual impairment and enhancing patient outcomes.

Keywords: *Herpes zoster,Herpes zoster ophthalmicus, neurotrophic keratitis,postherpetic neuralgia,valaciclovir, best-corrected visual acuity (BCVA).*

Introduction

The nosological compendium of Inborn Errors of Metabolism (IEM), as first illuminated by Sir Archibald Garrod (1908)[1], encompasses an Herpes zoster ophthalmicus (HZO) is a potentially vision-threatening condition caused by the reactivation of the varicella-zoster virus (VZV), also known as human herpes virus type 3. It represents a subset of shingles involving the ophthalmic (V1) division of the trigeminal nerve.[1] The virus, a member of the Herpes viridae family, remains dormant in sensory ganglia particularly the Gasserian (trigeminal) ganglion following primary infection with varicella (chickenpox).[2–4] Reactivation occurs when host immunity is compromised, leading to classical vesicular eruptions along the affected dermatome.

During reactivation, the virus travels anterogradely along sensory axons to the skin and mucosa, typically causing unilateral radicular pain and vesicular eruptions limited to the dermatome of a single cranial or spinal sensory ganglion.[5] The trigeminal dermatome is most frequently affected, followed by thoracic, cranial, cervical, lumbar, and sacral regions. Although recurrent episodes of herpes zoster are uncommon in immunocompetent individuals, they are more frequently observed in patients with HIV/AIDS.

Herpes zoster affects 20% to 30% of the population over their lifetime, with HZO accounting for approximately 10% to 20% of these cases.6 HZO is recognized as the second most common clinical manifestation of VZV reactivation. It may be categorized based on the presence or absence of ocular involvement. Ocular involvement occurs in approximately 50% -80% of all herpes zoster ophthalmicus patients.[7] HZO can occur at any age but is more prevalent in older adults, particularly those over 60 years of age.[8]

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DOI: 10.5455/im.56897

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Risk factors for HZO include advanced age and immunosuppressed states such as HIV infection, autoimmune diseases requiring corticosteroid or immunosuppressive therapy, malignancy, and organ or bone marrow transplantation. Additional contributing factors may include physical or emotional stress, acute illnesses, or other chronic conditions9. In patients with HIV, HZO often presents atypically, with multidermatomal involvement or lesions that are crusted, nodular, vesiculopustular, ulcerative, or widely disseminated.10–13

The prodromal phase of HZO typically mimics a viral illness, with symptoms such as low-grade fever, malaise, and fatigue occurring days before the rash appears. The dermatological manifestations begin as unilateral erythematous macules over the forehead, upper eyelid, and nose, evolving into papules, vesicles, and pustules that eventually crust and heal over several weeks. Dermatomal pain may precede the rash.[14] A classical sign indicating nasociliary nerve involvement is the presence of lesions at the tip of the nose, known as Hutchinson's sign, which has been associated with an increased risk of ocular complications due to shared innervation.[15]
HZO can affect virtually all ocular structures, from the eyelids to the retina, and is associated with a wide range of complications.[16] These include blepharoconjunctivitis, secondary Staphylococcus aureus infection ,episcleritis, scleritis, keratitis, uveitis, acute retinal necrosis (ARN), progressive outer retinal necrosis (PORN), optic neuritis, and cranial nerve palsies.[17] Cranial nerve involvement most commonly affects the third nerve, followed by the fourth, sixth, and seventh nerves. Recovery may be rapid or extend over several months.[18]
The most frequent and persistent complication of HZO is postherpetic neuralgia (PHN), characterized by neuropathic pain that continues after the skin lesions resolve.1 HZO can also lead to severe complications such as depression secondary to postherpetic neuralgia, persistent pain ,severe vision loss and even permanent vision loss.[19]
Early initiation of systemic antiviral therapy has been shown to significantly reduce the risk of both ocular and neurological complications in patients with HZO. Preventive strategies, including vaccination against herpes zoster, are strongly recommended, particularly for high-risk groups such as the elderly and immunocompromised individuals. It is imperative for primary care providers and ophthalmologists to prioritize vaccination and early intervention to mitigate the long-term consequences of HZO. 16

With the above background, the main.

AIMS AND OBJECTIVES

Primary Objective:
To analyze the spectrum of clinical presentations associated with Herpes Zoster Ophthalmicus (HZO).
Secondary Objective:
To evaluate the development of ocular complications during the course of the disease following treatment in patients diagnosed with HZO.

Materials and Methods

This observational and retrospective study was conducted after obtaining approval from the Institutional Ethics Committee of Chamarajanagar Institute of Medical Sciences, Karnataka. Purposive sampling was employed, and permission was obtained from the concerned authorities prior to data collection.
Clinical data were retrieved from outpatient department (OPD) registers maintained by the Department of Ophthalmology, which recorded findings from each patient visit. A total of 72 newly diagnosed cases of herpes zoster ophthalmicus (HZO), confirmed based on clinical history, examination findings, and relevant systemic evaluation, were included. The study covered a period of 18 months, from April 2022 to September 2023, with a mean follow-up duration of six months.

Statistical Analysis

Statistical analysis was not applicable to this descriptive observational study.

Inclusion Criteria

1.Patients of either sex aged 18 to 80 years diagnosed with herpes zoster ophthalmicus.
2.Patients willing to participate and comply with follow-up.

Exclusion Criteria

1.Patients with renal failure on dialysis.
2.Patients on immunosuppressive therapy following organ transplantation.
All participants underwent a comprehensive ophthalmological evaluation, including:
Visual acuity assessment using the Snellen chart.
Anterior segment examination with fluorescein and/or Rose Bengal staining.
Posterior segment examination.

Intraocular pressure measurement.

Laboratory investigations included complete blood count, random/fasting blood sugar, HIV 1 & 2 serology, urine routine, and renal function tests. Additional investigations were performed as required on a case-by-case basis.

Treatment Protocol

All patients were managed medically. Oral Valaciclovir 1000 mg was administered three times daily for at least 7 days and started within 3-4 days of rash onset. Systemic non-steroidal anti-inflammatory drugs (NSAIDs), such as Diclofenac or Ibuprofen, were also given. Skin lesions were treated with cold compresses, calamine lotion, and 5% acyclovir cream.

For ocular involvement:

Topical Ganciclovir 0.15% eye gel (five times daily), topical antibiotics, cycloplegics (Homatropine 2% eye drops), and lubricants were prescribed for keratitis.
In cases of anterior uveitis, topical corticosteroids (Prednisolone acetate 1%) with cycloplegics were initiated and tapered gradually based on clinical response.
Elevated intraocular pressure was managed with oral Acetazolamide (250 mg, 2-3 times/day) and topical Timolol maleate 0.5% eye drops twice daily.
Severely immunocompromised patients received intravenous Acyclovir at a dose of 10-15 mg/kg of ideal body weight (IBW) every 8 hours for a minimum of 2-3 weeks.
Patients were followed at regular intervals for at least six months. Clinical response to treatment and the occurrence of ocular and systemic complications were documented throughout the follow-up period.

RESULTS

Among the 72 patients with 74 eyes studied, 42 (58.3%) were male and 30 (41.7%) were female [Table 1]. The majority of cases occurred in the 50-60-year age group (n=32, 44.4%), followed by the 60-70-year age group (34.8%) [Table 2]. Unilateral ocular involvement was observed in 70 patients (97.2%), while bilateral involvement was noted in 2 patients (2.8%) [Table 3].

Visual acuity at presentation, assessed using the Snellen chart, was between 6/6 and 6/18 in 75.7% , 6/24 to 6/60 in 21.6%, and less than 6/60 in 2.7% of eyes [Table 4].

Associated systemic conditions included diabetes mellitus in 30 patients (41.6%), HIV infection in 10 (13.8%), tuberculosis in 5 (6.9%), and malignancy in 1 patient (1.38%). Additionally, 4 patients (5.5%) were undergoing chronic corticosteroid therapy [Table 5].

Ocular manifestations were varied [Table 6] , with lid edema observed in 42 eyes (56.7%), followed by blepharoconjunctivitis in 28 (37.8%). Blepharitis was noted in 10 (13.5%), and subconjunctival hemorrhage was reported in 2 eyes (2.7%). Conjunctivitis occurred in 14 eyes (18.9%). Among the less common presentations, episcleritis and scleritis were observed in 2 (2.7%) and 1 (1.35%) eye, respectively.

Keratoconjunctivitis was relatively common, affecting 24 eyes (32.4%) with superficial punctate keratitis as the most common corneal involvement. Keratitis was present in 9 (12.1%) and included epithelial involvement in 2 (2.7%), stromal involvement in 5 (6.7%), and endothelial involvement in 2 eyes (2.7%). Corneal hypoesthesia was documented in 6.7% of eyes. Anterior uveitis alone was evident in 18 (24.3%), while keratouveitis was observed in 15 eyes (20.2%). Iris atrophy was seen in 10 (13.5%), posterior synechiae in 6 (8.1%), and

pupillary distortion in 5 eyes (6.7%).

Elevated intraocular pressure (IOP) was observed in 18 eyes (24.3%), of which 13 eyes (17.5%) were successfully managed with medical therapy. Secondary glaucoma developed in 5 eyes (6.7%). No cases of retinal or orbital involvement were observed.

Neurological manifestations included oculomotor nerve palsy in 4.1% , Bell's palsy in 1.35% with spontaneous resolution over a few months and optic neuritis in 2.7% of eyes (Fig 1) .

In our assessment of complications related to ocular involvement in herpes zoster ophthalmicus (HZO), postherpetic neuralgia emerged as the most common, affecting 28 patients (39%) during follow-up. Paresthesia was reported in 25 (34.7%), and postherpetic itching was noted in 7 cases (9.7%) [Table 7]. Corneal scarring or opacification was observed in 2 eyes (2.7%), while lenticular opacification or cataract formation occurred in 1 eye (1.35%). Additionally, neurotrophic keratopathy was identified in 1 eye (1.35%) during follow-up [Table 8].

Among the systemic symptoms observed in patients with herpes zoster ophthalmicus (HZO) [Table 9], malaise was the most common, reported in 42 cases (58.3%), followed by ocular or periocular pain in 38 cases (52.7%). Headache occurred in 20 patients (27.7%), while fever was documented in 16 (22.2%). Dehydration was the least common systemic manifestation, occurring in only 2 individuals (2.7%).

Table 1 : PERCENTAGE OF GENDER AFFECTED

GENDER	FREQUENCY (%)
MALE	42(58.3)
FEMALE	30(41.7)

Table 2 : AGE DISTRIBUTION

AGE GROUPS(YEARS)	FREQUENCY (%)
<50	8(11.1)
50-60	32(44.4)
60-70	25(34.8)
70-80	7(9.7)

Table 3: PERCENTAGE OF OCULAR INVOLVEMENT

UL/BL	FREQUENCY (%)
UL	70(97.2)
BL	2(2.8)

Table 4 : VISUAL ACUITY AT PRESENTATION

BCVA	FREQUENCY OF EYE (%)
6/6-6/18	56(75.7)
6/24-6/60	16(21.6)
<6/60	2(2.7)

Table 5 : SYSTEMIC COMORBIDITIES OBSERVED IN HZO CASES

COMORBIDITIES	FREQUENCY (%)
DIABETES MELLITUS	30(41.6)
HIV	10(13.8)
ON STEROID	4(5.5)
MALIGNANCY	1(1.38)
TUBERCULOSIS	5(6.9)

Table 6 : PATTERN OF OCULAR INVOLVEMENT IN HZO-AFFECTED EYES

OCULAR INVOLVEMENT	FREQUENCY OF EYE (%)
Lid edema	42(56.7)
Blepharitis	10(13.5)
Blepharoconjunctivitis	28(37.8)
Subconjunctival haemorrhage	2(2.7)
Conjunctivitis	14(18.9)
Episcleritis	2(2.7)
Scleritis	1(1.35)
Keratoconjunctivitis	24(32.4)
Keratitis	9(12.1)
Epithelial	2(2.7)
Stromal	5(6.7)
Endothelial	2(2.7)
Corneal hypoesthesia	5 (6.7)
Anterior uveitis only	18(24.3)
Keratouveitis	15(20.2)
Iris atrophy	10(13.5)
Posterior synechiae	6(8.1)
Pupillary distortion	5(6.7)
IOP elevation	18(24.3)
Glaucoma	5(6.7)
Oculomotor nerve palsy	3(4.1)
Bell 's palsy	1(1.35)
Optic neuritis	2(2.7)

Fig 1 : PATTERN OF OCULAR INVOLVEMENT IN HZO - AFFECTED EYES

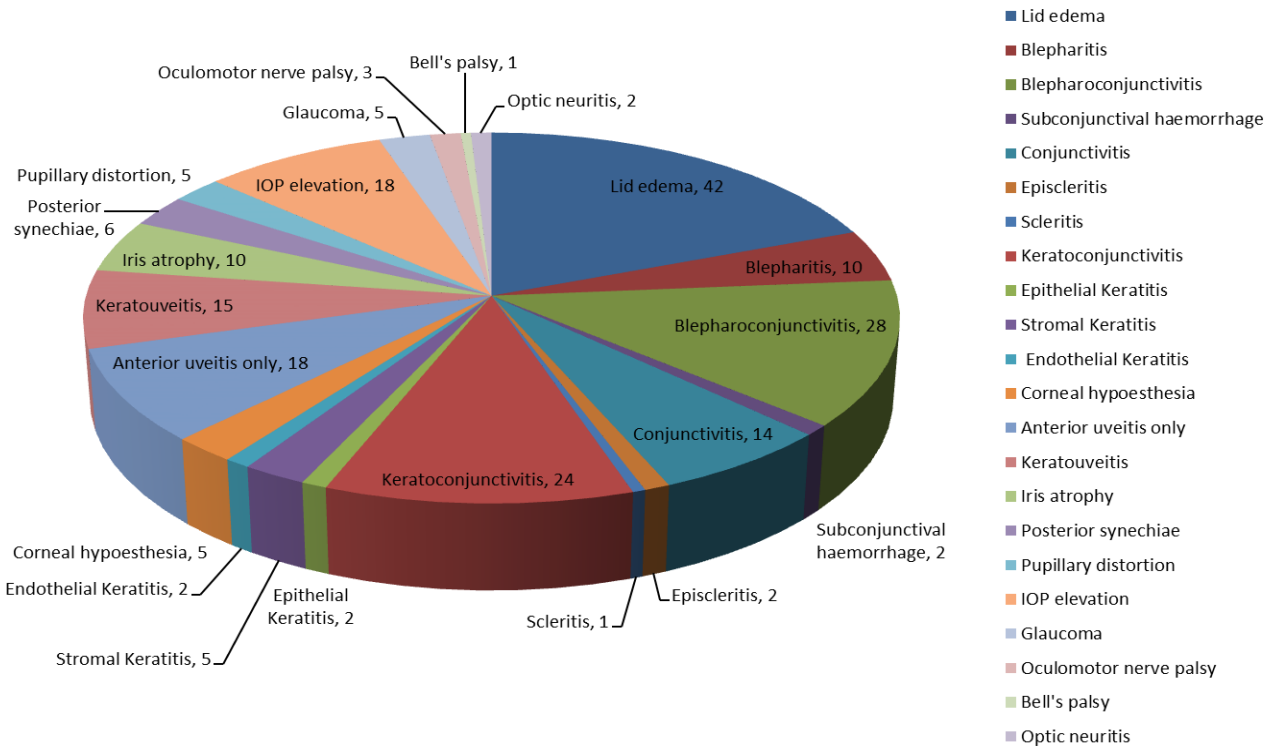
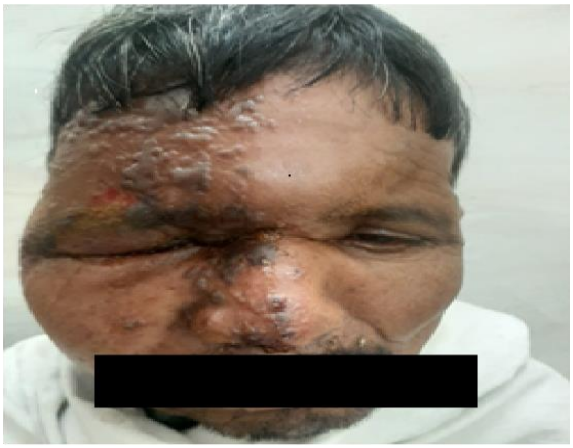


Table 7 : SYSTEMIC COMPLICATIONS OBSERVED IN HZO CASES	
SYSTEMIC COMPLICATIONS	FREQUENCY (%)
POSTHERPETIC NEURALGIA	28(39)
PARESTHESIA	25(34.7)
POSTHERPETIC ITCHING	7(9.7)

Table 8 : OCULAR COMPLICATIONS OBSERVED IN HZO EYES	
OCULAR COMPLICATIONS	FREQUENCY OF EYE (%)
CORNEAL SCARRING /OPACIFICATION	2(2.7)
CATARACT/LENTICULAR OPACIFICATION	1(1.35)
NEUROTROPHIC KERATOPATHY	1(1.35)

Table 9 : SYSTEMIC SYMPTOMS OBSERVED IN HZO CASES	
SYSTEMIC SYMPTOMS	FREQUENCY (%)
MALAISE	42(58.3)
EYEPAIN/PERIOCULAR PAIN	38(52.7)
HEADACHE	20(27.7)
FEVER	16(22.2)
DEHYDRATION	2(2.7)

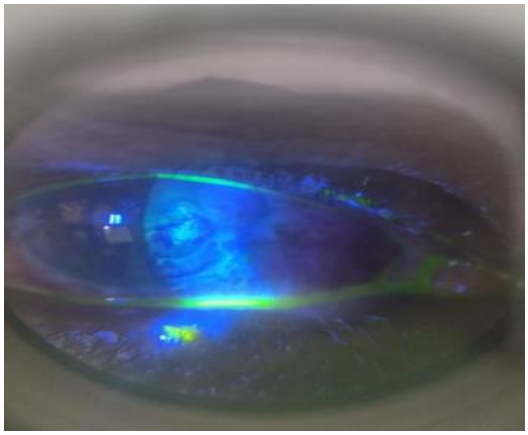


HZO with severe unilateral eye involvement

HZO with keratoconjunctivitis

HZO with blepharoconjunctivitis

HZO with bilateral eye involvement



HZO with dendritic keratitis

HZO with internal ophthalmoplegia

DISCUSSION

Herpes zoster ophthalmicus (HZO) is a clinically significant manifestation of herpes zoster, caused by reactivation of latent varicella-zoster virus (VZV) within the ophthalmic branch of the trigeminal nerve. It is associated with a broad range of ocular and systemic complications. While HZO is more frequently observed in elderly and immunocompromised individuals, it can also affect immunocompetent patients, sometimes resulting in severe ocular morbidity. Owing to its potential for vision-threatening complications and long-term irreversible ocular damage, HZO is considered an ophthalmic emergency. Early diagnosis and prompt initiation of antiviral therapy are essential to minimize the severity of ocular involvement and improve visual prognosis.

In the present study, the highest proportion of patients (44.4%) were in the 50-60 year age group, coinciding with the findings of Ghaznawi et al 20, who identified this decade as the most common period of HZO onset when comparing individuals above and below 60 years of age. This was followed by 34.8% of patients in the 60-70 year age group. Previous studies have consistently demonstrated an age-related increase in the incidence of HZO, largely attributed to the age-associated decline in cell-mediated immunity, which plays a critical role in suppressing reactivation of latent varicella-zoster virus 20.

In the current study, a higher prevalence of HZO among males was observed, aligning with findings from several earlier studies that reported a male predominance. However, studies by Maiya AS et al 3 and Womack LW et al 21 reported a female preponderance. In contrast, other investigations have found no significant gender difference in the incidence of HZO.22

Predominantly unilateral ocular involvement was observed in 97.2% of patients, with no significant laterality preference, consistent with findings reported in several previous studies [1]. Of the two bilateral cases, one patient was HIV-positive, suggesting that herpes zoster ophthalmicus (HZO) in the context of HIV infection may present with more extensive cutaneous and ocular involvement. The other patient had no significant medical history.

Among systemic comorbidities, diabetes mellitus was the most common, followed by HIV infection. However, 22 patients had no identifiable comorbid conditions. Ghaznawi et al. reported that younger patients were more likely to be systemically healthy compared to older individuals, with predisposing factors such as immunosuppressive therapy, cancer, or HIV infection observed in only 11.1% of early-onset HZO cases 20,23. In our study, among eight patients under the age of 50, four (50%) were HIV-positive and one (12.5%) was receiving chronic steroid therapy. These findings underscore age as a key determinant in the manifestation of HZO and highlight that the disease can occur even in immunocompetent individuals.

Lid edema was the most frequent ocular manifestation in our study, affecting 56.7% of eyes, followed by blepharoconjunctivitis (38.8%). Anterior uveitis (AU), with or without keratitis, was also a common finding, occurring in 44.5% of eyes. A previous retrospective study from India similarly identified AU with or without keratitis as the most frequent ocular presentation, occurring in over 50% of cases 24. In contrast, a study among Pacific Islanders reported a significantly lower AU incidence (6%) but noted keratitis in 28.3% of patients.25

In our study, keratitis was noted in 12.1% of eyes, with stromal involvement in 6.7%, and corneal hypoesthesia documented in 6.7% as well. Only one case of neurotrophic keratopathy was observed in a patient over 50 years of age. The relatively lower incidence of neurotrophic keratopathy may be attributed to the early initiation of antiviral therapy, with treatment started at a mean of 4 days after rash onset. In contrast, Ghaznawi et al. reported neurotrophic keratopathy in 19.6% of patients, primarily among older individuals 20, while Liesegang et al reported a prevalence of 25%.26

Optic neuritis, although rare, is a serious complication of HZO characterized by decreased visual acuity and central visual field defects. It often presents with a normal or swollen optic disc in early stages and may progress to optic atrophy and permanent vision loss. In the current study, optic neuritis was documented in two eyes. Previous studies have shown favorable outcomes in HZO-associated optic neuritis treated with systemic acyclovir and corticosteroids.27

Neurological complications also included oculomotor nerve palsy (4.1%) and Bell's palsy (1.35%), both of which resolved completely during follow-up. The reported incidence of extraocular muscle palsies in HZO varies between 7% and 31%.28,29

Postherpetic neuralgia (PHN) was observed in 28 cases (39%), representing a higher incidence than previously reported. Notably, PHN

occurred exclusively in patients over the age of 50. Ghaznawi et al. reported a PHN incidence of 17.8% in a series of 112 patients over 60 years of age in the United States 20, while a study in the Pacific region documented a prevalence of 20.9% 25. Advancing age remains the most significant risk factor for PHN, although factors such as severity of the acute episode, extent of rash, ocular involvement, and delayed initiation of therapy also contribute to its development.

The overall visual outcomes in our series were relatively favorable. The majority of patients presented with mild to moderate disease severity, while a smaller proportion exhibited severe involvement. At final follow-up, 5.4% of affected eyes had a best-corrected visual acuity (BCVA) of ≤6/60. This is consistent with prior reports on visual deprivation due to HZO 22.The primary causes of poor visual outcomes included neurotrophic keratopathy, optic atrophy secondary to optic neuritis, and corneal opacification.

Conclusion

The present study emphasizes the vital role of early recognition and timely treatment in reducing the risk of long-term ocular complications associated with Herpes Zoster Ophthalmicus (HZO). The diverse clinical presentations and potential for severe outcomes stress the need for increased clinical vigilance and prompt multidisciplinary intervention. Continued research and focused therapeutic strategies are essential to improve visual prognosis and enhance the quality of life for individuals affected by HZO.

Declaration of patient consent: The authors confirm that consent was obtained from all patients included in this study. Patients agreed to the use of their clinical information for academic and research purposes. They were informed that their identities will be kept confidential, although complete anonymity cannot be guaranteed.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Acknowledgements: The authors express their gratitude to all the faculty members of the department for their valuable support throughout the study. We are also grateful to the Institutional Ethics Committee for approving this study.

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