

TO STUDY THE CLINICAL AND EPIDEMIOLOGICAL DATA OF HERPES ZOSTER AND ASSESS THE RELATION BETWEEN RISK FACTORS AND DEVELOPMENT OF POSTHERPETIC NEURALGIA (PHN)

Atul Vijay¹, Naresh Rathod²

¹Associate Professor, Department of Dermatology, Venereology & Leprology, SRG Hospital & Medical College, Jhalawar.

²Junior Resident, Department of Dermatology, Venereology & Leprology, SRG Hospital & Medical College, Jhalawar.

ABSTRACT: BACKGROUND: Herpes zoster (HZ) is a common viral disorder with characteristic rashes and pain. Postherpetic neuralgia (PHN) is most common complication of HZ. There may be increased chances of PHN in the presence of various risk factors.

AIM: To study the clinical and epidemiological data of HZ and assess the relation between risk factors and development of PHN.

MATERIAL AND METHODS: In this prospective study cases of HZ attending the outdoor of dermatology department were included irrespective of age and sex. Relevant demographic and clinical findings of all the cases were recorded in a predesigned performa. Cases were followed up for next 6 months for the development of any complication and recorded the same if occurred. Relevant risk factors in cases of PHN were observed, recorded and analysed.

RESULTS: 123 cases were included in the study. Most common age group affected was 31-40 years, slightly more common in female sex and commonly occurred in immunocompromised cases. Most common dermatome affected was thoracic. PHN occurred in 23 (18.7%) cases. About 61% of PHN cases were above the age of 50 years and it occurred in 45.45% cases of HZ with ophthalmic involvement.

CONCLUSION: HZ is a common disease in the cases attending the dermatology OPD. PHN is most common complication which is more commonly associated with older age, female sex, presence of prodrome, severe rash and pain within 3 days and involvement of ophthalmic division of trigeminal nerve. But there is no significant relation between occurrence of PHN and antiviral drug treatment.

KEYWORDS: Varicella zoster virus, Postherpetic neuralgia, Risk factors.

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INTRODUCTION: Herpes zoster (HZ), a common viral disease caused by Varicella Zoster Virus (VZV). VZV belongs to herpesvirinae and has the characteristic feature that after primary disease (chicken pox) the virus goes into latency and on reactivation which may occur months to years after primary infection leads to HZ. Chicken pox usually occurs in 2-10 yrs of age group or occasionally in older age group. The reactivation of dormant VZV in sensory ganglion may occur spontaneously or may be due to immunosuppression.⁽¹⁾ Immunosuppression may be due to ageing, HIV infection, malignancy, immunosuppressive drugs, trauma, stress etc. In immunocompromised cases HZ may present with atypical presentations like, disseminated, multidermatomal, recurrent, crusted, haemorrhagic, ulcerative, ecthymatous etc.⁽²⁾

Typical manifestation of HZ is grouped vesicular lesions on an erythematous base present unilaterally involving a single or adjacent dermatome associated with pain and may be preceded by prodrome of pain.

But sometimes atypical visceral involvement can mimic different medical, surgical or gynaecological ailments.

Usually final outcome of HZ is uneventful but some complications may occur. Secondary bacterial infection, ulceration, post-inflammatory hyper/hypo-pigmentation, scar formation, keloid, ocular complications, cranial or peripheral nerve palsies, meningo-encephalitis, visceral involvement and postherpetic neuralgia are various complications of HZ.⁽³⁾

Among these complications most important and most troublesome complication is postherpetic neuralgia (PHN)^(4,5) which is persistence of pain exceeding one month after the disappearance of the rash but there is presently no universally accepted definition for PHN. But in HZ three specific phases of pain (acute herpetic neuralgia, subacute herpetic neuralgia and chronic pain or PHN) are suggestive of that PHN should be defined as pain lasting at least 3 months after resolution of the rash.^(6,7)

About 9-34% of the cases with HZ develop PHN.⁽⁸⁾ Pathologically there is degeneration of primary afferent neuronal cell bodies and axons, dorsal horn atrophy, dorsal root ganglion scarring, and epidermal innervations loss.⁽⁹⁾ Damaged sensory afferent fibres which occurs in PHN is responsible for constant pain besides mechanical allodynia in the area of sensory loss. In addition to continuous pain, paroxysms of pain occur because of discharges of abnormally generated impulses in demyelinated A β fibres.

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Corresponding Author:

Dr. Atul Vijay, Opp. SRG Hospital & Medical College,
NH-12, Jhalawar-326001.

E-mail: drvijayatul1@gmail.com

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Both sensitization and deafferentation are important in genesis of pain. Viral spread from nerve root to the corresponding dermatome causes inflammation and neural injury, leading to peripheral sensitization and increased afferent input to the spinal cord. Spontaneous burning pain is also common in these cases.

Risk factors for PHN in HZ cases include older age, female sex, more intense acute pain, more severe rash developing within 3 days after the onset of HZ, a prodrome of dermatomal pain before the rash appears and involvement of ophthalmic division of trigeminal nerve.⁽¹⁰⁾

PHN is directly associated with advanced age and incidence rises after the age of 60 years.⁽¹¹⁾ Older age is associated with subclinical polyneuropathy and degeneration of myelinated afferent fibres which may increase chances of PHN.

Females have longer life expectancy and are more likely to report more severe pain and pain of longer duration compared with males.⁽¹⁰⁾

The prodrome indicates early viral damage of affected sensory ganglion. Rash severity is related with the damage of epidermal nerve fibres. Severe acute pain probably enhances central sensitization and excitotoxic damage in the dorsal horn.

There are two different thoughts in association of PHN with number and location of dermatome involved. First one denies any association between dermatome and PHN⁽¹²⁾ while second thought supports it.⁽¹³⁾

Again there are two different opinions regarding relation between antiviral drug management and development of PHN. First group supports decreased chances of PHN with the use of antiviral treatment within 72 hours of eruption⁽¹⁴⁾ but second group is not in favour of the same.⁽¹⁵⁾

RESULTS: The study of HZ conducted in 123 cases showed that out of 123 cases 58% were below 40 years & 42 % were above 40 years. It mainly affects adults as the age group of 31-40 years has maximum number of cases (35=28.5%). Sex ratio favours slight female predominance (M:F=1.12:1).

Majority of cases (83%) had no provoking factors but in remaining (17%) common provoking factors were malignancy and PTB in 4 cases, HIV infection in 3 cases, chronic use of oral steroids for other diseases, DM, post operative period in 2 cases in each group, depression under treatment & renal disease each were present in 1 case.

76 cases (62%) had prodromal dermatomal pain but constitutional symptoms like nausea, vomiting, arthralgia, insomnia, headache, loss of appetite etc. were also present in 9 cases (7.3%) in prodromal period ranging from 1-3 days.

15 cases (12.19%) had tender lymphadenopathy at the time of presentation while 8 cases (6.5%) developed it during the course of the disease.

Almost all the cases had segmental neuralgia over the respective dermatome except in 3 cases among which one

had DM while other 2 cases presented very early. In 36% cases rashes & pain occurred concurrently.

Segmental distribution was as shown in pie diagram. Most common segment involved was thoracic in 51 cases (41.46%) among which T4 & T5 were the most common dermatomes affected.

More than half (11=55%) cases of trigeminal nerve had ophthalmic division involvement. Almost 80% of the cases had distribution of eruptions according to dermatome but in remaining 20% (24 cases) lesions were also present beyond the parental dermatome among which 8 cases had involvement of more than one adjacent dermatome, 15 cases had vesicles (ranging from 4-16) distant from the primary dermatome. Only one case who was HIV sufferer presented with more than 20 vesicles distant from primary dermatome (disseminated herpes zoster). 58 cases had lesions on right side while remaining 65 had on left side.

Out of 123 cases 49 (39.8%) developed complications including ulceration (11=8.94%), secondary bacterial infection (9=7.3%), scarring (5=4.06%), keloid (1=0.8%) & most importantly PHN in 23 (18.69%) cases.

PHN occurred in 23 cases out of which 10 were male & 13 were female. PHN was characterized as deep continuous pain in 5 cases, episodic shooting pain in 12 cases, burning & itching in 3 cases & 3 cases reported it as sensation of crawling insects. 14 cases out of 23 (60.87%) were in the age group of more than 50 years. According to dermatome involved in HZ who developed PHN most common dermatome was ophthalmic in which PHN occurred in 45.45% cases.

In our study cases of HZ came to the department within the range of 1-12 days after the eruption of rashes. Out of 52 cases who received antiviral treatment within 72 hours, 9 (17.30%) developed PHN & in other 71 cases who didn't receive antiviral treatment, 14 (19.71%) developed PHN.

DISCUSSION: HZ is a common viral disease usually occurring in adults & elderly cases. Age wise distribution shown in table-1 is in favour of previous studies which shows most cases are in age group 31-40 yrs.⁽¹⁶⁾ Similar to some earlier studies⁽¹⁷⁾ our study favours slight female predominance. But some studies also support male predominance.⁽¹⁸⁾ In majority of cases (83%) any provoking factors could not be elicited similar to other studies.⁽¹⁹⁾ Those who had any provoking factors (17%) could be somehow considered as immunocompromised as they were presented with the HIV infection, pulmonary TB, chronic use of oral steroids, postoperative cases or with DM. Higher incidence of HZ in immunocompromised cases were also reported in other studies.⁽²⁰⁾

Benbernou A et al reported prodromal pain in 74% cases in their study⁽²¹⁾ while in our study this data is 62%. But the prevalence of other constitutional symptoms were low during the prodromal period.

Similar to a study by Yawn BP et al our study also favours thoracic and lumbar dermatomes to be the most commonly involved dermatomes.⁽²²⁾

Similar to study by Katz et al (23) in our study pain was the one of the main complaint at the time of presentation and almost all the cases presented with it. This acute pain has its own morbidity and it is also associated with increased risk of development of PHN (24). Though the severity of pain may vary but those who developed PHN had severe pain at the time of presentation.

Risk factors associated with development of PHN include advanced age, female gender, prodrome of pain, severe acute pain, and severe rash.(10)

Main risk factor for PHN is increasing age as PHN is relatively uncommon below the age of 50 years. It may develop in 20% of those between 60 to 65 years of age and in greater than 30% of those older than 80 years.(25) Individuals older than 60 years account for 50 percent of these cases.(26) In our study 61% of PHN cases are more than 50 years of age & in 50-70 years of age 40% cases had PHN while in more than 70 years of age all the four cases had PHN. These figures are relatively higher from other studies which may be due to lesser number of cases. A Volpi et al reported a ratio of 3:2 of female to male developing PHN in HZ cases. Our study also had the same female to male ratio.(27) Cases who had prodrome of pain are more vulnerable to develop PHN as almost all the cases of PHN had prodromal pain but not all cases of prodromal pain developed PHN which may be related with the intensity of the pain during prodrome. This finding is also supported by the study by Jung BF et al.(10) In our study we categorized pain in mild, moderate & severe on basis of pain affecting case's daily routine activities or sleep. Almost all the cases of PHN had severe pain at the time of presentation, only 3 out of 23 cases had moderate pain who developed PHN. We didn't categorize rash severity but as compare to the cases who didn't developed PHN, rashes were more severe in cases who developed PHN. Rash severity is indicative of increased epidermal nerve fibre loss & severe acute pain enhances central sensitization and excitotoxic damage in the dorsal horn.(28)

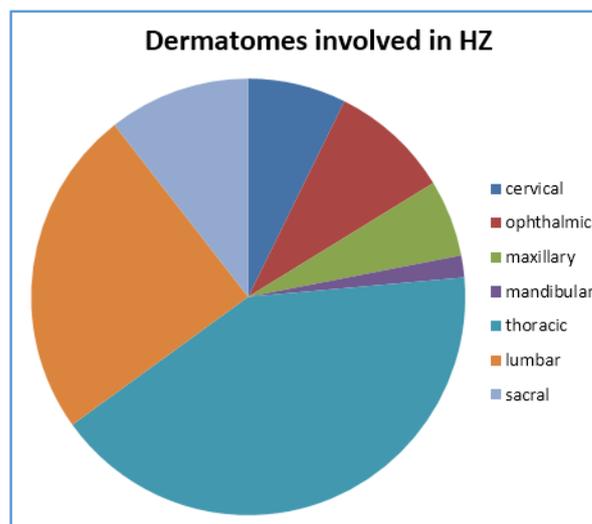
In our study PHN occurred in ophthalmic division of trigeminal nerve in 5 out of 11cases (45.45%) followed by thoracic dermatome (21.57%). Similar to our study Opstelten W et al also reported that involvement of ophthalmic division of trigeminal nerve has increased chances of development of PHN.(13) In some studies involvement of thoracic dermatome is strongly associated with development of PHN(29) though some other studies doesn't support that site or number of dermatomes involved have any association with occurrence of PHN.(12)

In our study among all the cases who received antiviral treatment within 72 hours, 17.30% cases developed PHN while in other group who didn't receive antiviral treatment, 19.71% cases developed PHN. This conclusion is similar to a previous study by Chen N et al which also denies that antiviral treatment decreases development of PHN.(15) But clinical trial by Shafran SD et al concludes that antiviral treatment is associated with decreased chances of PHN.(14)

CONCLUSION: HZ is a common clinical diagnosis in dermatology clinic. PHN is most common complication of HZ which is more common in elderly people and also occurs more in association with female sex, presence of prodrome, severe acute pain & more severe rash. Involvement of ophthalmic division of trigeminal nerve may be associated with increased chances of PHN but antiviral treatment is not associated with decreased chances of PHN. Some of our findings are supported by some previous studies while some other studies didn't support it which indicates requirement of more studies with large number of cases.

Age Group (in years)	HZ			PHN		
	Female (F)	Male (M)	Total	F	M	Total
0-10	3	1	4	-	-	-
11-20	3	11	14	-	-	-
21-30	12	6	18	-	-	-
31-40	25	10	35	4	1	5
41-50	8	15	23	2	2	4
51-60	9	7	16	4	2	6
61-70	3	6	9	2	2	4
71-80	2	1	3	2	1	3
>80	-	1	1	-	1	1
Total	65	58	123	14	9	23

Age & sex distribution in HZ & PHN



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