ORIGINAL ARTICLE

Hospital Based Study of Viral Keratitis: A Cross Sectional, Observational Study

Priyanka Sodani, Maneesha Sethi, Satinder Kumar, Vabita Bhagat

Abstract

Background Viral keratitis is one of the leading causes of corneal scarring and subsequent visual disability. An improved understanding of burden of viral keratitis and its clinical pattern can have a significant effect on prevention and treatment.**Materials & Methods** Our study was a descriptive, cross sectional, observational, hospital based study conducted over a period of 1 year. All patients with viral keratitis presenting to eye OPD during the 1 year period, were included in the study. History was taken with emphasis on symptoms, precipitating factors and any drug instillation. All patients underwent detailed ocular examination. Diagnosis of viral keratitis was made on basis of clinical presentation and slit lamp examination. Patients seen on 1st day were followed up on 3rd day, 7th day and 14th day.**Results** Total patients of viral keratitis in our study were 241 out of 22503 patients (1.07%). There were 123 cases (53.48%) of HSV keratitis, 81 cases (35.22%) of Adenoviral keratitis,26 cases(11.30%) of HZO keratitis. Commonest clinical presentation was epithelial keratitis (43.04%), followed by sub epithelial infiltration (35.22%) and stromal keratitis without ulceration (16.52% cases). Visual Acuity at presentation was 6/12-6/36 (64.77% of patients), while final visual acuity at two weeks follow up was 6/6-6/12(81.30% of patients). **Conclusion** Maximum cases were Herpes simplex keratitis and most common clinical presentation was epithelial keratitis . Very few epidemiological data is available on viral keratitis in developing countries so a long term study is required to estimate the burden of disease.

Key Words

Viral, Herpes Simplex, Keratitis

Introduction

Viral keratitis is one of the leading causes of corneal scarring and subsequent visual disability in both developing and developed countries. Herpetic eye disease remains a significant cause of blindness worldwide affecting over one million people annually. [1] It affects both pediatric and adult population especially if immunocompromised. [2] Both DNA and RNA viruses are responsible for keratitis, but common corneal infections are caused by DNA viruses -Herpes group viruses- Type 1, Type 2, Type 3-VZV(Varicella Zoster virus), Type 4 - CMV(Cytomegalovirus), Type 5- EBV(Ebstein Barr virus) and Adenoviruses. HSV -1(Herpes simplex Virus-1) is responsible for orofacial infections and HSV-2(Herpes simplex Virus-2) is responsible for genital herpes infections. HSV can affect any part of eye but keratitis is most common. [3,4] Herpes Zoster Ophthalmicus (HZO) represents 10-20% of herpes zoster cases. [5] It occurs when HSV- 3 reactivation presents in ophthalmic division of Trigeminal nerve. Hutchinson sign is much more predictive (50-80%) of ocular involvement and is strongly prognostic for ocular inflammation and corneal sensory denervation. [6] An improved understanding of burden of viral keratitis and its clinical pattern can have a significant effect on prevention and its early treatment.

Dept. of Ophthalmology Govt. Medical College, Kathua- J&K India

Correspondence to: Dr Maneesha Sethi, Associate Professor,Dept. Of Ophthalmology Govt. Medical College, Kathua

Manuscript Received: 10/9/2021; **Revision Accepted**: 12/11/2021

Published Online First: 10 April 2022

Open Access at: https://journal.jkscience.org

Cite this article as: Sodani P, Sethi M, Kumar S, Bhagat V. Hospital based study of viral keratitis: A cross sectional , observational study JK Science 2022;24(2):99-103

Materials and Methods

Our study was a descriptive, cross sectional , observational, hospital based study conducted over a period of 1 year from April 2019 to March 2020.Written informed consent was obtained from each patient or guardian (in case of pediatric patients) to participate in this study. Ethical approval was obtained from Institutional Ethical Committee and the study was conducted adhering to principles of Declaration of Helsinki.

All patients with viral keratitis presenting to Eye Out Patient Department of Government Medical College, Kathua, during one year period, were included in the study. Patient's demographic profile along with their occupation was recorded. History was taken with emphasis on symptoms and precipitating factors like fever, trauma, and any drug instillation. If patient had history of instillation of any drug, its dose, frequency and duration of application was enquired. Frequency more than two times and duration of application more than 15 days was recorded. All patients underwent detailed ocular examination, visual acuity assessment with Snellens chart, slit lamp examination, corneal staining (both with Fluorescein and Rose Bengal stains) and corneal sensations testing.

Diagnosis of viral keratitis was made on the basis of clinical presentation, slit lamp examination with decreased or absent corneal sensations. Diagnosis of epithelial keratitis was made if the lesion had dendritic ulcers (lesions with branching, linear pattern with terminal bulbs) [7], or geographic ulcers (broad ulcers with swollen, scalloped or geographic epithelial borders). Sub epithelial infiltration appeared as small nummular lesions just below the epithelium. Stromal lesions were divided into two categories; stromal keratitis without ulceration and stromal keratitis with ulceration (necrotizing keratitis). Stromal Keratitis without ulceration can manifest as focal, multiple or diffuse opacities often accompanied by corneal edema. Endothilitis included cases of disciform keratitis, which had stromal edema in a disc pattern with underlying keratic precipitates. In cases of kerato-uveitis, uveitis predominated with mutton fat keratic precipitates. Diagnosis of adenoviral keratitis was made if there was bilateral presentation with sub epithelial corneal infiltrates associated with fever and upper respiratory tract infection and preauricular lymphadenopathy. Diagnosis of Herpes Zoster Ophthalmicus was made if there was pustular, vesicular rashes involving tip of the nose (Hutchinson sign) with corneal involvement as pseudo dendrites [8] with negative fluorescein stain , stromal keratitis, nummular keratitis or disciform keratitis.

Fluorescein and Rose Bengal staining was done for each patient. In dendritic lesions, centre of the lesion was stained with fluorescein stain and the borders were stained with Rose Bengal stain. Geographic lesions edges too showed some dendritic pattern. Neurotrophic keratitis showed rolled up, smooth grey edges and stained only at the centre with fluorescein stain. In the pseudodendrites of HZO, fluorescein collected at the edges of epithelium, rather than staining the defect.

Patients were treated according to disease presentation with topical antiviral and cycloplegics. Topical steroid and oral antivirals were used in stromal keratitis, subepithelial keratitis and endothelitis.

All cases of viral keratitis were included. Viral keratitis with superadded bacterial, fungal or other infections and cases with associated uveitis were excluded. Old cases of viral keratitis with no signs of activity like congestion or ulceration were excluded. Recurrent cases were also excluded. Patients with history of any ocular surgery within past one year were excluded.

Patients seen on 1st day were followed up on 3rd day, 7th day and 14th day. Pre-treatment visual acuity and post treatment visual acuity was recorded at each follow up. In cases with bilateral disease, eye with worse best corrected visual acuity (BCVA) was recorded.

Results

Out of 22503 patients, who visited eye OPD in the study period, 241(1.07%) had viral keratitis. Out of which 3 had superadded bacterial infection, 4 had history of ocular surgery within past one year, 2 were recurrent cases and 2 were old cases of keratitis without activity but decreased sensations were excluded from the study. Therefore, total patients of viral keratitis included in our study were 230(1.04%)

Out of 230 patients, majority of cases were in the age group 21-50 years (79.53%), the mean age being 38.61years. There were 123 cases (53.48%) of HSV keratitis, followed by 81 cases (35.22%) of Adenoviral keratitis,26 cases(11.30%) were of HZO keratitis.(*Table 1*). Adenoviral cases were maximum in the months July-September with peak in August. Adenoviral keratitis had bilateral presentation.

Most common clinical presentation was epithelial keratitis (43.04%), followed by sub epithelial infiltration (35.22%) and stromal keratitis without ulceration (16.52% cases).(*Table 2*).

Overall, redness (83.04%) was most common presenting symptom in all types of viral keratitis.But foreign body sensation (91.35%) was seen commonly in epithelial keratitis. Diminution of vision was main complaint in stromal keratitis without ulceration (80%), sub epithelial keratitis (83%) and endothelitis (90%). Diminution of

Table 1 Type of Viral Keratitis

S. No	Type of Keratitis	Number of patients	Percentage (%)
1.	HSV Keratitis	123	53.48
2.	HZO Keratitis	26	11.30
3.	Adenoviral Keratitis	81	35.22
	Total	230	100

Table 2. Clinical Presentation

S.no	Clinical Pattern	No.of Patients	Percentage%
1.	Epithelial Keratitis	99	43.04
2.	Subepithelial infiltration	81	35.22
3.	Stromal keratitis without Ulceration	38	16.52
4.	Stromal keratitis with Ulceration	3	1.30
5.	Endothelitis	8	3.47
6.	Neurotrophic ulcer	01	0.43
	Total	230	100

Table3. Precipitating Factors Noted in Patients of Viral Keratitis

S.no	Precipitating cause	No.of Patients	Percentage%
1.	Fever	90	39.13
2.	Trauma	11	4.78
3.	Foreign body	13	5.65
4.	Upper Respiratory Tract Infection	49	21.30
5.	Steroid drops instillation.	31	13.48
6.	Some Ayurvedic drop instillation .	23	10
7.	Spontaneous (No history of any precipitating cause)	13	5.65
	Total	230	100

Table 4. Occupation of Patients of Viral Keratitis.

S.no	Occupation	No.of Cases	Percentage%
1.	Mannual worker/Farmer/Labourer	76	33.04
2.	Students	53	23.04
3.	House wives	56	24.35
4.	Technical workers	23	10
5.	Teachers	03	1.3
6.	Clerks/Office bearer	08	3.48
7.	Businessmen	05	2.17
8.	Others	06	2.61
	Total	230	100

vision (79.30%) with pain (81.01%) and watering (77.92%) were chief complaints in case of stromal keratitis with ulceration. Fever was the commonest precipitating cause in 90 patients (39.13%) followed by Upper Respiratory Tract Infection(URTI) in 49 patients (21.3%). 31 patients (13.48%) gave history of instillation of some steroid drops for more than 15 days with more than 2 times frequency per day.(*Table3*). Out of 54 patients with history of some drop instillation 49 patients(90.74%) had history of common vial usage by different family members. 11 cases (4.78%) reported trauma as precipitating factor. Majority of patients in the study population i.e. 33.04% were either laborers/farmers by occupation. Housewives constituted 24.35% and students 23.04% of the study participants.(*Table 4*) Visual Acuity at presentation fell maximum in the range 6/12-6/36 (64.77%), while final visual acuity at two weeks follow up, fell in the range 6/6-6/12(81.30%). (*Table 5)*

Discussion:

Developed nations have long term studies on viral keratitis, but more Indian subcontinent studies are required to estimate the incidence of viral keratitis. A French

Table: 5 Visual Activity at Presentation and After Two Week Follow up of Patients of Viral Keratitis

S.no	Visual Acuity	No.of Patients at Presentation(n) & Percentage (%)	No.of Patients and Percentage after two week follow up
1.	6/6	21 (9.13%)	114 (49.56%)
2.	6/9	37(16.09%	34 (14.78%)
3.	6/12	45 (19.56%)	39 (16.96%)
4.	6/18	38 (16.52%)	23 (10%)
5.	6/24	36(15.65%)	7 (3.04%)
6.	6/36	30 (13.04%)	4 (1.74%)
7.	6/60	8(3.48%)	3 (1.30%)
8.	5/60	7(3.04%)	2 (0.87%)
9.	4/60	4 (1.74%)	2 (0.87%)
10.	3/60	1 (0.43%)	1 (0.43%)
11.	2/60	2 (0.87%)	1 (0.43%)
12.	1/60	1 (0.43%)	0 (0%)
13.	FC/HM	0(0%)	0 (0%)
	Total patients	230	230

study [9] found incidence of HSV keratitis new cases as 13.2 per 100000, while Rochester Minnesota studies [10] found it to be 8.4-11.8 cases per 100000. Our hospital based study showed 1.07% (241 out of 22503) cases of viral keratitis

In our study majority of patients were in the age group 21-50 years with the mean age being 38.61years. Sain *et al* [11] also had maximum patients in the age group 31 to 50years (52.5%). Liesegang *et al* [4] found the mean age to be 37.4years. Most of the HZO patients were above 50 years of age. A study by Tran *et al* [12] also show peak incidence between ages 50-79 years with a skew towards older individuals. In our study Adenoviral keratitis was more common in 11-40years of age group while mean age in a study by Lee *et al* [13] was 33.58 ± 17.74 years.

Among the recruited cases maximum frequency of occurrence was of HSV Keratitis(53.48%). Liesegang *et al* [14] reported prevalence of ocular HSV as 149 per100,000 population. Adenoviral cases were maximum in July to September which corresponds with the study by Lee *et al* [13]. In a study by Das *et al* [14] , the peak prevalence was noted in the month of April. Adenoviral cases running in families had history of some Ayurvedic drops being instilled in the family suggestive of its contagious nature. HZO keratitis frequency was 11.30% in our study. Miami study [12] found frequency of HZO as 0.05% and Kaiser study [15] documented overall incidence of HZO as 30.9 per 100000person-years.These studies were retrospective and seem to have underestimated the incidence of HZO.

Though slit lamp findings are pathognomic for viral keratitis, atypical lesions can make diagnosis difficult.[16] Any previous medication or duration of disease can change the appearance of lesions on slit lamp. In a study conducted by Rubben *et al* [17] , 8% of the clinically diagnosed HSV lesions were identified on PCR assay as HZV lesions. Another study stated 5% of clinically diagnosed cases of HSV keratitis as adenoviral lesions, 3.2% by CMV and 2.7% by enterovirus. [18]

The different types of clinical presentations in this series were; 99 patients out of 230 had epithelial keratitis (43.04%),81(35.22%) patients had subepithelial infiltration, 36(16.52%) patients had stromal keratitis without ulceration and endothelitis in 8(3.48%) patients. The clinical pattern in a study by Kabra *et al* [19] showed 15.91% with dendritic ulcers, 4.09% with geographical ulcers, 53.64% with stromal keratitis and 8.64% as endothelitis. Shah *et al* [20] found 17.5% patients with epithelial keratitis, 51.6% with stromal keratitis without ulceration, 21.8% with endothelitis and 1.6% with neurotrophic ulcers. A study by Pramod *et al* [21] reported 65% with epithelial keratitis whereas 35% had stromal keratitis. In our study stromal keratitis and subepithelial lesions were taken as different manifestations.

In our study, indeterminate use of steroid drops by 13.48% cases especially in epithelial keratitis not only increased the duration of symptoms and treatment but also had effect on final visual outcome. In the Whilhelmus [22] study, 26% of the patients had history of previous steroid therapy. Similarly, Kabra *et al* [19] in his study reported usage of some form of medication in 50% of patients.

Major precipitating factor in our study was fever (22.6%). Saini *et al* [11] reported fever in 15% of patients, while history of minor trauma in 20% of patients. In our study, 49 patients with Adenoviral Keratitis (60.49%) had history of either some Ayurvedic drops instillation or some steroid drops instillation by a common vial by the family members. This inappropriate use of common vial by all the family members could have led to spread of adenoviral keratitis in them. This needs further study exclusively on Adenoviral keratitis. In our study majority of patients were in the manual worker/ labourer or farmers group. Teachers and office bearers were less affected. This shows that hygiene and education level may have impact on the disease occurrence.

A study at Aravind Eye hospital in India found that at least 2% had visual acuity worse than 20/1200 and 62% improved to better than 20/40. [19] A Moor fields Eye Hospital study found that 152 patients with epithelial keratitis; only 3% had final visual acuity less than 20/200 .[22] A study by Shah *et al* [20] 11.9% patients had visual acuity less than 3/60. Our study found that visual acuity finally improved to 6/6-6/12 in 81.30% patients. Only 2.60% patients had final visual acuity less than 6/60. This may be due to the fact that we have excluded keratouveitis patients, patients with increased intraocular pressure and recurrent cases. In the Rochester study only 4 eyes had visual acuity less than 20/100. [10] This again can be because of less of stromal disease in their study.

Conclusion:

Very few epidemiological data is available on viral keratitis in developing countries so a long term study is required to estimate the burden of disease.Our study documents different clinical presentations of viral keratitis in this dry dusty (Kandi, in local language) area of Kathua district of Jammu province. Maximum cases were Herpes simplex keratitis and epithelial keratitis was the most common clinical manifestation. Awareness needs to be created among people for discontinuing use of unprescribed drugs and sharing of common vials by all family members. There is need to train the community eye workers and pharmacists regarding injudicious use of steroid drops and emphasis should be laid on counseling of patients regarding usage of drop vials.

Financial Support and Sponsorship

Nil.

Conflicts of Interest

There are no conflicts of interest.

References

1. Vadoothker S, Andrews L, Jeng BH, Levin MR. Management of Herpes Simplex Viral Keratitis in the Pediatric Population. Pediatric Infect Dis J 2018; 37: 949-51.
2. Pandey M, Choudhury H, Abdul aziz A, et al. Advancement on sustained antiviral ocular drug delivery for Herpes simplex Virus keratitis: Recent update on potential investigation. Pharmaceutics 2021; 13:1.
3. Tsatsos M, Mac Gregor C, Athanasiadis I, Moschos MM, Hossain P, Anderson D. Herpes Simplex Virus Keratitis: An update of the pathogenesis and current treatment with oral and topical antiviral agents. Clin Exp Ophthalmol 2016; 44:824-37.
4. Liesegang TJ. Herpes Simplex Virus epidemiology and ocular importance. Cornea 2001; 20:1-13.
5. Liesagang TJ. Herpese Zoster Ophthalmicus natural history, risk factors, clinical presentation and morbidity. Ophthalmology 2008; 115:S3-S12.
6. 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.
7. Reidy JJ. 2011-2012 Basic and clinical Science Course-Section 8: External Disease and Cornea- San Francisco: American Academy of Ophthalmology 2011; 110-11.
8. Vrcek I, Choudhury E, Durairaj V. Herpes Zoster Ophthalmicus: A review for the internist. Am J Med 2017; 130:21-6.
9. Labetoulle M, Auquier P, Conrad H. Incidence of herpes simplex virus keratitis in France. Ophthalmology 2005; 112:888-95.
10. Young RR, Hodge DO, Liesegang TJ. Incidence, recurrence, and outcomes of herpes simplex virus eye disease in Olmsted County, Minnesota, 1976-2007: The effect of oral prophylaxis. Arch Ophthalmol 2010; 128:1178-83.
11. Saini JS, Agrawala R. Clinical pattern of recurrent herpes simplex keratitis. Indian J Ophthalmol 1999; 47:11-4.
12. Tran KD, Falcon MM, Choi DS. Epidemiology of herpes zoster ophthalmicus: recurrence and chronicity. Ophthalmology 2016; 123:1469-75.
13. Lee J, Bilonick RA, Romanowski EG. Seasonal variation in human adenovirus conjunctivitis: A 30 year observational study. Ophthalmic Epidemiol 2018; 451-6.
14. Das AV, Basu S. Epidemic Keratoconjunctivitis in India: Trend Analysis and implications for Viral Outbreaks. Ind J Ophthalmol 2020;68:732-36.
15. Borkar DS, Tham VM, Esterberg E. Incidence of herpes zoster ophthalmicus: Results from the Pacific Ocular Inflammation Study. Ophthalmology 2013; 120:451-56.
16. McGilligan VE, Moore JE, Tallouzi M. A comparison of clinical and molecular diagnosis of herpes simplex keratitis. Open J Ophthalmol 2014; 4:65-74.
17. Rubben A, Baron JM, Grussendorf-Conen EI. Routine detection of herpes simplex virus and varicella zoster virus by polymerase chain reaction reveals that initial herpes zoster is frequently misdiagnosed as herpes simplex. Br J Dermatol 1997; 137:259-61.
18. Marangan FB, Miller D, Alfonso E. Laboratory results in ocular viral diseases implications in clinical laboratory correlation. Arq Bras Oftalmol 2007; 70:189-94.
19. Kabra A, Lalitha P, Mahadevan K. Herpes Simplex Keratitis and visual impairment: A case series. Indian J Ophthalmol 2006; 54:23-27.
20. Shah A, Joshi P, Bhusal B. Clinical pattern and visual impairment associated with Herpes simplex keratitis. Clin Ophthalmol 2019; 13:2211-15.
21. Pramod NP, Rajendran P, Kannan KA, Thyagarajan SP. Herpes simplex keratitis in South India: clinic-virological correlation. Jpn J Ophthalmol 1999; 43:303-7.
22. Wilhelmus KR. Antiviral treatment and other therapeutic interventions for herpes simplex virus epithelial keratitis. Cochrane Database Syst Rev 2015; 1:CD002898.