

Study of ocular manifestations and factors affecting visual outcome in Herpes Zoster Ophthalmicus

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Abstract-

Background- Herpes zoster ophthalmicus results from reactivation of latent varicella zoster virus from trigeminal ganglia in previously exposed patients with low immunity.

Aims of the study- Aims of the study is to find out common ocular manifestations of HZO and factors affecting visual outcome.

Material and methods- This observational study was done on patients attending, Department of Ophthalmology, Patna medical college, Patna. The period of study was from October 2017 to December 2018. Total 35 patients were examined. Patients were followed on 7th, 14th, 30 day and 3 months after first visit.

Results- 28.57% cases were in age group 41-50 year. The males were 54.28% and female 45.71%. Conjunctivitis (77.1%) Corneal involvement (60%), Episcleritis (8.6%) Uveitis (57.1%) and Secondary glaucoma (5.7%) were common manifestations. Hutchinson signs was positive in 18 cases (n= 35). Corneal involvement and uveitis with Hutchinson signs were observed in 48.57%(p- value<0.001) and 45.71%,(p value <0.01) .Common predisposing factors were Diabetes mellitus(40%), HIV (22.85%), age->60 years 14.28%. 57.14% patients had no visual loss at 3 months follow up. 85.71% had vision 6/18 or better .

Conclusions-With the increasing incidence of HIV and diabetes , Herpes Zoster Ophthalmicus was presenting with at younger age group. Corneal involvement and uveitis was strong predictor of visual loss in HZO. The involvement of frontal,nasociliary and lacrimal nerves and positive Hutchinson signs were associated with increased incidence of ocular complications like keratitis and uveitis. The inflammatory and immune mediated lesions of HZO responded well to treatment with good visual outcome.

Key words- Herpes zoster ophthalmicus, Varicella zoster virus, Trigeminal ganglia, conjunctivitis, Corneal involvement, Uveitis, Hutchinson sign

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I. Introduction

Herpes Zoster Ophthalmicus results from reactivation of latent varicella zoster virus from trigeminal ganglia in which ophthalmic division of trigeminal nerve is involved. Varicella zoster virus persists in the sensory ganglia of the cranial nerves and the spinal dorsal root ganglia after varicella resolves.¹. Reactivation of varicella occurs when cellular immunity against virus falls. Patients of old age and patients who have neoplastic disease, organ transplant recipients or on immunosuppressive drugs are at risk of HZO. Other risk factors are HIV, diabetes, tuberculosis, irradiation and physical trauma. Incidence of herpes zoster ophthalmicus has increases 3.6% cases per 100000 person-years from 1994 to 2018².

II. Material and Methods

This observational study was done on patients attending, Department of Ophthalmology, Patna medical college, Patna. The period of study was from October 2017 to December 2018. Total 35 patients were included in the study. Patients were followed up on 7 days, 14 days, 30 days and 3 months after first visit.

Study duration- October 2017 to December 2018.

Sample size-35 patients

Subjects and selection methods-Those patients were enrolled who were attending OPD with specific clinical features which are suspicious for Herpes zoster ophthalmicus. Patients were from 11-80 year of age. Both male and female patients were included in this study

Inclusion criteria-

Patients presented with signs and symptoms of Herpes Zoster Ophthalmicus within 3 weeks of vesicle formation.

Exclusion criteria-

HZO patients who are terminally sick and bed ridden because it was difficult to follow up the cases regularly. Patients with previous history of primary open angle glaucoma, because in HZO patients IOP may be raised due to inflammation and by other complications.

Procedure methodology-

Written informed consent was obtained from eligible patients. Demographic characteristics such as age and sex, H/O systemic illness like Hypertension, Diabetes, anemia, and other diseases were obtained. Eligible patients were underwent comprehensive ocular examination. Visual acuity was recorded. Examination of orbit, eyelid, adnexa, corneal sensitivity, and ocular movement were performed and recorded. Slit lamp biomicroscopy with 90D were performed. Fundus examination was done by direct and indirect ophthalmoscopy. IOP was checked by NCT. Laboratory examination -blood sugar, HbA1c, ELISHA for HIV 1&2, routine urine, Complete blood count, were performed. Blood pressure was also measured.

Statistical analysis- Frequency, percentage, crosstab and chi-square test were used for statistical analysis.

III. Observations

Age distributions-

It was observed that maximum numbers of patients were between 41-50 years of age which was 28.57%. While age group 11-20 years and 71-80 years had minimum numbers of HZO in our study which was 5.71% each respectively.

Table 1 –Age Distributions

Age groups	Frequency	percentage	Chi square-12.800 p- value-0.046
11-20	2	5.71	
21-30	4	11.42	
31-40	5	14.28	
41-50	10	28.57	
51-60	9	25.71	
61-70	3	8.57	
71-80	2	5.71	

Sex distribution-

It was observed that number of male patients affected by HZO were 19(54.28%), while number of female patients were 16(45.71%). So in our study there was slightly more male preponderance.

Table2- Sex Distributions

Sex	Frequency	Percentage	Chi square-0.257, p value-0.612
Male	19	54.28%	
Female	16	45.71%	

Laterality-

In our study Right eye involvement seen in 19(54.28%) cases and left eye involvement in 16(45.71%) patients. No patients had bilateral involvement.

Table 3- Showing laterality

laterality	frequency	percentage	Chi square value-0.257, p value-0.6
left	16	45.71	
right	1	54.28	

Predisposing factors-

Diabetes mellitus was the most common predisposing factors and was observed in 14 (40%) cases. HIV infection was the second most common predisposing factors and seen in 8 cases(22.85%).

Table 4- Predisposing factors

Predisposing factors	Number of cases (n-35)	Percentage
Diabetes mellitus	14	40
HIV	8	22.85
Hypertension	6	17.14
Anemia	6	17.14

Age more than 60 years	5	14.28
Tuberculosis	2	5.71
Hypothyroidism	2	5.71
Chronic liver disease	1	2.9%

HIV association-

In study HZO patients affected by HIV infection were only 8(22.85%) HIV negative were 27(77.15%) patients.

Table 4- HIV association

	Number of patients	percentage
HIV Positive	8	22.85
HIV negative	27	77.15

Mean age of HIV positive was HZO patients was 47.38 years and for HIV negative patients 47.96.

Table 5- mean age of HIV positive HZO patients

	Number of patients	Mean age	SD	SE of Mean
HIV Positive	8	47.38	17.71	6.26
HIV negative	27	47.96	15.24	2.93
total	35			

Association of Diabetes with HZO-

Association of diabetes and HZO also studied, which was 50.93 with SD 14.66 and SE of mean 3.92.

Table 6 –Association of Diabetes with HZO

	Frequency	Mean age	SD	SE of mean
Diabetes present	14	50.93	14.66	3.92
Diabetes absent	21	45.76	16.16	3.52

Dermatological

involvement of branches of ophthalmic division of trigeminal nerve.

Frontal, Nasociliary and Lacrimal nerve branches together were most commonly involved followed by frontal nerve.

Table 7- Dermatological involvement of branches of trigeminal nerve

Branches	frequency	percentage
Frontal nerve	11	31.42
Nasociliary nerve	2	5.71
Frontal +nasociliary nerve	4	11.42
Frontal +lacrimal nerve	4	11.42
Naociliary +lacrimal nerve	2	5.71
Frontal +nasociliary +lacrimal	12	34.28

Table 8-Involvement of branches of ophthalmic division

Branch	Frequency	percentage	Chi-square	p-value
Frontal nerve	31	88.6	20.829	0.00
Nasociliary nerve	20	57.14	1.4	0.237
Lacrimal nerve	18	51.42	0.029	0.866

Frontal nerve (88.6 %) was the most common involved branches of ophthalmic nerve .This were followed by nasociliary (57.14%) and lacrimal nerve (57.14%).

Rashes- All Herpes zoster patients presented with erythematous macules and papules which changed to vesicle and healed by crust formation. These were along the dermatomes of affected nerves .In 2 patients skin rashes resulted into hemorrhagic blister, skin necrosis and secondary bacterial infection.

Herpetic pain- Acute severe hepatic pain was complained by 27 patients (77.14%).8 patients had mild pain. Post herpetic pain was seen in 9 patients (25.71%).

Table 9- presentation of different type of pain

Pain	Frequency of patients	percentage
Mild pain	8	22.85
Acute pain	27	77.14
Post herpetic pain	9	25.71

Ocular involvement

Conjunctivitis was observed in 27 patients (77.1%). Corneal involvement in 21 patients(60%),episcleritis in 3 patients(8.6%), uveitis in 20 patients(57.1%) and secondary glaucoma in 2 patients(5.7%).

Table 10- different ocular manifestations

Signs	No of patients	percentage	Chi-square	P value
conjunctivitis	27	77.1	10.31	0.001
Corneal involvement	21	60.0	1.4	0.237
Episcleritis	3	8.6	24.03	0.00
Uveitis	20	57.1	0.714	0.398
Secondary glaucoma	2	5.7	27.457	0.00

Corneal involvement-21 cases developed different corneal lesions.12 patient developed punctuate epithelial keratitis, 3 patients had pseudodendritic keratitis, 4 patients had nummular stromal keratitis, 1 patient had disciform keratitis and 1 patient had neurotropic keratitis.

Table 11 –different presentations of corneal involvement

Corneal lesions	frequency	percentage
Punctuate epithelial keratitis	12	34.29%
Pseudodendritic keratitis	3	8.57%
Nummular keratitis	4	11.4%
Disciform keratitis	1	2.86%
Neurotropic keratitis	1	2.86%

Age in relation to the ocular manifestation-

In our observations conjunctivitis and uveitis seen in older age group. The mean age of HZO with different ocular signs were 41.7 to 49.38 years.

Table 12- relation of age to various ocular manifestations

SIGNS	NO.OF CASES	AVERAGE AGE	STATISTICS	SIGNIFICANCE
CONJUNCTIVITIS	27	48.19	t -0.245 df=33 p-0.808	Not significant
CORNEAL INVOLVEMENT	21	49.38	t- 0.717 df=33 p-0.478	Not significant
EPISCLERITIS	3	41.7	t-0.712 df=33 p-0.482	Not significant
UVEITIS	20	47.9	t-0.031 df=33 p-0.976	Not significant
SECONDARY GLAUCOMA	2	42.5	t-0.493 df=33 p-0.625	Not significant

Hutchinson sign and ocular manifestations-

Hutchinson signs were positive in 18 cases out of 35 patients. Corneal involvement was observed in 17patients (48.57%, p value<0.001) with Hutchinson signs. Uveitis was seen in 16 patients (45.71%, p value <0.01) with positive Hutchinson signs.

Table 13- Prognostic effects of Hutchinson signs with different ocular signs

Signs	Hutchinson sign		statistics	Statistically significance
	positive	negative		
conjunctivitis	Absent	1	X ² =6.291 Df=1 P=0.12	Not significant
	present	7		
Corneal involvement	Absent	13	X ² =18.32 Df=1 P<0.001	significant
	present	4		

Uveitis	Absent	2	13	X ² =15.25 P<0.01 Df=1	significant
	present	16	4		
Episcleritis	Absent	22	10	X ² =0.006 Df=1 p =0.94	not significant
	present	2	1		
Secondary glaucoma	Absent	22	17	X ² =0.972 Df=1 P=0.32	Not significant
	present	2	0		

Follow up of common ocular manifestations -

Patients with HZO were treated with anti viral eye ointments, lubricating eye drops , steroid eye drop. Patients were also following the physician/ dermatologist advice for their complaints. In herpes zoster ophthalmicus, conjunctivitis was observed in 27 patients, which subsides in 2 weeks. Punctate keratitis was seen in 12 patients, which subsided by 4 weeks time, in most of the patients. But in two patients punctate keratopathy persist even at the 3 months followup. Stromal keratitis was observed on second week, which resolved by fourth week. Uveitis was present in 20 patients at the time of presentation and it was seen mostly in first and second week. On followup it was observed that all cases of uveitis resolved in four weeks. Episcleritis and secondary glaucoma also resolved in two weeks.

Table 14- followup of common ocular manifestations

Ocular complications	0 weeks	1 week	2 week	4 week	3 months
conjunctivitis	27	6	3	0	0
Punctate epithelial keratitis	12	11	5	3	2
stromal keratitis	0	0	4	2	0
uveitis	20	13	11	3	0
episcleritis	3	2	1	0	0
Secondary glaucoma	2	1	1	0	0

Visual outcome-

AT the time of presentations patients 17 patients had 6/6 vision and at the end of 3 months follow up 20 patients (57.14%) recovered to 6/6. 28.57% patients had vision more than 6/18, but 5 patient (14.28%) had VA<6/18 after 3 months follow up.

Table 15- Follow up of status of Visual outcome

Vision	At presentation	1 week	2 week	4 week	3 months
6/6	17	15	15	19	20(57.14%)
>6/18	6	10	14	10	10(28.57%)
<6/18	12	10	6	6	5(14.28%)

IV. Discussion

Age and sex distributions

Age is important predisposing factors. In our study peak incidence was noted in age group 41-50 years which was 28.57%. The mean age of HZO with different ocular signs were 41.7 to 49.38 year. Emma C Davies et al³ investigated the change in the age of occurrence of HZO, they found the mean age of occurrence reduced significantly from 61.2 years in 2007 to 55.58 years. Vikash Paudal et al⁵ also observed 40.4 years were average age. But contrary to our study, Durga S Borkar et al⁴, observed peak incidence in 65 years age. In this study the male patients were 19(54.28%) in number and female patients were 16(45.71%). So there was slightly male preponderance was observed in our study. This was in accordance with the study done by Puri et al⁶ in which 54.4% were males and 45.6% were females. Vikash Paudal et al⁵ found male to female ratio was 2.5:1. However no significant difference was found in sex distribution of patients in study done by Durga S Borkar et al⁴.

Laterality-

In our study right side was involved in 54.28% while left side was involved in 45.71%. In contrary to our study Womack et al study⁷ observed, 44% of the patients had right side involvement and 56% left side.

Predisposing factors-

In our study most common predisposing factor was Diabetes mellitus(40%) followed by HIV (22.85%). Other predisposing factors and associated disease were hypertension and anemia-17.14% each, age->60 years 14.28%,

tuberculosis 5.71%,hypothyroidism-5.71,and chronic liver disease-2.9% . keiserman⁸ et al also observed 25.2% of the patients of diabetes patients had herpetic eye disease . This was also supported by Puri et al ⁶who observed diabetes in 17.64% .HIV positivity was also risk factors in the young age group. In the study done by Sriprakash KS⁹ et al also observed 10.28% of HIV positive cases.

Mean age of HZO patients with HIV and DM-

Mean age of HIV positives HZO patients was 47.38 years and for HIV negative patients 47.96 years. The mean age of DM patients with HZO, was 50.93% .However Nooper et al ¹⁰ found mean age of 32 years (average age of cohort was 30 years) in patients with HIV, which is lower than the value noticed in present study.

Involvement of branches of ophthalmic division of trigeminal nerve-

In present study the frontal nerve was most commonly (88.6%) involved. Puri et al⁶ also noticed the involvement of frontal nerve was the commonest (57.35%). All Herpes zoster patients presented with erythematous macules and papules which changed to vesicle and healed by crust formation on area of involved dermatomes. Skin rashes in 2 patients resulted into hemorrhagic blister, skin necrosis and secondary bacterial infections. The most common dermatological presentation was that of the classical variety which involved frontal, nasociliary and lacrimal nerve branches together (34.28%). Acute severe hepatic pain was complained by 27 patients (77.14%). 8 patients had mild pain. Post herpetic pain was seen in 9 patients (25.71%).Harding et al described post neuralgic pain in 21% patients. Womack et al⁷ observed post herpetic neuralgia in 15 out of 86 cases. Zaal et al in their study noticed mild pain in 31%, moderate pain in10% and 5 patients had severe pain.

Hutchinson's sign-

In this study, Hutchinson signs was positive in 18 cases out of 35 patients.Corneal involvement was observed in 17patients (48.57%, p value<0.001) with Hutchinson signs and uveitis was seen in 16 patients (45.71%, p value <0.01) with positive Hutchinson signs. Both findings were statistically significant, and a positive Hutchinson's sign significantly correlated with the corneal lesions and uveitis.

Zaal et al¹¹ had also found Hutchinson's sign was a powerful predictor of ocular inflammations and corneal denervation in HZO with a relative risk of 3.35 and 4.02.Harding and associates¹² also observed that nasociliary nerve involvement was associated with subsequent ocular disease.

Conjunctivitis was present in 77.1 patients, which was resolved in 3 months time. This finding was statistically significant (p value 0.001). Puri et al⁶ observed 41.1% patients had conjunctivitis in their study. Corneal involvement was seen in 21 patients (60%), which is almost similar (60%) to the study of Zaal et al¹¹.In present study 12 patient had developed punctuate epithelial keratitis, 3 patients had pseudodendritic keratitis, 4 patients had nummular stromal keratitis, 1 patient had disciform keratitis and 1 patients had neurotropic keratitis who developed perforated corneal ulcer in affected eye, leads to corneal scarring and severe visual impairment. Womack etal⁷ also observed 65% of patients had corneal involvement Uveitis was seen seen 20 cases (57.14%) in form of anterior uveitis. Intermediate uveitis and choroiditis were not observed. In contrary to our study Puri et al⁶ reported uveitis in 19.1%, and Womak et al⁷ reported 43%, which is lower than our study. In our view this might be due to low sample size of our study group. Episcleritis was present in 3 patients (8.6%). Secondary glaucoma was observed in 2 patients (5.7%).Puri et al⁶ also observed secondary glaucoma in 5.8% of cases.

In our study we did not encountered any posterior segment complications and cranial nerve involvement. This might be due to small sample size of our study.

Visual acuity- In our study most of the patients had good visual outcome. 57.14% patients had no visual loss at 3 months follow up. 85.71% had vision 6/18 or better. Visual acuity was lower in those patients who had corneal involvement and uveitis. In the study done by Puri et al⁶ , 91.6% of the cases had vision better than 20/200 in the involved eyes. Zaal et al¹¹ also observed 96% patients had vision better than 20/200.

V. Conclusions

The following conclusions were derived from the study” Study of ocular manifestations and factors affecting visual outcome in Herpes Zoster Ophthalmicus” carried on thirty five patients from October2017 to December 2018 at Department of Ophthalmology, Patna Medical College Hospital, Patna.

1. Increasing age was the important predisposing factor.
2. With the increasing incidence of HIV, It was observed that Herpes Zoster Ophthalmicus was presenting with increased incidence at younger age group.
3. Diabetes was the most common predisposing factors followed by HIV. It was positively co-related to uveitis and was strong predictor of visual loss in HZO. So all patients of HZO need to be evaluated for Diabetes and for HIV.
4. Conjunctivitis, corneal involvement and uveitis were common presenting clinical features.

5. Visual acuity was found to be decreased in patients with punctate, pseudodendritic, nummular, neurotropic keratitis and uveitis.
6. The involvement of nasociliary and lacrimal nerves and positive Hutchinson signs were associated with increased incidence of ocular complications like keratitis and uveitis. So careful examination must be done in patients of HZO with Hutchinson signs.
7. The inflammatory and immune mediated lesions of HZO responded well to treatment and majority of patients received good visual outcome.

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