Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 5, 2024

Original Research Article

OCULAR MANIFESTATION OF HERPES ZOSTER OPHTHALMICUS IN A TERTIARY CARE CENTER MUZAFFARPUR, BIHAR

Dr. Sushma Kumari [1], Dr. Sweta Kumari [2]

[1] Senior Resident, Department of Ophthalmology, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, India

[2] Senior Resident, Department of Ophthalmology, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, India

Corresponding Author: Dr. Sushma Kumari

Abstract

Objectives: The present study aimed to evaluate the clinical profile, ocular manifestations, and visual outcomes in herpes zoster ophthalmicus patients in a tertiary care center in Muzaffarpur, Bihar.

Methods: All patients underwent an eye examination under a slit-lamp biomicroscope within 1 month of the onset of skin lesions. The degree of conjunctival injection was referenced from the Cornea and Contact Lens Research Unit grading scale (none, mild, moderate, and severe). The clinical grading of the intraocular inflammations was modified from the cell grading system of the Standardization of Uveitis Nomenclature (SUN) Working Group by using a 1 mm x 1 mm slit beam under a slit-lamp examination (grade 0 = none; grades 0.5–1+ = mild; grade 2+ = moderate; and grades 3–4+ = severe). Results: A total of 110 herpes zoster patients were enrolled in the present study. The mean age of the patients was 52.6 ± 17.34 years. Most of the patients were female 64 (58.81%). The rate of prevalence of ocular manifestation was 71.81%. The mean age of herpes zoster patients associated with ocular (47.56 ± 18.43) and non-ocular (51.48 ± 20.78) involvement showed no significant differences ($p = 0.335$). The duration of rash to eye examination >4 days between ocular (46.84%) and non-ocular (19.36%) involvement patients showed highly significant differences ($p = 0.008$). The duration of rash to acyclovir treatment >3 days between ocular (53.16%) and non-ocular (36%) involvement patients showed significant differences ($p = 0.039$). Conjunctivitis, keratitis, and iridocyclitis were seen in 77 (97.47%), 42 (53.16%), and 17 (21.52%) herpes zoster patients, respectively. Skin involvement on eyelids ($p = 0.009$), forehead ($p = 0.006$), and tip or alar of the nose ($p = 0.007$) between ocular and non-ocular involvement herpes zoster patients showed highly significant differences ($p < 0.05$), respectively. Conclusions: Herpes zoster infection was commonly seen in the older age population. It was more common in HIV infection, hypertension, diabetes mellitus, and tuberculosis patients. Significant involvement of eyelids, forehead, and tip or alar of the nose (Hutchinson's sign) was seen. Conjunctivitis, keratitis, and iridocyclitis are commonly associated with herpes zoster patients. Hence, early diagnosis and prompt aggressive treatment are required for the prevention of ocular complications in herpes zoster ophthalmicus patients.

Key words: Herpes zoster ophthalmicus, ocular manifestation, age group

INTRODUCTION

Herpes zoster ophthalmicus (HZO) is the clinical manifestation of the reactivation of latent varicella-zoster virus (VZV) infection in the ophthalmic branch of the trigeminal nerve . Herpes zoster (HZ), also known as "shingles," is caused by the reactivation of the varicella-

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 5, 2024

zoster virus in individuals who have had chicken pox, and there are approximately 1.2 million new cases of HZ annually in the United States . Although HZ typically results in a painful, unilateral, dermatomal, vesicular rash, zoster sine herpete (shingles without skin findings) has been reported. The demographics of individuals with HZ have been changing, and recently, new risk factors have been identified . For ophthalmologists, HZO continues to put patients at risk for vision loss. Efforts to combat vision loss from HZ require a multifaceted approach from vaccination to potential long-term suppressive therapy.

Although classically thought of as a disease of the elderly or immunosuppressed, HZ is frequently seen in younger individuals, and more than 90% of affected individuals are immunocompetent. The overall incidence of HZ is increasing: From the Olmstead County Study, the incidence of HZ has increased more than fourfold from the time periods 1945–1960 to 1980–2007, which translates into 2.5% per year . This increasing incidence also has been seen worldwide . Furthermore, the age at onset of HZ has been decreasing .

The clinical manifestation of herpes zoster is divided into three phases: preeruptive phase, acute eruptive phase, and chronic phase. The preeruptive phase is characterized by neuropathic-type symptoms, often described as burning, tingling, or shooting-type pain that may initially be mild and typically is limited to a particular dermatome . If cutaneous HZO is left untreated, ocular involvement occurs in more than half of patients and leads to chronic debilitating pain, visual impairment, and eventually, unilateral blindness . These ocular complications are more common among HIV-infected individuals and have a more severe clinical presentation and higher recurrence rate, especially in individuals with a low CD4 count .

The spectrum of ocular complications of HZO is diverse. Corneal inflammation and opacification (49–89%) and anterior uveitis (43–92%) are the most common complications, but ocular cranial nerve palsies, neuralgia, eyelid deformities, (blepharo-)conjunctivitis, (epi-)scleritis, and optic neuritis may also occur . In the acute phase of HZO, ‘early’ corneal complications may develop such as punctate epithelial keratitis and dendritic keratitis; these are associated with minimal risk of visual impairment. However, if left untreated, progression to chronic, late-stage corneal complications with serious visual impairment due to corneal opacification and ulceration may develop .

In cases where uveitis occurs, mild HZO-associated acute anterior uveitis may progress to sight-threatening stages due to chronic inflammation leading to corneal edema, iris atrophy, posterior synechiae, and cataract formation . Thus, early recognition of ocular involvement in HZO patients and subsequent initiation of targeted oral and topical treatment is essential to prevent ocular morbidity. The objectives of our study were to evaluate the clinical profile, ocular manifestations, and visual outcomes in herpes zoster ophthalmicus in a tertiary care center in Muzaffarpur, Bihar.

MATERIAL & METHODS

The present study was conducted in the Department of Ophthalmology, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, from August 2023 to December 2023. Patients who were clinically diagnosed with HZO and attended the Outpatient Department of Ophthalmology at Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, were enrolled. All patients underwent an eye examination under a slit-lamp biomicroscope within 1 month of the onset of skin lesions. The degree of conjunctival injection was referenced from the Cornea

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 5, 2024

and Contact Lens Research Unit grading scale (none, mild, moderate, and severe). The clinical grading of intraocular inflammations was modified from the cell grading system of the Standardization of Uveitis Nomenclature (SUN) Working Group by using a 1 mm x 1 mm slit beam under a slit-lamp examination (grade 0 = none; grades 0.5–1+ = mild; grade 2+ = moderate; and grades 3–4+ = severe).

Patients with previous ocular diseases, ocular trauma, or ocular surgery, or those who had an eye examination later than 1 month after the onset of their skin lesions were excluded from the study. Diagnoses of HZO were based on the presence of a unilateral group of vesicles on an erythematous base and a painful skin rash within the ophthalmic dermatome.

The following data were collected and recorded: demographic data (age, sex, and race), pre-existing diseases (acquired immune deficiency syndrome, diabetes mellitus, tuberculosis, autoimmune diseases, lymphoma, pregnancy, and others), and the date of onset of the skin rash. The extent of herpes zoster skin lesions was documented by marking anatomical drawings of the eyelids, forehead, alar, and tip of the nose.

Patients were treated with systemic oral acyclovir as soon as the diagnosis of HZO was established, and the time interval between the onset of HZO and the administration of the oral antiviral drug was recorded. Oral acyclovir (800 mg, 5 times per day) was prescribed for a period of 7–10 days, as per the guidelines of the American Academy of Family Physicians.

STATISTICAL ANALYSIS

Data was analysed by using latest version of SPSS software. Mean and standard deviations were observed. P-value was taken less than or equal to 0.05 for significant differences ($p \leq 0.05$).

OBSERVATIONS

A total of 110 herpes zoster patients were enrolled in the present study. The mean age of the patients was 52.6 ± 17.34 years. Most of the patients were female, with 64 (58.81%). The rate of prevalence of ocular manifestation was 79 out of 110 (71.81%).

Among 43 AIDS patients, 11 (25.58%) had herpes zoster infection. Hypertension was seen in 19 (14.4%) of the herpes zoster patients. Diabetes, tuberculosis, other immunodeficiencies, lymphoma, and systemic lupus erythematosus were seen in 8 (7.27%), 6 (5.45%), 5 (4.54%), 2 (1.81%), and 2 (1.81%) patients, respectively. Skin involvement was seen on the eyelids in 91 (82.72%), the forehead in 88 (80%), and the tip or alar of the nose (Hutchinson’s sign) in 35 (31.82%) patients.

In the present study, the rate of ocular involvement was 79 (71.82%). Ocular involvement of herpes zoster was observed in 44 (55.7%) right eyes and 35 (44.31%) left eyes. Conjunctivitis was seen in 77 (97.47%) herpes zoster patients. Conjunctival injection was graded as mild in 50 (63.3%), moderate in 24 (30.38%), and severe in 3 (3.8%) herpes zoster patients. Keratitis was observed in 42 (53.16%) patients. Among these 42 keratitis patients, dendritic involvement was seen in 37 (46.84%), stromal involvement in 3 (3.8%), and combined involvement in 2 (2.53%) patients. Iridocyclitis was seen in 17 (21.52%) herpes zoster patients, with mild, moderate, and severe cases in 10 (12.65%), 5 (6.33%), and 2 (2.53%) patients, respectively.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 5, 2024

Table 1: Demographic data of all 110 patients with acute herpes zoster ophthalmicus.

Characteristics	**Frequency (N=110)**
Age (years)	52.6 ± 17.34
Gender	
Male	36(32.73%)
Female	64(58.18%)
Underlying diseases	
Hypertension	19(14.4%)
Acquired immunodeficiency syndrome	11/43=25.58%
Diabetes mellitus	8(7.27%)
Tuberculosis	6(5.45%)
Lymphoma	2(1.81%)
Other immunodeficiency	5(4.54%)
Systemic lupus erythematosus	2(1.81%)
Skin involvements	
Eyelids	91(82.72%)
Forehead	88(80%)
Tip or alar of nose (Hutchinson's sign)	35(31.82%)

Table 2: Ocular findings in acute herpes zoster ophthalmicus patients.

Characteristics	**Frequency (N=79)**
Laterality	
Right eye	44(55.7%)
Left eye	35(44.31%)
Conjunctival injection	
No	2(2.53%)
Yes	77(97.47%)
Mild	50(63.3%)
Moderate	24(30.38%)
Severe	3(3.8%)
Keratitis	
No	37(46.84%)
Yes	42(53.16%)
Dendrite	37(46.84%)
Stromal	3(3.8%)
Combined	2(2.53%)
Iridocyclitis	
No	42(53.16%)
Yes	17(21.52%)
Mild	10(12.65%)
Moderate	5(6.33%)
Severe	2(2.53%)

In the present study, when we compared the mean age of herpes zoster patients associated with ocular (47.56 ± 18.43) and non-ocular (51.48 ± 20.78) involvement, the difference was not significant (p=0.335). The duration of rash to eye examination >4 days was significantly different between ocular (46.84%) and non-ocular (19.36%) involvement patients (p=0.008).

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 5, 2024

The duration of rash to acyclovir treatment >3 days was also significantly different between ocular (53.16%) and non-ocular (36%) involvement patients (p=0.039).

Comparisons of HIV infection (p=0.151), hypertension (p=0.717), diabetes (p=0.308), tuberculosis (p=0.521), immunodeficiency (p=0.550), lymphoma (p=0.373), and systemic lupus erythematosus (p=0.373) between ocular and non-ocular involvement herpes zoster patients showed no significant differences (p>0.05).

However, comparisons of skin involvement on the eyelids (p=0.009), forehead (p=0.006), and tip or alar of the nose (p=0.007) between ocular and non-ocular involvement herpes zoster patients showed highly significant differences (p<0.05).

Table 3: Showing the factors associated with ocular involvement in acute herpes zoster ophthalmicus.

Factors	**Ocular involvement (N=79)**	**No ocular involvement (N=31)**	**p-value**
Age (years)	47.56 ± 18.43	51.48 ± 20.78	0.335
Duration of rash to eye examination >4 days	37(46.84%)	6(19.36%)	0.008
Duration of rash to acyclovir treatment >3 days	44(55.69%)	8/25(32%)	0.039
Underlying diseases			
HIV infection	20/36(55.55%)	1/7(14.28%)	0.048
Hypertension	13(16.45%)	6(19.36%)	0.717
Diabetes	7(8.86%)	1(3.23%)	0.308
Tuberculosis	5(6.33%)	1(3.23%)	0.521
Immunodeficiency	3(3.8%)	2(6.45%)	0.550
Lymphoma	2(2.53%)	-	0.373
Systemic lupus erythematosus	2(2.53%)	-	0.373
Skin involvement			
Eyelid	70(88.61%)	21(67.74%)	0.009
Forehead	58(73.42%)	30(96.77%)	0.006
Tip or alar of nose (Hutchinson's sign)	31(39.24%)	4(12.91%)	0.007

DISCUSSIONS

Herpes zoster ophthalmicus (HZO) is the clinical manifestation of reactivation of the varicella-zoster virus (VZV) involving the ophthalmic division of cranial nerve V. This reactivation leads to ocular involvement in approximately 50% of HZO patients in the absence of prompt preventive antiviral therapy . HZO is often associated with significant ocular morbidity and can cause substantial visual impairment if not promptly and adequately treated.

Demographics and Prevalence

In our study, HZO was more common in older individuals, with a mean patient age of 52.6 ± 17.34 years. This finding aligns with previous research indicating that the incidence of HZO increases significantly with age . For instance, a recent study reported that individuals older than 65 years have an incidence rate approximately five times that of the rest of the population . The increased incidence in older populations is likely due to a decline in cell-mediated immunity, which is crucial in preventing the reactivation of latent VZV.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 5, 2024

Clinical Manifestations

HZO presents with variable ocular manifestations. In the acute eruptive phase, patients may exhibit eyelid swelling, conjunctivitis, punctate keratitis, and/or corneal pseudodendrites. If untreated, this can progress to more severe conditions such as stromal keratitis, neurotrophic keratopathy, and corneal mucous plaques. Severe ocular involvement, including serpiginous keratitis, acute retinal necrosis, optic neuritis, and orbital myositis, can result in retinal detachment or vision loss .

In our study, the rate of ocular involvement was 71.82%, similar to the 74% involvement reported by Adam et al. and slightly higher than the 63% found by Zaal et al. . The most common ocular manifestation was conjunctivitis (97.47%), followed by keratitis (53.16%), and iridocyclitis (21.52%).

Gender and Underlying Diseases

Females were more predominant in our study. Although previous studies by Nassaji-Zavareh et al. and Kaiserman et al. have shown a significant correlation between herpes zoster infection and diabetes mellitus, the proportion of diabetes mellitus patients in our study was relatively low at 7.27% .

Skin Involvement

The most common skin lesions in HZO were found on the eyelids, followed by the forehead, and least commonly, the tip of the nose. The virus tends to replicate and migrate along sensory nerves, affecting areas innervated by the ophthalmic division of the trigeminal nerve, particularly the supraorbital, supratrochlear, and nasociliary branches .

Factors Influencing Ocular Involvement

Our study highlighted several significant associations with ocular involvement. Hutchinson's sign, the duration from rash onset to eye examination (>4 days), and the duration from rash onset to acyclovir treatment (>3 days) were all significantly associated with higher risks of ocular manifestations. Skin involvement on the eyelids, forehead, and tip or alar of the nose also showed significant associations with ocular involvement.

Implications for HIV Patients

While our study did not find a significant relationship between HIV status and ocular involvement in HZO, this may be due to the low number of HIV-positive patients. However, other studies have demonstrated a strong association between HIV and severe ocular complications in HZO patients . Therefore, it is recommended that HIV-positive patients with HZO undergo thorough ophthalmological examinations to detect and prevent severe ocular complications.

Treatment

Prompt treatment with oral antiviral drugs is crucial in managing HZO. Systemic antivirals such as acyclovir, famciclovir, and valacyclovir are effective in reducing viral replication, minimizing ocular complications, and decreasing the duration of postherpetic neuralgia. Treatment initiated within 72 hours of rash onset is particularly beneficial .

In conclusion, early diagnosis and aggressive treatment of HZO are essential to prevent ocular complications and preserve vision. Our study underscores the importance of prompt medical

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 5, 2024

attention and antiviral therapy in managing HZO, especially in older individuals and those with significant risk factors.

CONCLUSIONS

The present study concludes that herpes zoster infection is commonly seen in the older age population. It is more common in HIV infection, hypertension, diabetes mellitus, and tuberculosis patients. There is significant involvement of eyelids, forehead, and the tip or alar of the nose (Hutchinson's sign) in herpes zoster patients. Conjunctivitis, keratitis, and iridocyclitis are commonly associated with herpes zoster. Hence, early diagnosis and prompt aggressive treatment are required for preventing ocular complications in herpes zoster ophthalmicus patients.

REFERENCES

1. Suaya JA, Chen SY, Li Q, et al. Incidence of herpes zoster and persistent post-zoster pain in adults with or without diabetes in the United States. Open Forum Infect Dis. 2014;1:ofu049.
2. Hernandez PO, Javed S, Medoza N, et al. Family history and herpes zoster risk in the era of shingles vaccination. J Clin Virol. 2011;52:344e348.
3. Liesegang TJ. Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. Ophthalmology. 2008;115(2 Suppl):S3eS12.
4. Kawai K, Yawn BP, Wollan P, et al. Increasing incidence of herpes zoster over a 60-year period from a population-based study. Clin Infect Dis. 2016;15:221e226.
5. Ivan Vrcek, Eileen Choudhury, Vikram Durairaj. Herpes Zoster Ophthalmicus: A Review for the Internist. The American Journal of Medicine 2017; 130: 1.
6. Vafai A, Berger M. Zoster in patients infected with HIV: a review. Am J Med Sci 2001: 321: 372–380.
7. Bayu S, Alemayehu W. Clinical profile of herpes zoster ophthalmicus in Ethiopians. Clin Infect Dis 1997: 24: 1256– 1260.
8. Veenstra J, Krol A, Van Pragg RM et al. Herpes zoster immunological deterioration and disease progression in HIV-1 infection. AIDS 1995: 9: 1153–1158.
9. Harding SP, Lipton JR, Wells JC. Natural history of herpes zoster ophthalmicus: predictors of postherpetic neuralgia and ocular involvement. Br J Ophthalmol 1987: 71: 353–358.
10. Liesegang TJ. Herpes zoster virus infection. Curr Opin Ophthalmol 2004: 15: 531–536.
11. Shaikh S, Ta CN. Evaluation and management of herpes zoster ophthalmicus. Am Fam Physician 2002: 66: 1723–1730.
12. Phillips AJ, Speedwell L, Makepeace C. CCLRU grading scales (Appendix D). Contact Lenses. 1997.p.863-7.
13. Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol 2005;140:509-16.
14. Borkar DS, Tham VM, Esterberg E, Ray KJ, Vinoya AC, Parker JV, Uchida A, Acharya NR (2013) Incidence of herpes zoster ophthalmicus: results from the Pacific ocular inflammation study. Ophthalmology 120:451–456.
15. Ghaznawi N, Virdi A, Dayan A, Hammersmith KM, Rapuano CJ, Laibson PR, Cohen EJ (2011) Herpes zoster ophthalmicus: comparison of disease in patients 60 years and older versus younger than 60 years. Ophthalmology 118:2242–2250.
16. Vrcek I, Choudhury E, Durairaj V. Herpes Zoster Ophthalmicus: A Review for the Internist. Am J Med. 2017;130:21-6.

17. Rousseau A, Bourcier T, Colin J, Labetoulle M. Herpes Zoster Ophthalmicus—Diagnosis and Management. US Ophthalmic Review 2013;6:119-24.
18. Nassaji-Zavareh M, Taheri R, Ghorbani R, Aminian M. Undiagnosed diabetes mellitus in patients with Herpes Zoster. Indian J Dermatol 2008;53:119-21.
19. Kaiserman I, Kaiserman N, Nakar S, Vinker S. Herpetic eye disease in diabetic patients. Ophthalmology 2005;112:2184-8.
20. Zaal MJ, Volker-Dieben HJ, D'Amaro J. Visual prognosis in immunocompetent patients with herpes zoster ophthalmicus. Acta Ophthalmol Scand 2003;81:216-20.
21. Albrecht MA. Clinical manifestations of varicella-zoster virus infection: Herpes zoster. UpToDate, UpToDate, Inc., Waltham, MA. 2014.
22. Szeto SK, Chan TC, Wong RL, Ng AL, Li EY, Jhanji V. Prevalence of Ocular Manifestations and Visual Outcomes in Patients with Herpes Zoster Ophthalmicus. Cornea 2017;36:338-42.
23. Van Dyk M, Meyer D. Hutchinson's sign as a marker of ocular involvement in HIV-positive patients with herpes zoster ophthalmicus. S Afr Med J 2010;100: 172-4.
24. Adam RS, Vale N, Bona MD, Hasanee K, Farrokhyar F. Triaging herpes zoster ophthalmicus patients in the emergency department: Do all patients require referral? Acad Emerg Med 2010;17: 1183-8.
25. Harding SP, Lipton JR, Wells JC. Natural history of herpes zoster ophthalmicus: predictors of postherpetic neuralgia and ocular involvement. Br J Ophthalmol 1987;71:353-8.
26. Bak E, Kim N, Khwarg SI, Choung HK. Case Series: Herpes Zoster Ophthalmicus with Acute Orbital Inflammation. Optom Vis Sci 2018;95:405-10.
27. Chiang E, Bajric J, Harris GJ. Herpes Zoster Ophthalmicus With Orbital Findings Preceding Skin Rash. Ophthalmic Plast Reconstr Surg 2018;34:e113-e5.
28. Tran KD, Falcone MM, Choi DS, et al. Epidemiology of herpes zoster ophthalmicus: recurrence and chronicity. Ophthalmology. 2016;123(7): 1469-1475.
29. Marsh RJ, Cooper M. Oral acyclovir in acute herpes zoster. Br Med J (Clin Res Ed). 1987;294(6573):704.
30. Balfour HH Jr. Varicella zoster virus infections in immunocompromised hosts. A review of the natural history and management. Am J Med. 1988;85:68-73.
31. Seitz B, Heiligenhaus A. "Herpetic keratitis". Various expressions require different therapeutic approaches. Ophthalmologe. 2011;108(4): 385-395.