

# Early and Late-Stage Ocular Complications of Herpes Zoster Ophthalmic in Saudi Arabia

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## Abstract

To describe the spectrum of ocular complications of HZO and to distinguish between early- and late-stage ocular complications. A retrospective cross-sectional study was carried out on patients who were diagnosed with ocular complications from herpes zoster in both the early and late stages. Patients who passed three months from the last eye examination were collected for re-examination in the Optometry Clinic, College of Science Applied Medical for the detection of late-stage complications of herpes zoster disease using a visual acuity chart (VA), lamp examination, and optical coherence tomography (OCT). The study proved that there is a positive statistically significant relationship regarding early eye complications versus complications in the late stage of herpes zoster with age ( $P = 0.004$ ). According to the gender that suffers from complications and early visual complications in the late stage of herpes zoster, there is no statistical significance at ( $P = 0.513$ ). Moreover, there was no statistically significant relationship regarding the time between the onset of ophthalmic complaints and their presentation to the ophthalmology outpatient clinic with the early stage regarding eye complications and the complications in the late stage at ( $P = 0.576$ ). The study concluded there is an association between advanced age and increased early eye complications vs. complications in the late stage. In addition, there was no relationship between sex and those with early ocular complications in the late stage of herpes zoster.

**Keywords:** Herpes zoster ophthalmic (HZO), Herpes zoster (HZ), Varicella-zoster virus, Ophthalmic, Chickenpox, Saudi Arabia

## INTRODUCTION

In general, infection with varicella zoster virus most commonly occurs in childhood, as it is spread through the air droplets, in addition to transmission by contact, as herpes zoster results through reactivation of the shingles virus, which resides within the nodule. Sensory neurosis, as the disease usually presents as a skin rash, is unilateral or vesicular in relation to a single cutaneous distribution [1].

Herpes zoster occurs globally, without seasonal differences in terms of infection, as the incidence of herpes zoster depends on age, and there are many common factors related to herpes zoster, such as age over fifty years, immunosuppression, infections, in addition to psychological stress. Studies have shown that the incidence of herpes zoster is rising in older individuals [2].

Reactivation of the varicella-zoster virus causes herpes zoster, as it lies dormant in the medullary ganglia, the sensory ganglia in the skull after the initial infection takes place in infancy. In addition to the limitations of the individual cutaneous skin, this treatment is available through antivirals. However, there are many complications with regard to the eye and blood vessels. In addition to the visceral and nervous vessels with regard to herpes zoster, these complications lead to an increase in the cost in terms of

health care, for all reasons, in addition to placing financial burdens on patients [3].

Moreover, depending on the patient's medical history, the diagnosis of herpes zoster, and the findings on a conventional physical examination, it is necessary to perform other techniques, for example, tonometry and keratometry, for a more thorough analysis to detect problems. Ocular herpes zoster is rarely diagnosed without additional diagnostic tests, such as viral.

Cultures, polymerase chain reaction (PCR), and antibody testing. It makes sense to consider HIV testing for patients who have severe disease, disseminated herpes zoster (a

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disease of several skin conditions), or those who have significant risk factors. Additional laboratory and imaging tests are rarely necessary [1].

In Saudi Arabia, data on the incidence and complications of herpes zoster are unknown; a study was conducted that aimed to assess trends regarding herpes zoster and its complications.

A retrospective survey was conducted among patients with a history of herpes zoster in Saudi Arabia during the year 2021 between June and December. The study found that herpes zoster is one of the common cases affecting a group of patients. Expanding access to the vaccine is required because the incidence of herpes zoster and its complications have been reduced by the available vaccine products [4].

According to one of the studies conducted on herpes zoster on patients with diabetes and high blood pressure, whose average age was seventy-one years, with ages ranging from fifty-two years to eighty-eight years, the results of the study reached Fifty-seven percent of the patients had decreased visual acuity when compared to the fellow eye, as it ranged from one to six strings related to vision, as most of them are due to inflammation related to the epithelial cornea, in addition to ocular perfusion. In most cases, the eye did not change compared to the fellow eye. The study concluded that no elevation was found related to intraocular pressure or posterior segment complications in any case [4].

On the other hand, one of the studies conducted in Saudi Arabia, due to the prevalence of herpes zoster and the serious impact on patients, recommended products that help reduce the incidence of herpes zoster. In addition, the study recommended expanding vaccinations to be delivered to all regions of the Kingdom of Saudi Arabia [5].

### Research Problem and Significance

No studies were performed in Saudi Arabia to describe the ophthalmic complications and eye examination abnormalities of patients suffering from ophthalmic herpes zoster diseases. So, this study aimed to describe the spectrum of ocular complications of herpes zoster ophthalmic (HZO) in the Riyadh region of Saudi Arabia and focus on the importance and effectiveness of vaccines to reduce the incidence of herpes zoster disease.

### Purpose of the Study

To describe the spectrum of ocular complications of HZO and, in particular, to distinguish between early- and late-stage ocular complications as these impact on visual prognosis and to improve the awareness among subjects about the important herpes zoster vaccine.

### Research Hypothesis

Herpes Zoster is now a prevalent condition affecting a wide range of patients; researchers recently hypothesized that

herpes zoster condition plays a significant role in Ocular Complications.

## MATERIALS AND METHODS

### Study Design

A Retrospective cross-sectional study.

### Setting

A Retrospective cross-sectional study. The study was conducted at King Khalid University Hospital in Riyadh and at Al-Aqiq General Hospital in Al-Baha.

### Subjects

Three hundred patients were diagnosed with herpes zoster (HZ); out of the 300 patients found (n=27), patients diagnosed with herpes zoster ophthalmic (HZO). (n=16) were from the King Khalid University Hospital in Riyadh, and (n=16) from the Al-Aqiq General Hospital in Al-Baha. All patient information, including demographic, diagnostic, and examination data, was extracted from the participant files. Patients who had passed three months since their last eye exam were re-examined at the optometry clinic of the College of Applied Medical Sciences using the visual acuity chart (VA), slit-lamp examination, and Optical Coherence Tomography (OCT) to detect the late-stage ocular complications of herpes zoster.

### Inclusion Criteria

Patients diagnosed with early and late-stage ocular complications of herpes zoster are either male or female.

### Exclusion Criteria

Participants who do not meet the inclusion criteria are either male or female.

### Tools

1. Visual acuity (VA), slit lamp examination, and optical coherence tomography (OCT) were performed as part of a comprehensive ophthalmologic examination of participants. \ Best corrected visual acuity on a Snellen chart would be required to satisfy the inclusion criteria.
2. A slit lamp is a microscope with a brilliant light that is utilized during eye examinations. It provides a detailed examination of the anterior and posterior structures of the eye. It is essential for detecting abnormalities during an eye exam.
3. OCT refers to optical coherence tomography: is a non-invasive optical tomography that provides in vivo retinal cross-sectional images.

### Statistical Analysis

Descriptive statistics were calculated using the SPSS v.28 software to provide an overview of the study's data, including frequency distributions, percentage shares, and means and standard deviations expressed as means SD. Second, we compared the two groups using chi-square tests for categorical variables (with Fisher's exact if necessary)

and Mann-Whitney U tests for continuous variables. Information may be seen as a mean plus SD, median plus range, or odds ratio (OR) with 95% CI. The statistical significance level used was a p-value of less than 0.05.

**Ethical Consideration**

The Human Research Ethics Committee at King Saud University approved the initiative. Before inclusion in the study, all participants provided informed consent.

**RESULTS AND DISCUSSION**  
*Socio-Demographic Data*

**Table 1. Socio-demographic variables (n=27)**

		N (%)
Gender	Male	15 (55.6)
	Female	12(44.5)
Hospital	King Khalid University Hospital- Riyadh	16 (59.3)
	Al-Aqiq General Hospital- Al-Baha	11(40.7)

**Table 1** shows that 55.6% of the total patients were male, while 44.4% were female. About the Hospital, 59.3% of the total patients were from King Khalid University Hospital-Riyadh, while 40.7% were from Al-Aqiq General Hospital-Al-Baha.

**Table 2. Patient's age (n=27)**

		N	Mean	Std. Deviation
Age	Male	15	57.60	15.240
	Female	12	41.00	18.625

**Table 2** shows that patients' ages ranged between 12 and 90 years, with a mean of 50.22 and Std. Deviation 18.506. Among the male group, patients' ages ranged between 30 and 90 years, with mean 57.60 and Std. Deviation 15.240, while Among the female group, patients' ages ranged between 12 and 77 years with a mean of 41 and Std. Deviation 18.625.

**Comparison Results**

**Table 3. Visual acuity of the eye (n=27)**

VA	OD		OS	
	N	%	N	%
20/20	4	14.8	4	14.8
20/25	4	14.8	2	7.4
20/30	4	14.8	4	14.8
20/40	4	14.8	2	7.4

**Table 5. Early- versus late-stage ocular complications of herpes zoster**

		Early-stage (n = 19)	Late -stage (n = 8)	Odds Ratio (95% CI)	P-value
Gender	Age	45(12-64)	65(34-90)	na	0.004
	Male	9 (60%)	6 (40%)		

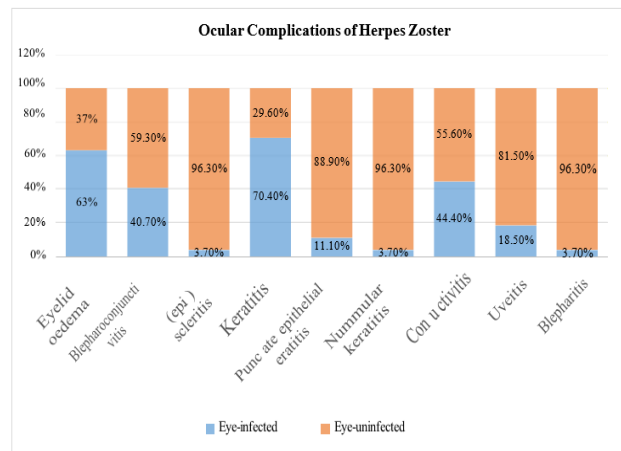
	20/60	7	25.9	9	33.3
Visual Impairment		2	7.4	4	14.8
Legally Blindness		2	7.4	2	7.4

**Table 3** shows that the visual acuity of the OD eye (20/60) was 25.9% vs. 33.3% for the OS eye. Visual impairment in the OD eye was 7.4% vs. 14.8% for the OS eye, while Legal blindness had an equality percentage at both OD and OS.

**Table 4. Ocular complications of herpes zoster**

	Eye-infected	Eye-uninfected	Total (n = 27)
Eyelid oedema	17 (63%)	10 (37%)	27 (100%)
Blepharoconjunctivitis	11 (40.7%)	16 (59.3%)	27 (100%)
(Epi-) scleritis	1 (3.7%)	26 (96.3%)	27 (100%)
Keratitis	19 (70.4%)	8 (29.6%)	27 (100%)
Punctate epithelial Keratitis	3 (11.1%)	24 (88.9%)	27 (100%)
Nummular Keratitis	1 (3.7%)	26 (96.3%)	27 (100%)
Conjunctivitis	12 (44.4%)	15 (55.6%)	27 (100%)
Uveitis	5(18.5%)	22 (81.5%)	27 (100%)
Blepharitis	1 (3.7%)	26 (96.3%)	27 (100%)

**Table 4** shows ocular complications of herpes zoster among patients (n=27). The highest percent was 70.4% for Keratitis, followed by 63% for Eyelid edema, 44.4% for Conjunctivitis, followed by 40.7% for Blepharoconjunctivitis, followed by 18.5% for Uveitis and 11.1% for Punctate epithelial keratitis, while (epi-) scleritis, Nummular Keratitis and Blepharitis occurred in one eye by present 3.7% (**Figure 1**).



**Figure 1. Ocular Complications of Herpes Zoster**

	Female	10(83.3%)	2(16.7%)		
<b>HZO</b>	Active HZO	1 (50%)	1 (50%)	0.39	0.513
	Healed HZO	18 (72%)	7 (28%)	(0.021-7.11)	
Time between onset of eye complaints and presentation to the ophthalmology outpatient department	(1-3wks)	18 (66.67%)	7 (25.93%)	na	0.576
	<b>Poor vision</b>				
	OS	1 (50%)	1 (50%)	na	na
	<b>Painful eye</b>				
Reported ocular symptom	OD	8 (66.67%)	4 (33.33%)	0.85	0.665
	OS	11(78.6%)	3(21.4%)	(0.52-1.38)	
	<b>Photophobia</b>				
	OD	3(75%)	1(25%)	1.88	0.524
	OS	2(40%)	3(60%)	(0.56-6.31)	

Data are shown as numbers (%) or median (range); HZO, herpes zoster ophthalmicus; CI, Confidence interval; P-value, Pearson Chi-square or Mann-Whitney U test; na, not applicable. \*Crude odds ratio and P-value were calculated for active HZO vs. healed HZO between early- and late-stage ocular complications.

**Table 5** shows that early ocular complications were observed in 19 (70.4%) patients, and late-stage ocular complications were observed in 8 (29.6%) patients.

Chi-square results show that late-stage ocular complications were associated with age ( $P=0.004 < 0.001$ ); since the median of late-stage cases was 65 years, ranging between 34 and 90 years, while patients with early-stage had a median age of 45, ranging between 12 and 64 years. Otherwise, the results did not record any significant relationships, perhaps due to the small sample size and the close percentages between the groups.

Depending on the demographic characteristics and ocular complications, the study observed a slightly higher male ratio than female patients (55.6% and 44.4%). This gender distribution indicates the need to explore additional potential gender-specific factors that may affect the development and management of visual complaints due to HZO and associated ocular complications. According to a study by Goswami *et al.*, (2021), the male-to-female ratio was 2:1 among HZO cases (66.67% and 33.33%), respectively [6]. Males were more likely to experience ocular manifestation [6]. In contrast, a study was conducted by Sundström showed that the incidence of herpes zoster more common in females than in males and older patients compared to younger individuals [7].

In the current study, 27 patients were included, the majority from King Khalid University Hospital (Riyadh district) (59.3%), and (40.7%) were from Al-Aqiq General Hospital in Al-Baha, which may be affected by various factors such as the location and reputation of the hospitals, referral patterns, or differences in population density. Therefore, this may cause a rise in patients in Riyadh; however, it is essential to consider potential biases in patient selection and recruitment for each Hospital and any differences in the healthcare infrastructure and resources available at each site. Similar findings were shown in a study conducted in

England showed that from 25.67 (95% CI 25.23-26.10) in 1999 to 38.98 (95% CI 38.48-39.48) in 2019 per 100,000 subjects, hospital admissions for various reasons increased by 51.9% (trend test,  $p < 0.01$ ). Zoster (herpes zoster), varicella (chickenpox), herpes viral (herpes simplex) infections, and virus warts were the most common viral diseases identified by the skin and mucous membrane lesions hospital reasons, accounting for 26.9%, 23.4%, 18.7%, and 17.6%, respectively [8].

Interestingly. The total in the current study hospital admissions is two patients due to decreased immunity.

Furthermore, the study also provides important information about the age range of the patients; the subjects' age in the total 27 patients in the study ranged from 12 to 90 years, with a mean of 50.22 years. The mean age of males and females was (57.60 and 41) respectively. Corresponding results were shown in a study by Szeto *et al.*, showing 259 patients altogether. 42.5% of patients are <60 years old, and 57.5% are  $\geq 60$  years old [9].

On the other hand, a study found that in HZO with an elderly age group, the visual results are subpar. Affected eyes have worse vision than unaffected eyes. Keratitis, anterior Uveitis, posterior Uveitis, and optic neuritis are the main causes of vision loss [6], which is inconstant to our study.

Regarding visual acuity, the study found that the visual acuity of the OD (20/60) was reported in 25.9% of patients, while the OS had a slightly higher percentage of 33.3%. Visual impairment was observed in 7.4% of the OD compared to 14.8% of the OS eye, indicating a higher prevalence of visual impairment in the left eye. Interestingly, legal blindness was equally prevalent in both the OD and OS eyes. These findings suggest the need for regular monitoring of visual acuity and the implementation of appropriate interventions to prevent or manage visual impairment in

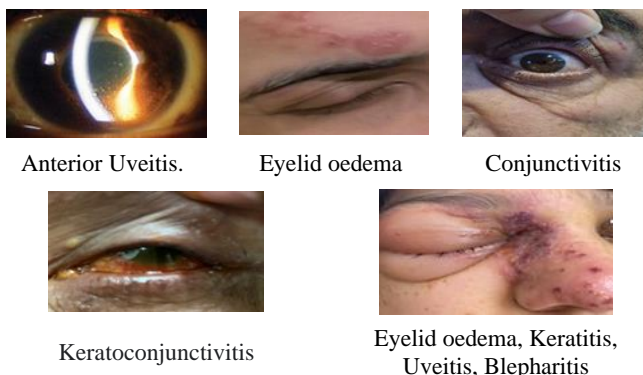


patients with visual complaints and HZO. Similar findings were shown in a study conducted by Niederer *et al.*, who observed that one in ten subjects with HZO might have moderate or severe vision loss, commonly due to corneal involvement [10]. Severe loss of vision caused by HZO is related to aging, immunosuppression, and Uveitis, and this result appropiates our study, whereas four.

Individuals considered legal blindness age over 55 years and visual impairment of OD and OS (7.4% vs. 14.8%), respectively, and was due to Uveitis.

However, the current research details the onset and progression of ocular problems in HZO patients who visited the ophthalmology outpatient clinics of two Saudi Arabian hospitals. There was a wide range of ocular HZO problems. Inflammation of the eyelid, cornea, conjunctiva, and uvea were the most common early-stage ocular problems (70.4%).

Unlike the previous research, Schaftenaar, Erik, *et al.* (2016) performed a study on 48 patients in rural South Africa who presented to the ophthalmology outpatient department with either active or healed HZO. The study included 10 males and 38 females with a median age of 40. While early-stage issues such as punctate epithelial Keratitis and anterior Uveitis were uncommon, the research found that most (65%) presented with late-stage ocular disorders linked with permanent vision loss. The correlation between late-stage problems and delays in visiting the ophthalmology outpatient department stems from patients waiting to start antiviral medication (which may be effective as soon as 72 hours after developing a rash) (**Figure 2**).



**Figure 2.** Spectrum of ocular complications of herpes zoster ophthalmicus.

In one study on HZO complications, conducted by Goswami *et al.* in India [6], 869 patients were included, and ocular involvement of HZO was detected in 737 of them (84.8%) within the first month of presentation. Lid involvement, Conjunctivitis, Keratitis, and Uveitis were the most common ocular signs (73.81 percent, 69.05 percent, and 59 percent, 30 percent, respectively). Consistent with the present research, Goswami *et al.* (2021) found that inflammation of

the cornea, swelling of the eyelids, and inflammation of the conjunctiva and uvea were the most common eye disorders. While almost 70.4% of our patients had Keratitis, nummular Keratitis affected just one patient, a 41-year-old male. Possible explanation: Antiviral treatment started an average of three days after the beginning of HZO in these individuals [11].

Herpes zoster ophthalmicus (HZO) is a frequent disorder induced by the involvement of the trigeminal nerve in herpes zoster infection, as shown by Li's (2018) paper, "Acute keratitis" Herpes zoster ophthalmicus (HZO). One of the most often seen ocular consequences of HZO is acute Keratitis. Herpes zoster (HZO) has become more common in recent years, and the average age at which people get the disease has dropped.

Presentation. In zoster stromal Keratitis, improved imaging methods have shed light on the corneal involvement of HZO by identifying virus particles inside keratocytes. When oral antiviral treatment fails to alleviate the symptoms of acute zoster keratitis, topical ganciclovir is effective. Acute zoster keratitis may cause irreversible eyesight loss if not treated quickly. Herpes zoster immunizations are essential for disease prevention, while oral and topical antiviral medicines are important in treating the acute phase. Herpes zoster anterior segment problems need further study to provide uniform procedures for treatment.

Herpes zoster seldom causes problems in the posterior region. Due to immunosuppression, one patient in our research developed necrotizing retinitis, which is linked with considerable ocular morbidity (eye discomfort, blindness, etc.). The posterior segment was implicated in this instance. This is the conclusion reached by the researcher Lobo-Chan (2020) [12].

In addition, the research categorized ocular problems into early, mid, and late stages. Seventy-four percent of patients had early ocular problems, whereas 29.6 percent experienced late-stage difficulties. According to chi-squared research, there is a correlation between advanced age and ocular problems. Patients experiencing late-stage difficulties were, on average, 65 years old, with a range of ages of 34 to 90 years, whereas those experiencing early-stage issues were, on average, 45 years old, aged 12 to 64 years. This provides evidence that advanced age may pose a threat to healthy development. Disease development may be predicted using prediction models that consider phenotypic, demographic, environmental, genetic, and molecular risk variables, according to research by Heesterbeek *et al.*

However, many risk variables will be calculated for each person's specific risk estimate based on their present illness stage. To wit: [13].

### Strengths of the Study

- **Comprehensive data collection:** The study provides valuable insights into demographic characteristics, ocular complications, gender distribution, hospital distribution, age range, visual acuity, and timing of ocular complications among patients with visual complaints and herpes zoster ophthalmicus (HZO). The comprehensive data collection is available for a more thorough understanding of the topic.
- **Comparison with existing literature:** The study compares its findings with previous research, providing a broader context and facilitating the identification of similarities and differences. This strengthens the validity of the study and allows for a more comprehensive interpretation of the results.
- **Multidisciplinary approach:** The study incorporates various disciplines, such as ophthalmology, epidemiology, and healthcare management, which enhances the depth and breadth of the analysis. The multidisciplinary approach contributes to a more comprehensive understanding of the topic.

### Limitations of the Study

- **Retrospective design:** The study is likely to have a retrospective design, which relies on the analysis of existing data. This design limits the control over data collection and may introduce biases or missing information.
- **Potential selection bias:** The study may be subject to selection bias, as the sample of patients may not be representative of the general population. Patients included in the study may have different characteristics or disease severity compared to those who were not included, which can affect the generalizability of the findings. The results were collected from two different areas, and some data were collected from previous files.
- **Lack of causality determination:** The study provides associations and observations but may not establish causal relationships between variables. It is important to interpret the findings with caution and recognize that further research is needed to determine the underlying mechanisms and causality.
- **Potential confounding factors:** The study may not have accounted for all potential confounding factors that could influence the outcomes. Factors such as comorbidities, socioeconomic status, and access to healthcare services could confound the observed relationships.

### Recommendations

- Herpes zoster, commonly known as shingles, is a viral infection caused by the reactivation of the varicella-zoster virus. While the primary manifestation of herpes zoster is a painful rash, there is a need for further research focusing on the complications that can arise from this infection. Understanding the various complications associated with herpes zoster is crucial for improving patient care, developing preventive strategies, and enhancing treatment approaches. Therefore, this

recommendation aims to highlight the importance of conducting research in this area.

- As for the HZ vaccine, we suggest that vaccines be available to individuals under 50 years old and who suffered previously from chickenpox, especially patients with immunocompromised.
- COVID-19 decreases cell-mediated immunity and could also increase HZ's potential reactivation. Further studies should be investigated to clarify the possible connection between COVID-19 vaccination and the reactivation of herpes virus infections [14].
- This type of information is important to increase awareness about the Herpes zoster vaccine in our country.

### CONCLUSION

The study concluded Patients with early-stage ocular complications more than Patients with late-stage ocular complications. The study reported a statistically significant relationship between the ocular complications in the late stages of herpes zoster and age at (P- value =0.004), suggesting that older age may be a risk factor for the development of HZO.

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