

Comprehensive Review of Clinical Manifestations and Management of Herpes Zoster

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Abstract

Herpes zoster, commonly known as shingles, is caused by the reactivation of the Varicella-zoster virus, the same virus responsible for chickenpox. After a person recovers from chickenpox, the virus remains dormant in the nervous system and may reactivate later in life, particularly when immunity decreases with age or illness. This review discusses the latest updates on the epidemiology, clinical features, complications, treatment, and prevention of herpes zoster. The occurrence of herpes zoster increases with advancing age and is more common in individuals with weakened immune systems, metabolic disorders, malignancies, or infections such as COVID-19 and AIDS. In recent years, cases of viral reactivation following COVID-19 vaccination have also been reported.¹ Clinically, herpes zoster presents with painful skin eruptions that may vary in severity and can lead to serious complications. Among these, postherpetic neuralgia is the most common and is characterized by persistent nerve pain even after the skin lesions heal. Other complications may involve the nervous system, blood vessels, kidneys, and gastrointestinal tract. Early diagnosis and prompt antiviral treatment with drugs such as acyclovir or brivudine play an important role in reducing disease severity and preventing complications. Proper pain management is also essential for improving patient quality of life. Vaccination remains the most effective preventive strategy, and currently available vaccines include a live attenuated vaccine and a recombinant subunit vaccine, which can also be administered to immunocompromised individuals. This review highlights current knowledge and recent advances in the understanding and management of herpes zoster, especially in elderly and immunocompromised

patients, with special attention to its relevance during the COVID-19 era.²

Keywords: Herpes zoster; Varicella-zoster virus; postherpetic neuralgia; antiviral therapy; vaccination; complications; COVID-19.

I. INTRODUCTION

Herpes Zoster, commonly known as shingles, is a viral infection caused by the reactivation of the Varicella zoster virus (VZV), a neurotropic virus belonging to the alpha-herpesvirus family. Primary infection with VZV usually occurs during childhood and results in varicella (chickenpox). After the primary infection resolves, the virus remains dormant in the sensory dorsal root ganglia of the nervous system for years or even decades. Reactivation of the latent virus, often associated with aging, immunosuppression, stress, or underlying diseases, leads to herpes zoster.

Herpes zoster is characterized by painful unilateral vesicular eruptions distributed along the affected dermatome. The disease is commonly associated with severe neuropathic pain and may lead to complications such as postherpetic neuralgia, ophthalmic involvement, bacterial superinfection, and neurological disorders. The incidence of herpes zoster increases with advancing age and in immunocompromised individuals, making it an important global public health concern.

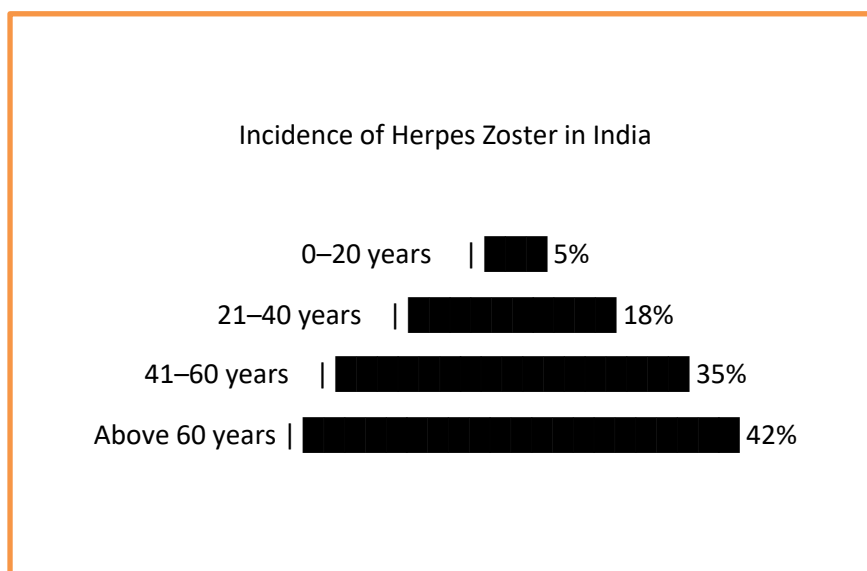
Early diagnosis and appropriate antiviral therapy play a significant role in reducing disease severity, complications, and duration of symptoms. Vaccination has also emerged as an effective preventive strategy against herpes zoster and its complications. This review aims to provide an overview of the epidemiology, pathogenesis, clinical manifestations, diagnosis, management, and

prevention of herpes zoster. The incidence of herpes zoster increases with advancing age due to the gradual decline in cell-mediated immunity. Individuals with immunosuppressive conditions such as malignancies, organ transplantation, AIDS, diabetes mellitus, and infections like COVID-19 are at higher risk of developing the disease. In recent years, reactivation of VZV following COVID-19 vaccination has also been reported, drawing increased clinical attention to the disease.³

EPIDEMIOLOGY

The disease is distributed worldwide and affects individuals of all age groups, although it is more common in older adults and immunocompromised patients. The global incidence of herpes zoster ranges from approximately 3–5 cases per 1,000 person-years in the general population and increases significantly with age, particularly in individuals above 50 years. In elderly populations, the incidence may rise to 8–12 cases per 1,000 person-years due to declining cell-mediated immunity associated with aging. Both males and females are affected, though some studies report a slightly higher prevalence among females.⁴

BAR GRAPH



ETIOLOGY

Herpes zoster occurs due to the reactivation of latent Varicella zoster virus (VZV) in sensory nerve ganglia. The following factors specifically contribute to viral reactivation:

1. Advanced Age

Several risk factors contribute to the development of herpes zoster, including advanced age, immunosuppressive conditions, malignancies, HIV infection, organ transplantation, psychological stress, and chronic diseases such as diabetes mellitus. Patients receiving chemotherapy, corticosteroids, or immunosuppressive therapy are also at increased risk of viral reactivation. The lifetime risk of developing herpes zoster is estimated to be about 20–30% in the general population and may exceed 50% in individuals living up to 85 years of age. Recurrence of herpes zoster can occur, especially in immunocompromised individuals.

Postherpetic neuralgia (PHN), the most common complication of herpes zoster, occurs more frequently in elderly patients and significantly affects quality of life. The introduction of varicella and zoster vaccines has contributed to reducing the incidence and severity of herpes zoster in many countries. However, the disease continues to remain an important public health concern due to aging populations and increasing numbers of immunocompromised individuals worldwide⁵

Incidence of Herpes Zoster in India

Aging leads to a decline in cell-mediated immunity, increasing susceptibility to VZV reactivation, especially after 50 years of age.

2. Immunosuppression

Conditions that weaken the immune system increase the risk of herpes zoster.

3. HIV/AIDS

Patients with HIV infection have reduced immune function, making VZV reactivation more common.

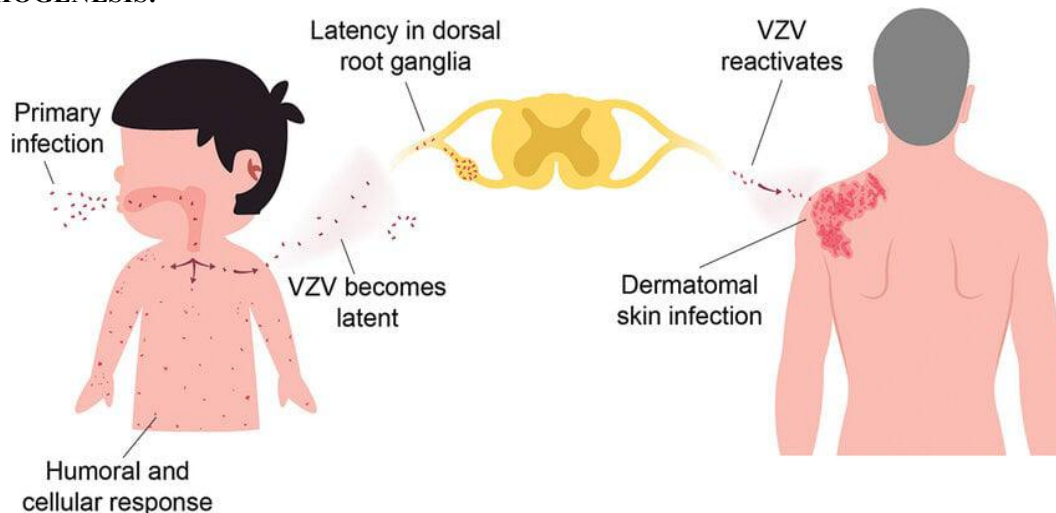
4. Cancer and Malignancies

Leukemia, lymphoma, and other malignancies can suppress immunity and trigger herpes zoster.

5. Chemotherapy and Radiotherapy

Cancer treatments may impair immune responses and promote viral reactivation.⁶

PATHOGENESIS:



Herpes zoster is caused by the reactivation of the varicella-zoster virus (VZV), the same virus that causes chickenpox. After a person recovers from chickenpox, the virus remains inactive in the sensory nerve ganglia for many years. When the body's immunity decreases due to aging, stress, illness, or immunosuppression, the latent virus becomes active again. The reactivated virus travels along sensory nerves to the skin, causing pain, inflammation, and a unilateral vesicular rash distributed along the affected dermatome. In some patients, nerve damage may persist and lead to postherpetic neuralgia.⁷

CLINICAL MANIFESTATIONS:

A painful, raised or blistered rash is the most common symptom of shingles. It might appear near your waist or on one side of your face, neck, chest, belly or back. Sometimes, it shows up on other parts of your body. Other symptoms that can appear before or along with the rash

Include:

- Deep, burning or shooting nerve pain
- Itching or tingling
- Areas of reddish or discolored skin
- Fever
- Chills
- Headache
- Generally feeling unwell (malaise)

- Stomach upset

Some early symptoms, like **nerve pain and discoloration, can appear weeks before the rash.** Others might show up in the days leading up to it. The rash turns into blisters about three to four days after it appears. Within about 10 days, the blisters dry out and crust over into scabs. The scabs may take a few weeks to completely go away.

Some people don't get a rash with shingles. See a healthcare provider if you have symptoms of shingles, even if you don't have the rash.⁸

COMPLICATIONS:

Herpes Zoster may cause the following specific complications:

1. **Postherpetic Neuralgia (PHN)** – Persistent burning or stabbing nerve pain after the rash heals. It is the most common complications.
2. **Herpes Zoster Ophthalmicus** – Involvement of the eye due to infection of the ophthalmic branch of the trigeminal nerve, which may cause keratitis, uveitis, glaucoma, and vision loss.
3. **Ramsay Hunt Syndrome** – Occurs when the virus affects the facial nerve near the ear, causing facial paralysis, ear pain, hearing loss, and vertigo.
4. **Secondary Bacterial Infection** – Open skin lesions may become infected with bacteria, leading to cellulitis or abscess formation.

5. **Meningitis and Encephalitis** – Inflammation of the meninges or brain, resulting in headache, fever, confusion, or neurological deficits.

6. **Myelitis** – Inflammation of the spinal cord that can lead to weakness or paralysis.

7. **Disseminated Herpes Zoster** – Widespread vesicular lesions and systemic involvement, especially in immunocompromised patients.

8. **Cranial and Peripheral Nerve Palsies** – Damage to nerves causing motor weakness or sensory disturbances.

9. **Pneumonitis and Hepatitis** – Rare visceral complications involving the lungs or liver.

10. **Scarring and Pigmentary Changes** – Permanent skin marks or discoloration after healing of lesions.¹⁰

11. **Meningitis Retention Syndrome** -A rare neurological complication characterized by acute urinary retention associated with aseptic meningitis. Patients may present with fever, headache, neck stiffness, and bladder areflexia.

12. **Acute Colonic Pseudo-Obstruction (Ogilvie Syndrome)** -A rare gastrointestinal complication causing severe constipation, abdominal distension, and colonic dilatation without mechanical obstruction.

13. **Keloids and Isotopic Skin Reactions** -Healing herpes zoster lesions may develop keloids, especially in darker skin types. Previously affected skin areas can also develop secondary dermatoses or infiltrative disorders.

14. **pseudohernia Formation** -Weakness or paresis of abdominal muscles may cause unilateral abdominal bulging known as post-herpetic pseudohernia.

15. Rarely, cysts may develop in areas previously affected by herpes zoster, particularly in patients with postherpetic neuralgia.

16. **Erythema Multiforme** -A hypersensitivity reaction presenting with target-shaped skin

lesions, macules, and papules associated with herpes zoster infection.

17. **Vasculitis and Vasculopathy**

Varicella-Zoster Virus Infection may involve blood vessels and lead to:

Retinal vasculitis

CNS arteritis

Giant cell arteritis

Leukocytoclastic vasculitis

IgA vasculitis

These complications can result in stroke, visual impairment, or systemic inflammation.

18. **Recurrent Herpes Zoster** -Reactivation of the virus may occur repeatedly, especially in elderly or immunocompromised individuals and patients receiving immunosuppressive therapy.

19. **Occult Neoplasia Association** -Severe or atypical herpes zoster may indicate underlying malignancies, particularly hematological cancers and lung cancer.

20. **Reactivation Following COVID-19 or Vaccination** -Reactivation of VZV has been reported after COVID-19 infection and following COVID-19 vaccination in some individuals, especially those with immunosuppression or comorbidities.¹¹

MANAGEMENT AND PREVENTION:

The standard treatment for Herpes Zoster includes antiviral drugs such as Acyclovir, its prodrug Valacyclovir, and Brivudin. Oral valacyclovir has better bioavailability than acyclovir, making it more effective and convenient. These antiviral drugs act as nucleoside analogues and inhibit viral DNA replication in infected cells. Resistance to acyclovir may occur due to mutations in viral thymidine kinase or DNA polymerase enzymes.¹²

DRUGS	DOSE	REMARKS
Acyclovir	Adults: 800 mg orally 5 times/day	Limited bioavailability
	Intravenous: 500 mg 3 times/day	Used in severe cases or immunosuppression
	Children: 10 mg/kg 3 times/day Maximum daily dose 2.5 g	
Brivudin	125 mg once daily orally for 5 days	No renal toxicity
Valacyclovir	1000 mg orally 3 times/day for 7 days	Better absorption

Famciclovir	250–500 mg orally 3 times/day	Used in acyclovir-resistant cases
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A rare **adverse effect** of antiviral therapy is **renal toxicity**, especially with **acyclovir**. Dose adjustment may be necessary in patients with kidney impairment. **Brivudin** does not cause renal toxicity, but it should never be used with 5-fluorouracil or related drugs within the previous four weeks because of severe drug interactions.

In cases resistant to acyclovir, Famciclovir can be used as an alternative. **Valganciclovir** has also shown activity against the Varicella-Zoster Virus Infection. A newer class of drugs called helicase-primase inhibitors blocks viral DNA synthesis. **Amenamevir** is the first approved drug of this class and is used in Japan for herpes zoster treatment.

Preventing reactivation of VZV is important in immunocompromised patients, especially transplant recipients. Low-dose acyclovir or famciclovir may be used for prevention. Recent studies have shown that extracts from *Elaeocarpus sylvestris* may inhibit VZV replication and reduce inflammatory pain, although more research is needed before routine clinical use.¹³

1. Vaccination:

Vaccination helps prevent herpes zoster and its major complication, postherpetic neuralgia (PHN). Two vaccines are currently available:

1. Zostavax – a live attenuated vaccine
 2. Shingrix – a recombinant glycoprotein E vaccine
- Shingrix is more effective than Zostavax and is considered safer for immunocompromised individuals because it is a non-live vaccine. Clinical studies have shown strong and long-lasting immune responses after vaccination. Large studies from China and the United States demonstrated that recombinant vaccination significantly reduces cases of herpes zoster, postherpetic neuralgia, hospitalizations, and outpatient visits. Vaccine effectiveness has been reported to be around 70–85% depending on age and number of doses. A rare adverse effect reported after recombinant vaccination is optic neuritis related to myelin oligodendrocyte glycoprotein antibodies.

2. Maintaining Strong Immunity:

A healthy immune system helps reduce the risk of VZV reactivation.

Preventive measures include:

- Balanced nutritious diet
- Regular physical exercise
- Adequate sleep and rest
- Stress management

- Avoidance of smoking and excessive alcohol use.¹⁴

3. Prevention in Immunocompromised Patients:

Patients with weakened immunity, such as transplant recipients or cancer patients, may require preventive antiviral therapy.

Acyclovir or Famciclovir may be used in low doses to prevent reactivation.

4. Early Treatment of Infection

Early diagnosis and prompt antiviral treatment within 72 hours of rash appearance can reduce disease severity and complications.

5. Avoiding Transmission

People with active shingles should:

- Keep rashes covered
- Avoid scratching lesions
- Maintain good hand hygiene

Avoid close contact with pregnant women, newborns, and immunocompromised individuals until lesions crust over.¹⁵

II. CONCLUSION

Herpes zoster is an important viral disease caused by the reactivation of latent Varicella-zoster virus, primarily affecting elderly and immunocompromised individuals. The incidence of the disease continues to increase with advancing age and in patients with conditions that weaken the immune system. Herpes zoster is characterized by painful dermatomal skin eruptions and may result in serious complications, with postherpetic neuralgia being the most frequent and debilitating outcome affecting quality of life. Other complications involving the eyes, nervous system, blood vessels, and internal organs may also occur. Early diagnosis and prompt initiation of antiviral therapy are essential for reducing disease severity, duration, and risk of complications. Appropriate pain management further improves patient outcomes and quality of life. Vaccination remains the most effective preventive strategy, significantly reducing the incidence of herpes zoster and its associated complications. The availability of recombinant vaccines has expanded protection, particularly among immunocompromised individuals. Recent observations of VZV reactivation associated with COVID-19 infection and vaccination have highlighted the need for continued clinical awareness and research. Overall, improving knowledge regarding epidemiology, risk factors,

prevention, and treatment strategies is essential for effective management of herpes zoster and reducing its healthcare burden worldwide.

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