A study of HIV seropositivity among herpes zoster patients

By

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In

Dermatology, Venereology and Leprosy

Under the guidance of

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DECLARATION BY THE CANDIDATE

I hereby declare that the dissertation entitled "**A study of HIV seropositivity among herpes zoster patients**" is a bonafide and genuine research work carried out by me under the guidance of **Dr. B. Siddaramappa** M.D,D.V.D, Professor and H.O.D, Department of Dermatology, Venereology and Leprosy, Jawaharlal Nehru Medical College, Belgaum.

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List of abbreviations used

AIDS	Acquired Immunodeficiency Syndrome
CNS	Central Nervous System
DC	Differential Count
ELISA	Enzyme Linked Immunosorbent Assay
ESR	Erythrocyte Sedimentation Rate
FAMA	Fluorescent Antibody to Membrane Antigen
HAART	Highly Active Anti Retroviral Therapy
HIV	Human Immunodeficiency Virus
KLES	Karnataka Lingayat Education Society
MRC	Medical Research Centre
OPD	Out Patient Department
PCR	Polymerase Chain Reaction
PHN	Post Herpetic Neuralgia
RBS	Random Blood Sugar
TC	Total Count
VZV	Varicella Zoster Virus

Abstract

Background and objectives: The aim of the study was to determine the HIV seropositivity among herpes zoster patients and the various clinical presentations of herpes zoster.

Methods: The present study was a one-year time bound observational study from December 2006 to November 2007. All new clinically diagnosed cases of herpes zoster were included in the study. The patient's demographic data, symptoms, location of lesions, risk factors, associated systemic disease and complications were noted. Routine investigations were carried out and a blood sample was taken for HIV serology in all patients after informed consent and counseling.

Results: A total number of 72 herpes zoster cases were recorded. The HIV seropositivity ratio was 22.22%. The maximum number of cases were seen in the 21-30 years age group (25%) followed by 31-40 years age group (19.44%) and 51-60 years age group (18.06%). The mean age of the study population was 41.17 years and the male to female ratio was 1.88:1. In the present study, most of the patients had thoracic dermatome involvement (50%). Five out of those 36 patients were HIV seropositive (13.89%). The next dermatome groups commonly involved were the Cervical (20.83%) followed by the Lumbar (13.89%) group. HIV seropositivity was 26.67% in the cervical dermatome group and 50% in the lumbar dermatome group. Most of the patients (91.67%) had classical vesicular type of herpes zoster. Two patients each had bullous, ulcerative and hemorrhagic skin lesions. HIV seropositivity was noted in one patient each of herpes zoster with bullous and hemorrhagic skin lesions.

Interpretation and conclusion: Occurrence of herpes zoster in young adults who give history of high-risk sexual behaviour may require HIV testing. Herpes zoster can be useful to the clinician as a clinical marker of HIV infection.

Key words: Herpes zoster; HIV; VZV

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Introduction

Herpes zoster is a localized disease characterized by unilateral radicular pain and grouped vesicular eruption that is generally limited to the dermatome innervated by a single spinal or cranial sensory ganglion. It occurs as a result of reactivation of varicella zoster virus (VZV) that had persisted in latent form within sensory ganglion following an earlier attack of varicella.[1]

Herpes zoster has traditionally affected persons with more than 60 years of age. Recently, herpes zoster has been observed in young adults infected with human immunodeficiency virus infection. The incidence of complicated and atypical herpes zoster has increased due to increasing prevalence of HIV infection. Herpes zoster should be recognized as a marker condition, indicating the necessity for HIV screening.[2]

It is observed in India that most of the patients afflicted with herpes zoster are of the middle age group.[3,4,5] There are many possible explanations for this, and an increasing prevalence of HIV among young adults is one of them. Studies in this part of Karnataka are lacking, and it is yet to be established whether HIV is a significant cause for the occurrence of herpes zoster in younger individuals, or whether there are any other predisposing factors for the same.

Hence, this study is undertaken to determine the seropositivity of HIV in patients suffering from herpes zoster, and to know the clinical and morphological characteristics of herpes zoster.

Objectives

1. To determine the HIV seropositivity rate among patients suffering from herpes zoster.

2. To study the various clinical presentations of herpes zoster, the common sites, extent of involvement, risk factors and demographic characteristics.

Review of literature

Historical aspects

Herpes zoster is derived from the Greek language.[6] Herpes means '*to creep*' and zoster means '*girdle'*. '*Zona'* is also a Greek word meaning '*girdle'*. It is also known as shingles, which is derived from a Latin word '*cingulum'*, meaning girdle. It is has been referred to as '*holy fire*' by the Romans, [7] a '*belt of roses from hell*' by the Norwegians, and '*hell fire*' by the Danes.[8]

The following is a timeline of significant historical events pertaining to herpes zoster.

- **1831**- Ricard Bright recognized the implications of the segmental distribution of the rash.[9]
- **1862**- Von Barensprung proved the correctness of Bright's deduction by demonstrating at autopsy the damage in sensory nerve and ganglion.[9]
- **1865**- Charcot and Cotard noted an association between cancer and zoster. They reported a case of cervical zoster associated with the presence of spinal metastases from a carcinoma of the breast.[10]
- **1866**- William Broadbent first described the association of muscular paralysis and zoster.[11]
- **1888**- Von Bokay proposed that susceptible children acquired varicella after contact with individuals suffering from herpes zoster and showed the relationship of herpes zoster to varicella.[9]

- **1900**- Head and Campbell published a study including detailed postmortem examinations of 20 persons who had zoster. All gross and minute pathology of the disease was described and illustrated; the acute haemorrhagic inflammation in recently infected ganglia and sensory nerves, the nerve damage linking the affected neurons peripherally to the sensory endings and centrally to the cord and brain, the recovery and the permanent damage. From their experience they were able to map the sensory areas related to each ganglion.[9]

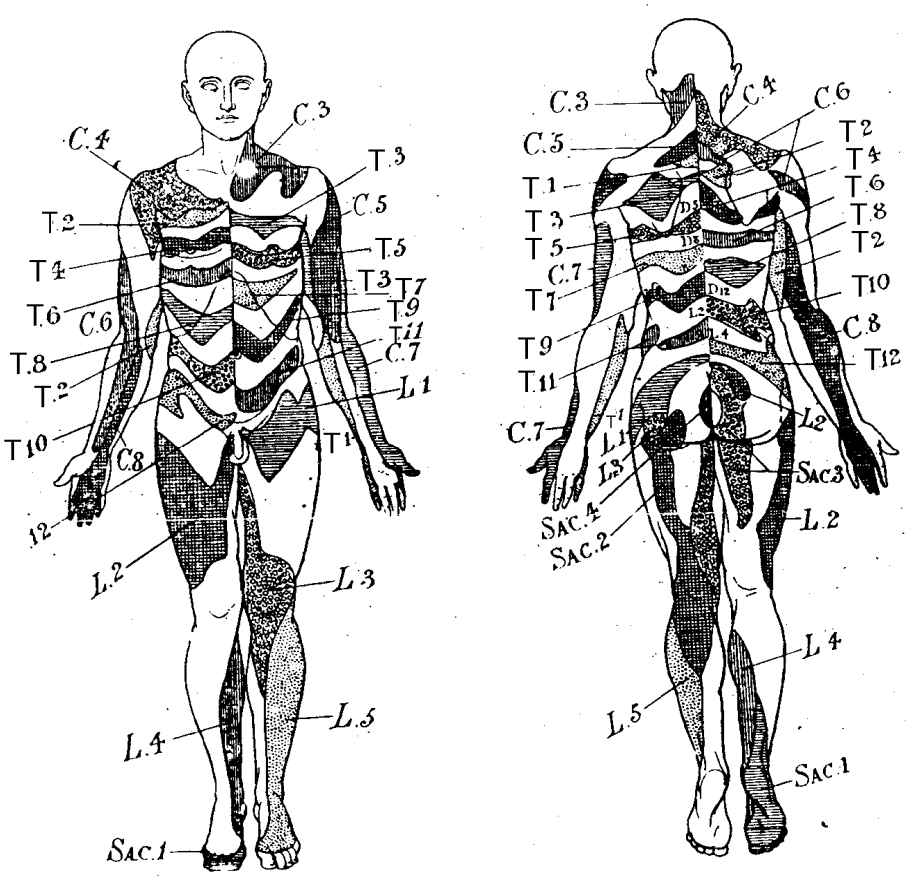


Figure 1: Zoster areas allocated to sensory ganglia by Head and Campbell

- **1915**- Paschen demonstrated viral elementary bodies in vesicle fluid by light microscopy.[12]
- **1925**- Kundratitz and Brungaard showed that children inoculated with zoster vesicle fluid might develop varicella and also transmit it to their uninoculated companions.[9]
- **1943**- Ruska showed viral elementary bodies in vesicle fluid by using the electron microscope.[13]
- **1944**- Abrahamson stored the plasma of a convalescent herpes zoster patient, and then later used it successfully to protect children in contact with varicella.[9]
- **1949**- Halpern and Covern reported an association between diaphragmatic paralysis and herpes zoster.[14]
- **1952**- Weller and Stoddard succeeded in growing varicella virus in a tissue culture system.[9]
- **1954**- Weller and Coons showed that the virus was the same whether it came from a case of varicella or a case of herpes zoster.[9]
- **1959**- Taylor-Robinson and Downie had shown by immunological methods that herpes zoster and varicella are closely related.[9]
- **1983**- Varicella zoster virus disease was first recognized in the context of infection with HIV.[15]

Definition

Herpes zoster is a localized disease characterized by unilateral radicular pain and grouped vesicular eruption that is generally limited to the dermatome innervated by a single spinal or cranial sensory ganglion. It occurs as a result of reactivation of varicella zoster virus (VZV) that had persisted in latent form within sensory ganglion following an earlier attack of varicella.[1]

Alternatively, it can be defined as a reactivation of an endogenous varicella zoster virus infection, which persists in a latent form in sensory neurons following an earlier varicella attack.[16]

Epidemiology

Incidence:

The incidence of herpes zoster ranges from 0.24% to 0.6% in various studies.[3,4,9,17] It is estimated that there are more than a million new cases of herpes zoster each year, more than one-half of which occur in persons 60 years of age or older, and this number increase as the population ages.[1]

Age:

One strong risk factor of herpes zoster is age. It's incidence increases with age.[18] Earlier studies have indicated that most cases of herpes zoster occur at an older age,[19,20] one study showing that 118 cases out 192 were aged above 50 years,[9] and another one showing that 61 out of 81 were beyond the age of 45 years.[17]

However, there are many studies which point out that herpes zoster occurs more commonly in the younger populations. It is observed that majority of the herpes zoster cases occur in the 2nd to 4th decades of life.[3,4,5]

Herpes zoster is rare during the first few years of life.[1] It is uncommon in childhood except in those who are immunocompromised. Recurrent herpes zoster is very rare in children.[16]

Sex:

Herpes zoster affects both sexes and all races with equal frequency.[21] Many international studies have noted an equal sex incidence.[18,19,20,22] There are a few Indian studies which

have noted a higher incidence of herpes zoster in males, with male to female ratios ranging from 1.74:1 to 3:1.[3,4,5,23,24]

Seasonal variation:

Herpes zoster occurs sporadically throughout the year without seasonal prevalence.[1] No seasonal variation was noted in some studies,[4,9,17] and an increased incidence was noted in the months of March, April, August, September and December in some studies.[3,23,24]

Etiological agent

The herpes virus family contains over a hundred species of enveloped DNA viruses that affect humans and animals. They are characterized by their ability to establish latent infections, enabling the virus to persist indefinitely within infected hosts and to undergo periodic reactivation.[25]

Varicella zoster virus belongs to Alpha herpes virus subfamily of herpes viridae and is also known as human herpes virus 3 (HHV-3).[25]

The herpes virus capsid is icosahedral and composed of 162 capsomeres. It encloses the core, which contains a linear double stranded DNA genome. The nucleocapsid is surrounded by a lipid envelope. This is derived from the modified host cell nuclear membrane through which the naked virions bud during replication. The envelope carries surface spikes, each about 8mm long. Between the envelope and the capsid is an amorphous structure called the tegument, which contains several proteins. The enveloped virion measures about 200nm in diameter and the naked virion is about 100nm in diameter.[25]

Herpes viruses replicate in the host cell nucleus. They form Cowdry type A intranuclear (Lipschutz) inclusion bodies. Like other enveloped viruses, herpes viruses are susceptible to organic solvents like alcohol, ether, chloroform and bile salts. They are heat labile and are affected by extremes of pH.[25]

The VZV genome encodes about 70 genes, most of which have a DNA sequence and functional homology similar to that of genes of the other herpes viruses. Immediate early

gene products regulate VZV replication. Early gene products, such as the virus-specific thymidine kinase and the viral DNA polymerase, support viral replication. Late genes encode virus structural proteins that serve as targets of antibody and cellular immune response.[1]

Davison and Scott published the complete DNA sequence of VZV in 1986. Buoyant density estimations as well as sequence data show a (G+C) content of 46%, which is much lower than most herpes viruses.[26]

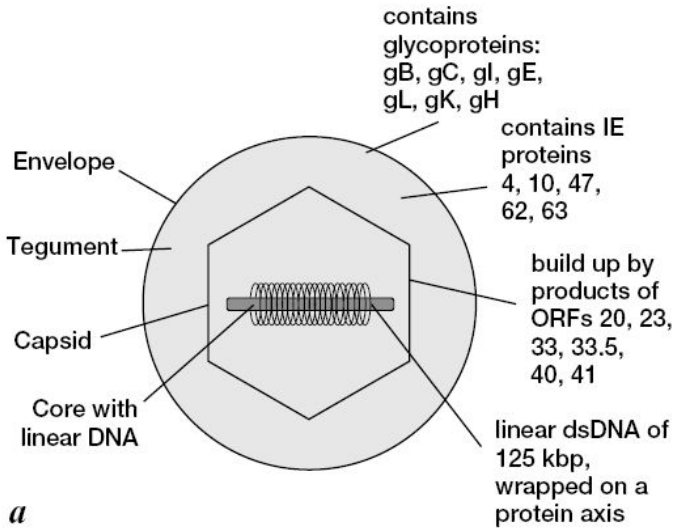


Figure 2: Schematic drawing of the VZV - The important elements – envelope, tegument, capsid and core are shown on the left-hand side, important components of each element are given on the right-hand side.

Pathogenesis

The concept that herpes zoster represents the reactivation of latent varicella zoster virus was first proposed in 1943 by Garland J.[27] This concept was proved by molecular analysis of viruses recovered from primary and reactivation infections in same patient.[28]

It is hypothesized that after a primary attack of varicella, the virus enters the body through the skin and mucosal membranes to the contiguous endings of sensory nerves. It is transported up the sensory fibers until it arrives at the sensory ganglion, where it becomes established as a latent infection in the nuclei of the neurons. Here, the virus persists silently and harmlessly. It is no longer infectious and does not multiply but it retains the capacity to revert to full infectiousness.[9]

Herpes zoster occurs with highest frequency in the dermatomes where the rash of varicella achieves the greatest density, presumably because the areas of the skin with denser rash during varicella transmit larger amounts of virus to the corresponding sensory ganglia and this establishes latent infection in a larger number of sensory neurons.[9]

Even when the latent virus does revert, usually nothing perceptible happens. The minute dose of infectious virus that results is immediately neutralized by circulating antibodies or destroyed by cellular immune responses before it can infect other cells. The small quantity of viral antigen released into the blood stream during such "contained reversions" stimulates host immune response and this raises the level of host resistance. When host resistance falls below a critical level, the reactivated virus can no longer be contained and the infectious virus multiplies and spreads within the ganglion causing

neuronal necrosis and intense inflammation, a process that is usually accompanied by severe neuralgia. The infectious virion then spreads antidromically down the sensory nerve, causing an intense neuritis, and is released around the sensory nerve endings into the skin to produce the characteristic cluster of zoster vesicles.[9]

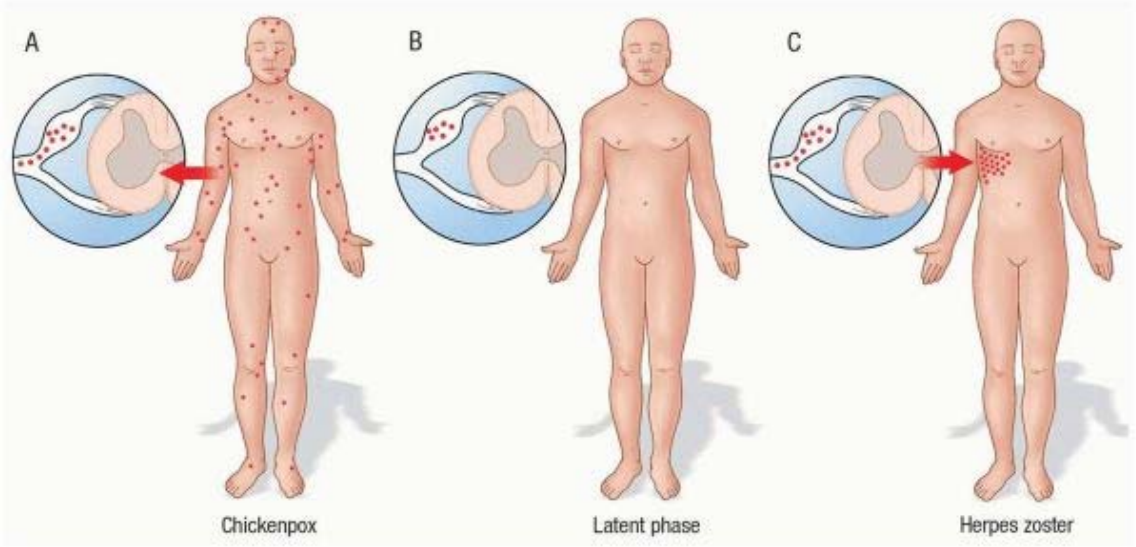


Figure 3: Pathogenesis of herpes zoster - **A**. During primary varicella-zoster virus (VZV) infection (varicella or chickenpox), virus infects sensory ganglia. **B**. VZV persists in a latent phase within ganglia for the life of the individual. **C**. With diminished immune function, VZV re-activates within sensory ganglia, descends through sensory nerves, and replicates in skin.

Spread of the ganglionic infection proximally along the posterior nerve root to the meninges and cord results in local leptomeningitis, cerebrospinal fluid pleocytosis, and segmental myelitis. Infection of motor neurons in the anterior horn and inflammation of the anterior nerve root account for the local palsies that may accompany the cutaneous eruption, and extension of infection within the central nervous system may result in rare complications of herpes zoster (e.g., meningoencephalitis, transverse myelitis).[1]

Immunology of herpes zoster

Humoral Response:

Specific antibody persists at low levels during the constraint period. With the appearance of herpes zoster in normal subjects, there is a rapid rise in specific levels of IgG, IgM, and IgA.[29] The unexpected rise in IgM, a response usually associated with a primary exposure to an infectious agent, has been studied extensively.[30] The results of several studies confirm that an IgM response may occur with a frequency of demonstration ranging from 20% to 78%.[31]

Circulating antigen-antibody complexes have been demonstrated in the serum from 50% of healthy subjects with localized herpes zoster. This observation suggests that a new mechanism, i.e. tissue damage resulting from immune complex deposition is almost certainly involved in the pathogenesis of severe infections.[32]

Cellular Responses:

The cellular immune responses to herpes zoster have been examined extensively. Lymphocytes from elderly people who are healthy show little blastogenic response to the viral antigen in the first five days after the appearance of the eruption. Thereafter, specific responses occur.[33]

Skin tests with Oka-strain antigen are usually negative when the eruption appears. Five days later, 56 percent of tests are positive, and thereafter, all are positive.[34] Thus, a depressed cellular immune state is a major factor in the process of viral recrudescence.[30]

Pathology of herpes zoster

Skin changes:

Lesions of herpes zoster are histologically indistinguishable from those of herpes simplex. The earliest changes include nuclear swelling of keratinocytes. With haematoxylin and eosin stain, these nuclei appear slate grey and homogenous with margination of the nuclear chromatin. A few necrotic keratinocytes are seen. The changes usually begin along the basal keratinocytes and then involve the entire epidermis. Later it produces profound degeneration of keratinocytes, resulting in acantholysis.[35]

Degeneration of epidermal keratinocytes occurs in two forms - ballooning degeneration and reticular degeneration. Ballooning degeneration consists of swelling of epidermal keratinocytes. Balloon cells have a homogenous, eosinophilic cytoplasm, and they may be multinucleated (Tzanck cells). Balloon cells lose their intercellular bridges and become separated from one another (Secondary acantholysis) and unilocular vesicles result. Vesicles are found intraepidermally or subepidermally.[35]

Reticular degeneration is the result of rupture of the ballooning cells due to progressive hydropic swelling. It occurs in the upper portions and at the peripheries of viral vesicles. It results in multilocular vesicles, but later the walls disappear to become unilocular.[35]

Inclusion bodies are observed in the center of enlarged, round nuclei of balloon cells. They are eosinophilic and surrounded by a clear space or halo. They measure about 2-3 μm in diameter. In disseminated herpes zoster, it may also be seen in the dermis within

nuclei of capillary endothelia and adjoining fibroblasts. The upper dermis beneath viral vesicles contains inflammatory infiltrate of variable density.[35]

The degree of vessel damage, micro thrombi and hemorrhage are more pronounced than in varicella. Herpes zoster vasculitis may mimic giant cell arteritis.[36]

Neural changes:

It begins either in a dorsal root ganglion or in a cranial nerve ganglion. The ganglion shows intense lymphocytic infiltration, which is associated with necrosis of the ganglion cells and nerve fibers along with haemorrhage.[37]

Inclusion bodies have been demonstrated within neurilemmal cells of the small nerves in the dermis underlying the vesicles.[35]

It has been reported that there is a pronounced diminution in the number of nerve fibers in some nerve bundles of the dermis in lesions, ranging from 14 days to a year after the onset of the eruption.[38]

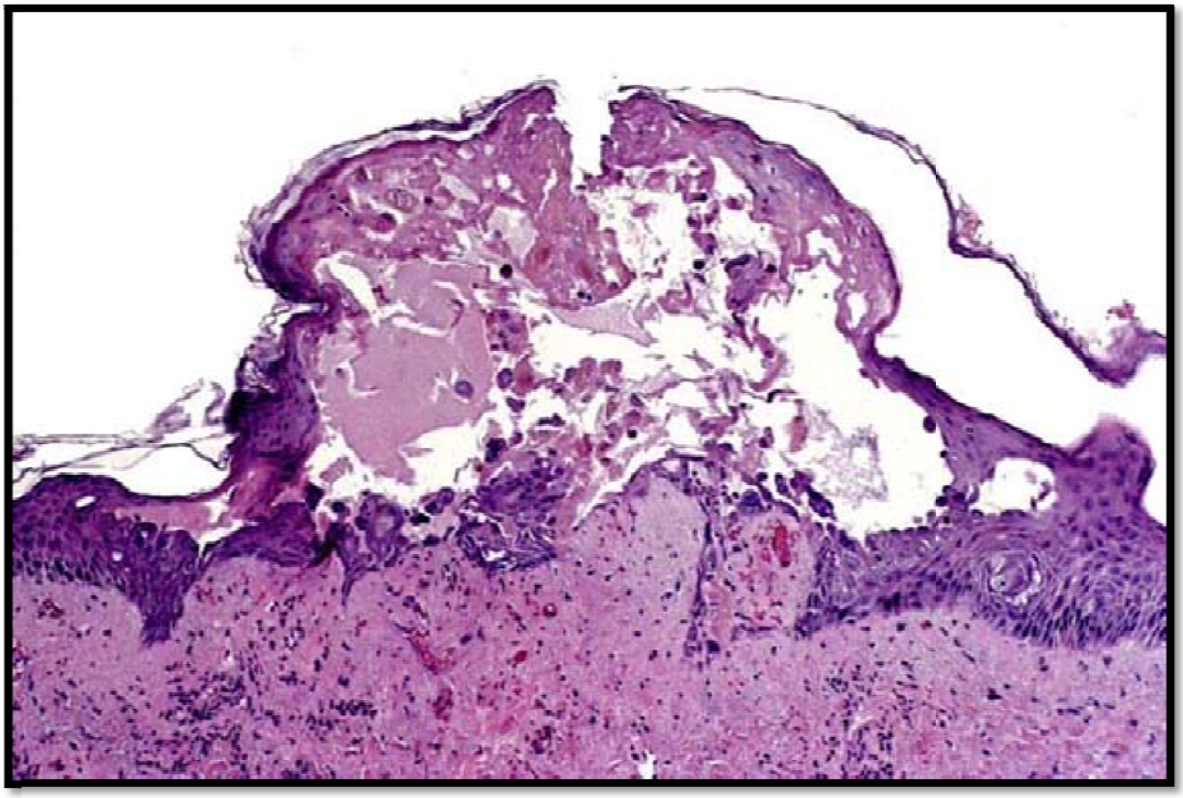
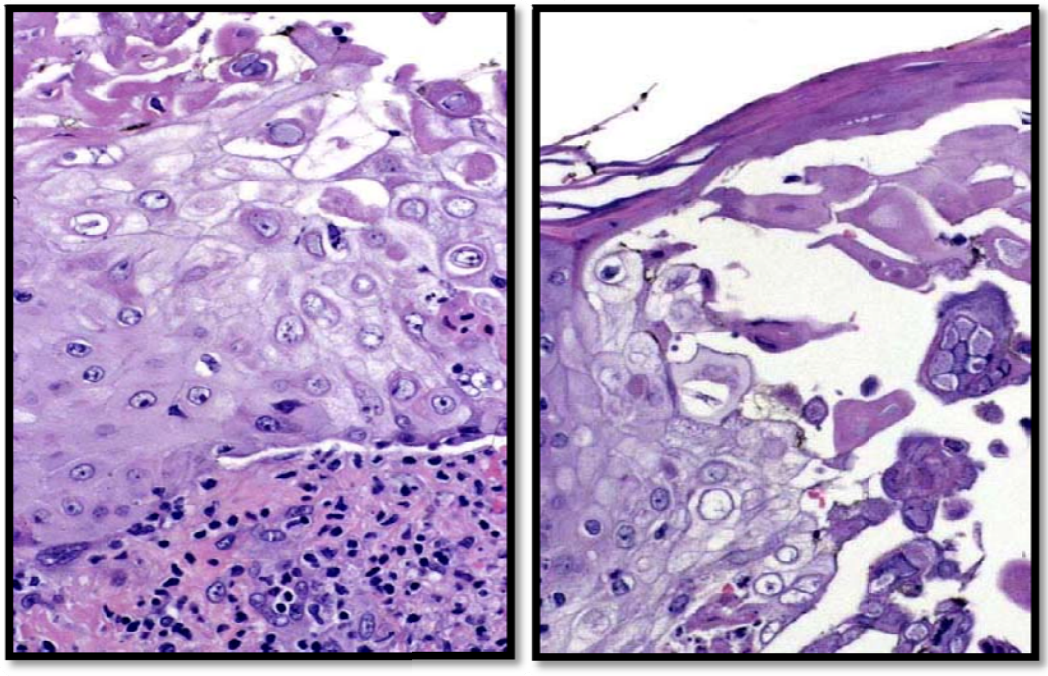


Figure 4: Intraepidermal blister of herpes zoster



Figures 5 and 6: Ballooning degeneration and multinucleate giant cell

CNS changes:

Upward extension of the virus along the spinal cord from the dorsal root ganglion to the brain is common. Pleocytosis of the spinal fluid is present in 1/4th of patients with herpes zoster.[39]

The frequent occurrence of the herpes zoster meningoencephalitis in association with disseminated zoster suggests that virus often reaches the brain because of viremia.[40]

Visceral lesions:

In fatal cases of pneumonia due to herpes zoster, the autopsy showed focal areas of hemorrhagic necrosis, giant cells and macrophages with eosinophilic inclusion bodies.[41]

Autopsy findings in a female patient of disseminated herpes zoster with underlying Hodgkin's disease revealed intranuclear inclusion bodies and focal necrosis within the esophageal mucosa, myenteric plexus of stomach, dorsal root ganglia, sympathetic ganglion at the level of affected dorsal root ganglia, pancreas, adrenal glands and one ovary.[37]

Precipitating factors

The majority of herpes zoster cases occur in otherwise healthy persons who are without evidence of precipitating factors. These cases are classified as primary or spontaneous.[42]

Recent chemotherapy is associated with herpes zoster, although no single chemotherapeutic regimen or agent has been consistently implicated.[43] It has been reported that local X-ray irradiation followed by chemotherapy was associated with greatest risk of developing herpes zoster.[44]

Herpes zoster may be precipitated by a variety of stimuli, after contact with a case of varicella, in immunosuppressive states, Hodgkin's disease and other malignancies, irradiation of the spinal column, tumour involvement of the cord, dorsal root ganglion or adjacent structures, surgical manipulation of spine, heavy metal poisoning or therapy.[1]

In an analysis of 45 cases of herpes zoster that developed after irradiation in 39 cases of malignant disease and 6 of non-malignant disease, it was found that the maximum incidence of zoster is at the somatic level of the neoplasm and thus at the site of irradiation. It was also found that herpes zoster occurred on the side of the body opposite to that irradiated and the maximum incidence was noted between three to six months following treatment.[45]

Clinical features

Prodromal symptoms:

Pre-eruptive prodromal symptoms like itching, tingling, burning sensation or pain in the involved dermatomes usually precedes the eruption by 2-4 days but may continue for several days.[16]

Prodromal symptoms vary from superficial itching, tingling or burning to severe deep or lancinating pain. It may be constant or intermittent and it is often accompanied by tenderness and hyperaesthesia of the skin over the involved dermatome.[21]

The pre-eruptive pain of herpes zoster may simulate pleurisy, myocardial infarction, duodenal ulcer, cholecystitis, biliary or renal colic, appendicitis, prolapsed intervertebral disk or early granuloma.[1]

A recent study of 107 cases of herpes zoster found that pain was the presenting complaint in 97(90.65%) cases. The most common prodromal symptom seen was paresthesia in 25(23.30%) cases, followed by itching in 21(19.62%) cases.[5]

The time between the start of pain and the onset of eruption averages 1.4 days in trigeminal zoster and 3.2 days in thoracic zoster.[18]

Rash of herpes zoster:

Herpes zoster lesions begin as erythematous macules and papules that often first appear where superficial branches of the affected sensory nerve are given off, for example, the posterior primary division of spinal nerves. Vesicles form within 12-24 hours and evolve into pustules by the third day. They then dry and form crusts in 7-10 days. The crusts generally persist for 2-3 weeks. In normal individuals, new lesions continue to appear for 1-4 days and occasionally as long as 7 days. The rash is most severe and lasts longer in older people and is least severe and of shortest duration in children.[1]

The ophthalmic division of trigeminal nerve and the trunk from T_3-L_2 are most frequently affected.[1] It is noted that thoracic (53%), cervical (20%), trigeminal including ophthalmic (15%) and lumbosacral (1%) dermatomes are most commonly involved at all ages, but the relative frequency of ophthalmic zoster increases in old age.[18]

A recent study reported that thoracic segments were most commonly involved in 59.8% cases followed by cervical segments in 15.8% cases. Unidermatomal involvement was seen in 75.7% cases, multidermatomal in 16.8% and disseminated in 7.4% cases.[5]

Another study noted that thoracic segments are most commonly affected (52.5%) followed by cervical (20%), Lumbosacral (15.8%) and cranial (8.8 %).[4]

In uncomplicated cases, recovery is complete in 2-3 weeks in children and young adults, and 3-4 weeks in older patients.[18]

Figure 7: Herpes zoster affecting the left C3 and C4 dermatomes

Figure 8: Herpes zoster affecting the left T5 dermatome

Figure 9: Herpes zoster affecting left L1 and L2 dermatomes

Figure 10: Herpes zoster affecting left S1 and S2 dermatomes

Variations in presentation

Disseminated herpes zoster (herpes zoster generalizatus):

It is a generalized varicelliform eruption accompanying the segmental eruption.[46] It has been defined as more than 20 lesions scattered outside the initial dermatome or systemic infections (hepatitis, pneumonitis, encephalitis).[16]

It is seen in 2-10% of patients with localized herpes zoster. The lesions usually appear within a week of onset of the segmental eruption. Such disseminated lesions commonly occur in immunocompromised patients, especially those with internal malignancies such as lymphoma, patients with acquired immunodeficiency such as HIV infection, or those receiving immunosuppressive therapy. Disseminated herpes zoster may also occasionally be seen in immunocompetent people, especially elderly patients where a selective decline of CMI to VZV occurs.[16]

There is a 5-10% risk of meningoencephalitis and other visceral involvement, which may be fatal.[47]

The dermatomal lesions are sometimes hemorrhagic or gangrenous. The outlying vesicles or bullae which are usually not grouped resemble varicella and are often umbilicated and may be hemorrhagic. Fever, prostration, headache and signs of meningeal irritation or viral meningitis may be present.[46]

Herpes zoster with aberrant vesicles is seen in some patients who, in addition to the localized eruption, develop a few scattered vesicles elsewhere on the body. Such lesions

do not constitute generalized herpes zoster. Aberrant lesions may occur during the early phase of zoster by hematogenous spread of the virus prior to the neutralizing antibodies.[16]

Herpes zoster at two different sites at the same time, involving more than two segments at each site occurs in the immunocompromised.[48]

Zoster sine herpete:

This refers to herpes zoster without skin eruptions. Hematogenous dissemination of the virus from the affected ganglion, which occurs during reactivation, stimulates the immune response. Sometimes this response is rapid enough to neutralize the virus which is released into the skin during reactivation and thus prevents development of cutaneous lesions. This results in only an episode of acute segmental neuralgic pain without vesiculation. Involvement of the geniculate ganglion in this manner can lead to facial palsy without cutaneous herpes zoster.[16]

Ramsay Hunt syndrome:

Now known as herpes zoster cephalicus or oticus, this is due to herpes zoster affecting the geniculate ganglion.[16]

It is characterized by facial palsy in combination with herpes zoster of the external ear or tympanic membrane, with or without tinnitus, vertigo, and deafness, and results from involvement of the facial and auditory nerves.[1]

Although the syndrome of facial palsy associated with herpes zoster oticus was first described by Kerner in 1904, the name of Ramsay Hunt became linked with it following his paper of 1907.[49] It accounts for 2-7% of all facial palsies.[16]

Herpes zoster ophthalmicus:

It occurs due involvement of the ophthalmic branch of the trigeminal nerve.[16]

The eye is affected in two-thirds of cases, and when vesicles on the side of the nose occur, it indicates involvement of the nasociliary nerve. This is known as Hutchinson's sign.[18]

Complications of herpes zoster ophthalmicus include superficial and deep keratitis, neuroparalytic keratitis with corneal ulcerations, panophthalmitis, iritis leading to iris atrophy, ocular palsies, neuralgia and rarely choroidal detachment, retinal vasculitis and optic neuritis. Recurrent attacks of episcleritis and scleritis as well as conjunctivitis may occur for years after the primary disease.[16]

Zoster of other divisions of the trigeminal nerve:

Herpes zoster of the maxillary division of the trigeminal nerve produces vesicles on the uvula and tonsillar area, whereas involvement of the mandibular division results in vesicles that appear on the anterior part of the tongue, floor of the mouth and buccal mucous membrane.[18] Maxillary herpes zoster can present with corneal involvement.[50]

Glossopharyngeal zoster:

This produces pain in the ear and pharynx with vesiculo-ulcerative lesions of the soft palate and vesicles on the ear, uvula, pharynx, tonsil and posterolateral part of tongue.[22]

Vagal zoster:

This may cause paresis of the larynx and pharynx, as well as cardiac and epigastric distress. Pharyngeal paresis leads to dysphagia. Typical vesicles are seen on the base of the tongue, epiglottis, arytenoid cartilage and aryepiglottic folds.[22]

Phrenic nerve zoster:

This may paralyze the ipsilateral diaphragm.[22]

Sacral zoster:

This can lead to retention of the urine as a preceding manifestation, as reported in a case of herpes zoster of the 3rd posterior sacral root.[51] Colonic pseudo-obstruction can also occur due to herpes zoster involving the sacral nerves.[52]

Figure 11: Ophthalmic herpes zoster affecting the right side

Figure 12: Maxillary herpes zoster on the left side with scarring

Complications of herpes zoster [1]

Table 1: Complications of herpes zoster

Cutaneous	Visceral	Neurologic
Bacterial superinfection	Pneumonitis	Postherpetic neuralgia
Scarring	Hepatitis	Meningoencephalitis
Zoster gangrenosum	Esophagitis	Transverse myelitis
Cutaneous dissemination	Gastritis	Cranial nerve palsies
	Pericarditis	Sensory loss
	Cystitis	Deafness
	Arthritis	Ocular complications
		Granulomatous angiitis
		Peripheral nerve palsies -Motor -Autonomic

Various granulomatous lesions can arise within sites of recent involvement of herpes zoster. These include granuloma annulare, sarcoidal granuloma, tuberculoid granuloma, pseudolymphoma, lymphoplasmacytoid lymphoma, Kaposi's sarcoma and granulomatous vasculitis.[53]

This is termed as 'Isotopic response', which is defined as the occurrence of a new skin disorder at the site of another, unrelated, and already healed skin disease.[54]

Post herpetic neuralgia (PHN)

It is defined as the persistence or recurrence of pain more than a month after the onset of herpes zoster, but better considered after 3 months. It occurs in about 30% of patients over 40 years of age and most frequently when the trigeminal nerve is involved.[18]

PHN has also been variably defined as any pain after rash healing or any pain 1 month, 3 months, 4 months or 6 months after rash onset, with most recent definitions focusing on 90 to 120 days after rash onset.[55, 56]

In clinical and community studies, the overall incidence of PHN is 8 percent to 15 percent, depending on the definition.[57, 58, 59] Age is the most significant risk factor for PHN. Clinically significant pain lasting 3 months or more is rare in immunocompetent persons younger than 50 years of age, but complicates 12 percent to 15 percent of cases of herpes zoster in persons 60 years of age and older.[60]

Increasing age, greater acute pain severity, presence of prodromal pain and greater rash severity have each been reported to be independent predictors of PHN.[56]

Patients with PHN may suffer from constant pain (described as burning, aching, throbbing), intermittent pain (stabbing, shooting), and/or stimulus-evoked pain, including allodynia (tender, burning, stabbing). Allodynia (pain elicited by stimuli that are normally not painful) is a particularly disabling component of the disease that is present in approximately 90 percent of patients with PHN. Patients with allodynia may suffer severe pain after even the lightest touch of the affected skin by things as trivial as a breeze or a piece of clothing.[1]

These sub-types of pain may produce disordered sleep, depression, anorexia, weight loss, chronic fatigue, and social isolation, and they often interfere with dressing, bathing, general activity, traveling, shopping, cooking, and housework.[1]

Pathogenesis:

The cause of PHN is not known, but there are various hypotheses put forward.

1. Reduction in the number of large myelinated axons and an increase in small unmyelinated fibers.[61]
2. Abnormal impulses arising in the dorsal root ganglion neurons as the direct result of viral infection.[61]
3. Post inflammatory fibrosis in the ganglia or sensory roots and perpetuation of pain by a central mechanism.[62]
4. An endogenous neuropeptide, substance P, distributed in the small peripheral sensory neurons which terminate in the skin and substantia gelatinosa plays an important role in the mediation of pain.[63]

Pregnancy and the infant

Herpes zoster during pregnancy is not as serious a problem as primary varicella during pregnancy because it does not result in serious morbidity or intrauterine varicella infection.[64]

Transplacental transmission of the virus does not occur with maternal herpes zoster as the preexisting maternal immunity protects the fetus by preventing viremia. However if maternal zoster develops just a few days before delivery, the infant may acquire varicella.[65]

Passively acquired varicella virus specific IgG antibodies may not have time to accumulate within the infant, thereby decreasing the protective effect of maternal immunity.[66]

When the infant's level of maternal antibody wanes, the relative immunosuppression may lead to early viral reactivation and herpes zoster in the infant.[67]

Infants who are exposed to varicella in utero may develop herpes zoster early in life without having had previous varicella.[68]

Laboratory diagnosis of herpes zoster

Tzanck Smear:

Cytology was first used in cutaneous disorders by Tzanck in 1947, for the diagnosis of vesiculobullous disorders, particularly herpes simplex.[69]

Tzanck smear is a very simple and rapid technique. The material is scraped from the base of an early vesicle and stained with Giemsa, Hematoxylin-Eosin, Wright, Methylene Blue, Papanicolaou or Toluidine Blue. Quick staining can be done by Hemacolor or Diff-Quik within one minute. The typical features include characteristic multinucleated syncytial giant cells and secondary acantholytic cells.[70]

Skin biopsy:

The earliest changes include nuclear swelling of keratinocytes. With haematoxylin and eosin stain, these nuclei appear slate grey and homogenous with margination of the nuclear chromatin. A few necrotic keratinocytes are seen. The changes usually begin along the basal keratinocytes and then involve the entire epidermis. Later it produces profound degeneration of keratinocytes, resulting in acantholysis.[35]

Degeneration of epidermal keratinocytes occurs in two forms - ballooning degeneration and reticular degeneration. Ballooning degeneration consists of swelling of epidermal keratinocytes. Balloon cells have a homogenous, eosinophilic cytoplasm, and they may be multinucleated (Tzanck cells). Balloon cells lose their intercellular bridges and become separated from one another (Secondary acantholysis) and unilocular vesicles result. Vesicles are found intraepidermally or subepidermally.[35]

Reticular degeneration is the result of rupture of the ballooning cells due to progressive hydropic swelling. It occurs in the upper portions and at the peripheries of viral vesicles. It results in multilocular vesicles, but later the walls disappear to become unilocular.[35]

Electron microscopic examination:

It reveals viral particles in the axons of dermal nerves in herpes zoster but does not differentiate varicella zoster virus from herpes simplex virus.[35]

Culture:

Varicella zoster virus grows only in human fetal diploid kidney cells or human foreskin fibroblasts.[35] It is extremely labile, so it should be inoculated immediately onto cell culture. The cytopathic effect is characterized by the formation of acidophilic intranuclear inclusion bodies and multinucleated giant cells.[1]

The cytopathic effects are slow to develop and remain focal because varicella zoster virus extends from cell to cell only by direct contact and is not released into the medium.[16]

There is a modification of the cell culture assay in which vesicle fluid or lesion scraping is centrifuged onto cells growing on cover slips at the bottom of thin glass walled ‘shell’ vials. The cells are then stained with fluorescein or enzyme-labeled monoclonal antibodies to VZV proteins. This assay can confirm the presence of varicella zoster virus within 24-72 hours, well before the cytopathic effects are evident in conventional cell cultures.[1]

Other tests:

- Immunofluorescent or Immunoperoxidase staining[1]
- Nucleic acid hybridization, PCR[1]
- ELISA[1]
- FAMA (Fluorescent Antibody to Membrane Antigen)[1]
- Latex agglutination test [71]

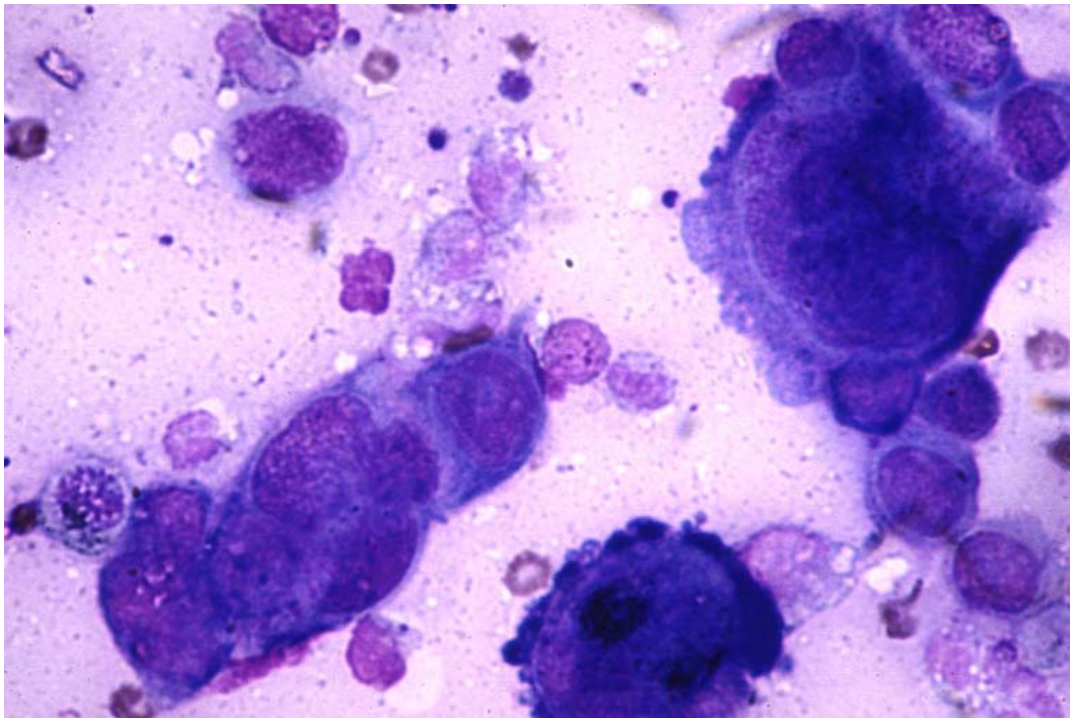


Figure 13: Tzanck smear preparation showing multinucleate giant cells

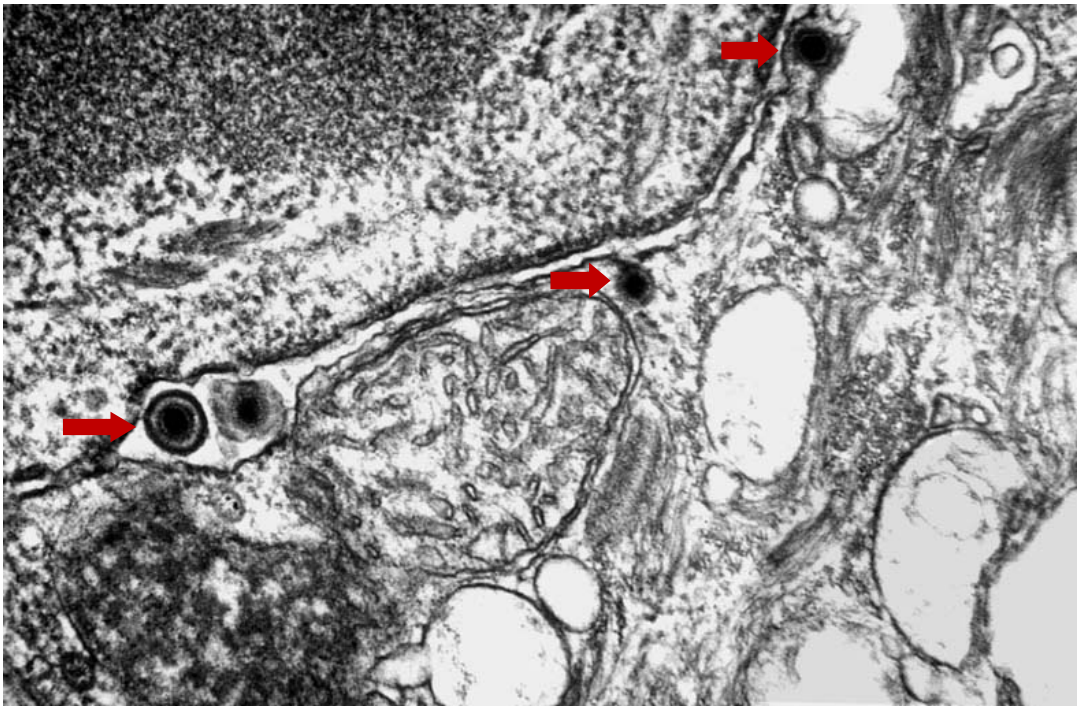


Figure 14: Electron microscopy showing viral particles in nerve endings

Herpes zoster and HIV

Epidemiology:

Incidence of herpes zoster increases with age.[18] Recently herpes zoster infections have been observed in young adults infected with HIV.[72] In patients infected with HIV, herpes zoster is 10 times more common than in the normal population and may become disseminated and chronic.[18]

Pathogenesis:

Cell mediated immunity plays a critical role in inactivating varicella zoster and maintaining its latent state. It appears that T-lymphocytes are necessary for viral inactivation and that a relative loss of CD4+ cells and an excess of CD8+ cells accompanies acute herpes zoster out breaks.[73]

HIV infection causes a gradual loss of CD4+ cell number and function. However, a study did not find any increase in risk of herpes zoster with increasing duration of HIV infection, as expected with a fall in CD4+ cell number. They believed that CD8+ cells might also play an important role in reactivation of VZV virus, especially in the early stages of HIV infection, a time when CD4+ cell function is still relatively intact.[74]

Studies on herpes zoster and HIV infection:

A study on 115 men of 21-55 years of age suffering from herpes zoster found that 11 (9.5%) were HIV positive. More than one dermatome was involved in 7 (63.6%) HIV positive and in 2 (1.9%) HIV negative cases. Two HIV positive cases had multiple cranial nerve involvement and one had generalized herpes zoster. Out of 11 HIV positive

cases, 9 (81.8%) gave history of multiple unprotected sexual exposure with female commercial sex workers and 2 (18.1%) with amateurs. None of them had used a condom during sexual intercourse. None gave history of blood transfusion in the past or intravenous drug use.[2]

In a comparative study of herpes zoster of 196 HIV positive individuals and 34 HIV negative individuals between ages of 16 and 50 years, the duration of illness in the HIV positive group was longer (32 vs. 22 days). The HIV positive group was more likely to have generalized lymphadenopathy (74% vs. 3%), severe pain (69% vs. 39%), bacterial super infection (15% vs. 6%) and more than one affected dermatome (38% vs. 18%). Cranial nerve lesions occurred exclusively in the HIV positive group. The mean CD4 count at presentation was 333/mm^3 in the HIV positive group and 777/mm^3 in the HIV negative group. Herpes zoster is often recognized as an initial HIV related illness.[75]

A study in rural Uganda concluded that the mean rate of herpes zoster was 53.6/1000 person years in HIV positive and 4.4 in HIV negative participants. The cumulative incidence of a first episode of herpes zoster was 7.6% at 2 years, 12.6% at 4 years and 24.0% at 6 years after seroconversion. The incidence rate was 35.6/1000 person years. They stressed the fact that herpes zoster was an indicator of HIV-1 infection.[76]

A study on 1,198 HIV seropositive individuals for herpes zoster diagnosed herpes zoster in 48 individuals (4%). They concluded that herpes zoster occurs more frequently in individuals acquiring HIV infection through sexual transmission rather than injection drug users. They observed that patients with febrile episodes of herpes zoster progress faster to AIDS.[77]

In a study of 966 homosexuals for herpes zoster, the incidence of first episode was 3.31 per 1000 person years in HIV seronegative and 51.51 per 1000 person year in HIV seropositive individuals. Recurrences only occurred in HIV positive patients (25.6%). The incidence of herpes zoster was 31.2 per 1000 person year at CD 4+ cells ≥ 500/ mm^3, 47.2 per 1000 person year at CD4+ cells 200-499/mm^3 and 97.5 per 1000 person year at CD4+ cell < 200/mm^3. The study concluded that incidence of herpes zoster increases with the decrease of CD4+ cell counts and T-cell reactivity.[78]

A study on 112 homosexual men with herpes zoster for development of AIDS showed that the cumulative incidence of AIDS was 22.8% within 2 years of herpes zoster, 45.5% within 4 years and 72.8% after 6 years. They concluded that herpes zoster could be used as a predictor of AIDS.[72]

HIV seropositivity in herpes zoster:

The HIV seropositivity rates widely vary from 9.5% to 92% in various studies that have been conducted in the last 20 years.

Table 2: HIV seropositivity rates of herpes zoster in different studies

Author	Year	Place	Number of herpes zoster cases	% HIV positive
Van de Perre et al [79]	1989	Kigali	131	92
Colebunders R et al [80]	1988	Zaire	146	91
Dehne KL et al [81]	1992	Karol	182	89
Vasconcellos MR et al [82]	1990	Sao Paulo	66	10.6
Varsha D et al [83]	1998	Mumbai	74	47.3
Desylva et al [84]	1998	Mumbai	120	22.5
Kar PK et al [2]	2003	Bangalore	115	9.5

Laxmisha C et al [85]	2004	Pondicherry	40	35
Onunu AN et al [86]	2004	Nigeria	52	69.2
Dubey AK et al [5]	2005	Pondicherry	46	13.04

Clinical features:

A study conducted on 527 HIV seropositive males for herpes zoster found an overall incidence of 11.8%. Herpes zoster was the presenting symptom in 50% of cases. Majority of the cases were in an age group of 20 to 40 years (89%). Thoracic dermatome (68%) was the commonest to be involved, followed by cervical (14.5%), trigeminal (9.7%) and lumbosacral (8%). Among other associations of HIV positive herpes zoster cases, 24.2% had tuberculosis and 4.8% had hepatitis B virus infection. The skin lesions of herpes zoster in majority of cases were bullous, hemorrhagic and necrotic.[87]

Herpes zoster occurring in HIV disease is most often unidermatomal, but it may be multidermatomal, recurrent within the same dermatome or disseminated. The eruption may be bullous, hemorrhagic, necrotic, hyperkeratotic, ulcerated and be accompanied by severe pain. The majority of HIV infected patients with herpes zoster experience an uneventful recovery. However, atypical clinical courses of herpes zoster are common. Lesions may persist for months, either in localized or disseminated form.[88]

Concerning skin involvement, the distribution pattern (two and more dermatomes involved, herpes zoster duplex or generalisatus), a tendency to relapse or even to persist and the severity of cutaneous lesions (hemorrhagic, ulcerating, necrotizing, hyperkeratotic, scarring) are of special interest. A higher frequency of disseminated

herpes zoster lesions in immunocompromised patients was already reported in the pre-AIDS era.[89]

Virus shedding persists 2 days longer (7.0 vs. 5.3 days) in the immunocompromised host compared to immunocompetent patients.[90] Painful ulcerating and/or hyperkeratotic lesions with persistence of viral replication for months have been rarely described. Such lesions are clinically very unusual and restricted to sites of the initial herpes zoster eruptions. Necrotic and ecthymatous zoster have also been described.[91-94]

Chronic verrucous VZV lesions are very rare in HIV negative patients. Disseminated verrucous rashes have been recently described in a renal transplant recipient.[95]

In a study of 45 patients of herpes zoster with 1614 person-years of follow up, an incidence of 3.2 episodes per 100 person-years was noted. Complications of herpes zoster occurred in 12 patients (27%). Ocular complications were seen in 5 patients, neurological complications in four patients, and chronic atypical skin lesions in 5 patients. Six patients each had post herpetic neuralgia and bacterial super-infection, which were the common minor complications of zoster.[96]

Herpes zoster and HAART:

Herpes zoster occurring during HAART in AIDS patients is an immunopathological consequence of the improvement of the host immune response, correlating with the beginning of immune restoration.[97]

Risks for developing herpes zoster includes no protective varicella specific antibody despite previous varicella infection, severe immunodeficiency at baseline, and vigorous immunologic and virological responses to HAART.[98]

Management of herpes zoster

Antiviral agents:

The nucleoside analogues acyclovir, famciclovir, valacyclovir, brivudin and the pyrophosphate analog foscarnet show efficacy in treating VZV infections. Acyclovir is a guanosine analog that is selectively phosphorylated by VZV thymidine kinases and thus is concentrated in infected cells. Cellular enzymes then convert acyclovir monophosphate to acyclovir triphosphate, which interferes with viral DNA synthesis by inhibiting viral DNA polymerase.[1]

Two prodrugs, valacyclovir (L-valyl ester and prodrug of acyclovir) and famciclovir (diacetyl ester prodrug of 6-deoxy penciclovir), are better and more reliably absorbed than acyclovir after oral administration. Thus, they produce much higher blood levels of antiviral activity and permit less frequent dosing than acyclovir.[1]

Because of their superior pharmacokinetics, famciclovir, or valacyclovir are preferred to acyclovir for oral therapy of VZV infections. Acyclovir-resistant herpes zoster has been documented in patients with advanced AIDS. Because of the mechanism of acyclovir resistance in VZV (mutations in the viral thymidine kinase gene), these infections are cross-resistant to ganciclovir, valacyclovir, famciclovir, and penciclovir. They usually respond to foscarnet, 40 mg intravenously every 8 hours; however, the infections commonly recur after treatment has ended.[1]

Topical treatment of herpes zoster:

During the acute phase of herpes zoster, the application of cool compresses, calamine lotion, cornstarch, or baking soda may help to alleviate local symptoms and hasten the drying of vesicular lesions. Occlusive ointments should be avoided, and creams or lotions containing glucocorticoids should not be used. Topical treatment of the herpes zoster rash with antiviral agents is not effective.[1]

Antiviral therapy:

The major goals of therapy in patients with herpes zoster are to:

(1) Limit the extent, duration, and severity of pain and rash in the primary dermatome

(2) Prevent disease elsewhere

(3) Prevent PHN

Randomized controlled trials indicate that oral acyclovir (800mg five times a day for 7 days), famciclovir (500mg three times a day for 7 days), and valacyclovir (1g three times a day for 7 days) reduce time to rash healing, and the duration and severity of acute pain in older adults with herpes zoster who are treated within 72 hours of rash onset.[1]

Because of the lower risk of PHN, antiviral therapy is less valuable or not necessary for treatment of uncomplicated herpes zoster in healthy people younger than 50 years of age. The use of antiviral agents is unproven if treatment is initiated more than 72 hours after rash onset. Nevertheless, it is prudent to initiate antiviral therapy even if more than 72 hours have elapsed after rash onset in patients who have ophthalmic zoster or who continue to have new vesicle formation.[99]

Treatment of herpes zoster in immunocompromised patients:

A randomized, double-blind, placebo-controlled trial in immunocompromised patients with herpes zoster showed that intravenous acyclovir (500 mg/m^2 every 8 hours for 7 days) halted progression of the disease, both in patients with localized herpes zoster and in patients with cutaneous dissemination before treatment.[100]

Acyclovir accelerated the rate of clearance of virus from vesicles and markedly reduced the incidence of visceral and progressive cutaneous dissemination. Pain subsided faster in acyclovir recipients, and fewer reported PHN, but these differences were not statistically significant. In patients with mild immunosupression and localized herpes zoster, oral acyclovir, valacyclovir, or famciclovir usually suffices. A randomized, controlled trial of oral famciclovir versus oral acyclovir in patients with localized herpes zoster after bone marrow or organ transplantation or cancer chemotherapy showed that the two treatments were equivalent in rash healing and loss of acute pain and that both were well tolerated.[101]

Treatment of post herpetic neuralgia:

Once established, PHN is difficult to treat. Fortunately, it resolves spontaneously in most patients, although this often requires several months. Clinicians have advocated a wide range of treatments, including many oral and topical medications, epidural injection of local anesthetic and glucocorticoids, acupuncture, biofeedback, subcutaneous injections of triamcinolone, trans-epidermal electric nerve stimulation, spinal cord stimulators, and systemic administration of a variety of compounds, but most have not been validated by controlled trials.[1]

Topical therapy for PHN:[1]

- Topical anesthesia delivered by means of a 5 percent lidocaine patch
- EMLA (eutectic mixture of local anesthetics) cream
- Capsaicin cream (0.025%, 0.075%), an extract of hot chili peppers
- Intralesional or subcutaneous injection of triamcinolone 0.2 mg/mL into the affected dermatome
- Repeated cryosurgery to limited areas affected by PHN has been reported to reduce the sensitivity of trigger areas and produce long-term relief from pain
- Transcutaneous electrical stimulation has brought pain relief to a high percentage of patients

Oral therapy for PHN:[1]

- Gabapentin: 300mg/day, gradually increased over 4 weeks
- Pregabalin
- Tricyclic antidepressants: Amitryptiline (75 to 100 mg daily), Nortryptiline and Desipramine
- Opioid analgesics, especially oxycodone
- Antiepileptics: Carbamazepine (600 to 800 mg/day) or phenytoin sodium (300 to 400 mg/day)

Prevention of herpes zoster: Zoster vaccine

One approach to the prevention of herpes zoster is the stimulation of immunity to VZV, which wanes in the elderly and in other high-risk individuals.[102]

Studies of healthy adults older than 55 years of age with a history of varicella have demonstrated an increase in VZV-specific T lymphocytes and humoral immunity after vaccination with live attenuated VZV vaccine that is similar to the increase observed after an episode of herpes zoster. These findings suggest that vaccination of older persons may be useful in preventing herpes zoster and its complications.[102]

A recent study tested the hypothesis that vaccination against VZV would decrease the incidence and/or severity of herpes zoster and PHN among older adults. The study enrolled 38,546 adults 60 years of age or older in a randomized, double-blind, placebo-controlled trial of a live attenuated (Oka/Merck) VZV vaccine of much greater potency than the currently licensed varicella vaccine. A total of 957 confirmed cases of herpes zoster (315 among vaccine recipients and 642 among placebo recipients) and 107 cases of PHN (27 among vaccine recipients and 80 among placebo recipients) were included in the efficacy analysis. The zoster vaccine reduced the burden of illness due to herpes zoster by 61.1 percent ($p < 0.001$), reduced the incidence of PHN by 66.5 percent ($p < 0.001$), and reduced the incidence of herpes zoster by 51.3 percent ($p < 0.001$). Reactions at the injection site were more frequent among vaccine recipients but were generally mild.[60]

This landmark study showed that the zoster vaccine markedly reduced morbidity from herpes zoster and PHN among older adults. The FDA licensed the zoster vaccine 'Zostavax' for the prevention of herpes zoster in adults 60 years of age and older in 2006.

It is to be given subcutaneously as a single dose of 19,000 plaque forming units (PFU) only if the following criteria are fulfilled in the recipient.[60]

- Has not had a life-threatening allergic reaction to gelatin, the antibiotic neomycin, or other component of the herpes zoster vaccine.
- Does not have a weakened immune system due to HIV/AIDS or another disease or medications (such as steroids, radiation and chemotherapy) that affect the immune system.
- Does not have a history of cancer affecting the bone marrow or lymphatic system, such as leukemia or lymphoma.
- Does not have active, untreated tuberculosis.

It is however not yet available in India. With the development of the varicella zoster vaccines, antiviral therapy, and neuropathic pain treatments, clinicians now have multiple effective tools to markedly reduce human suffering from herpes zoster.[1]

Figure 15: Hemorrhagic herpes zoster affecting the left L2 and L3 dermatomes (HIV+)

Figure 16: Disseminated herpes zoster lesions in the same patient

Figure 17: Bullous herpes zoster with disseminated lesions

Figure 18: A case of Ramsay Hunt syndrome (HIV+)

Methodology

The present study is a one-year time bound observational study from December 2006 to November 2007. The source of data for the study includes all cases of herpes zoster attending the dermatology OPD and referred cases from other departments, at KLES Dr.Prabhakar Kore Hospital and MRC, Belgaum.

Inclusion criteria: All new clinically diagnosed cases of herpes zoster were included in the study. Only the patients who were willing to enroll themselves in the study were included.

Exclusion criteria: Old cases of herpes zoster and those in whom a history of herpes zoster is unreliable were excluded. Patients in whom HIV status is already known were excluded from the study. Patients unwilling to undergo tests and enroll themselves in the study were excluded.

A sample size of **50** was selected and this was calculated by taking 80% of the average yearly number of cases of herpes zoster over the last five years attending the dermatology OPD at KLES Dr.Prabhakar Kore Hospital and MRC, Belgaum.

The patient's demographic data, symptoms, location of lesions, risk factors, associated systemic disease and complications was noted in a pre-tested and pre-designed proforma after taking informed and written consent. Diagnosis was made by history and clinical examination.

Routine haematological and urine investigations such as Hb%, TC, DC, ESR, RBS, Urine routine and microscopy were done in all patients. Tzanck smears were done and a blood sample was taken for HIV serology in all patients after informed consent and counseling.

Analysis was done by recording the data in the form of tables and noting the proportion of HIV positive individuals in each category. As this was a descriptive study, no tests of statistical significance were required.

Results

The present study is a one-year cross-sectional descriptive study and included 72 cases of herpes zoster who attended the OPD in KLES Dr. Prabhakar Kore Hospital and MRC, Belgaum from December 2006 to November 2007.

Frequency of herpes zoster and HIV seropositivity rate

In our study, 72 patients were clinically diagnosed to have herpes zoster out of 13,308 patients who attended the OPD. Hence, the frequency of herpes zoster in our hospital works out to be 0.54 %. As 16 of them were seropositive for HIV, the seropositivity ratio is **22.22%**.

Month wise distribution

In the present study, the maximum number of cases presented in the month of March (15.28%), followed by September (12.50%), January and December (11.11% each). The least number of cases were in June (2.78%), followed by April and May (4.17% each).

Figure 19: Month wise distribution of cases

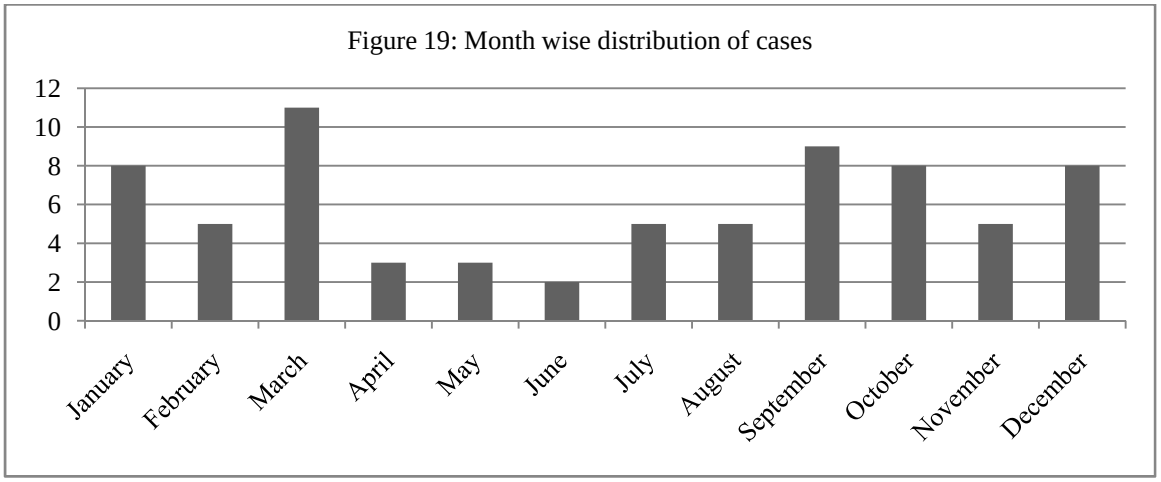


Table 3: Month wise distribution of cases

Month	Number of patients	% of total
December 2006	8	11.11
January 2007	8	11.11
February 2007	5	6.94
March 2007	11	15.28
April 2007	3	4.17
May 2007	3	4.17
June 2007	2	2.78
July 2007	5	6.94
August 2007	5	6.94
September 2007	9	12.50
October 2007	8	11.11
November 2007	5	6.94

Age distribution

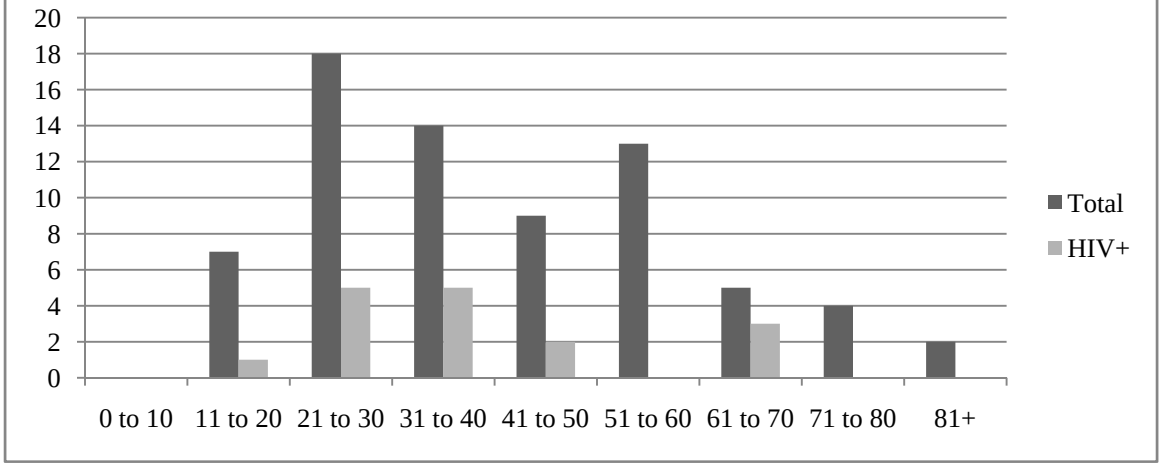
In the present study, the youngest patient was 12 years and the oldest was 83 years old. The maximum number of cases were seen in the 21-30 years age group (25%) followed by 31-40 years age group (19.44%) and 51-60 years age group (18.06%). Very few patients were afflicted with herpes zoster at the extremes of age in this study. The mean age of the study population was 41.17 years. The youngest HIV seropositive patient was 12 years and the oldest was 64 years old. Most of the HIV seropositive patients were from the 21-30 and 31-40 years age group, accounting for five cases each. The proportion

of HIV seropositivity in those age groups was 27.78% and 35.71% respectively. However, the maximum proportion of HIV seropositivity was noted in the 61-70 years age group, which accounted for 60% of the total cases in that age segment.

Table 4: Distribution of cases according to age group

Age group	Number of patients	% of total	HIV+	% in age group
0-10	0	0	0	0
11-20	7	9.72	1	14.29
21-30	18	25.00	5	27.78
31-40	14	19.44	5	35.71
41-50	9	12.50	2	22.22
51-60	13	18.06	0	0
61-70	5	6.94	3	60.00
71-80	4	5.56	0	0
81+	2	2.78	0	0

Figure 20: Distribution according to age group

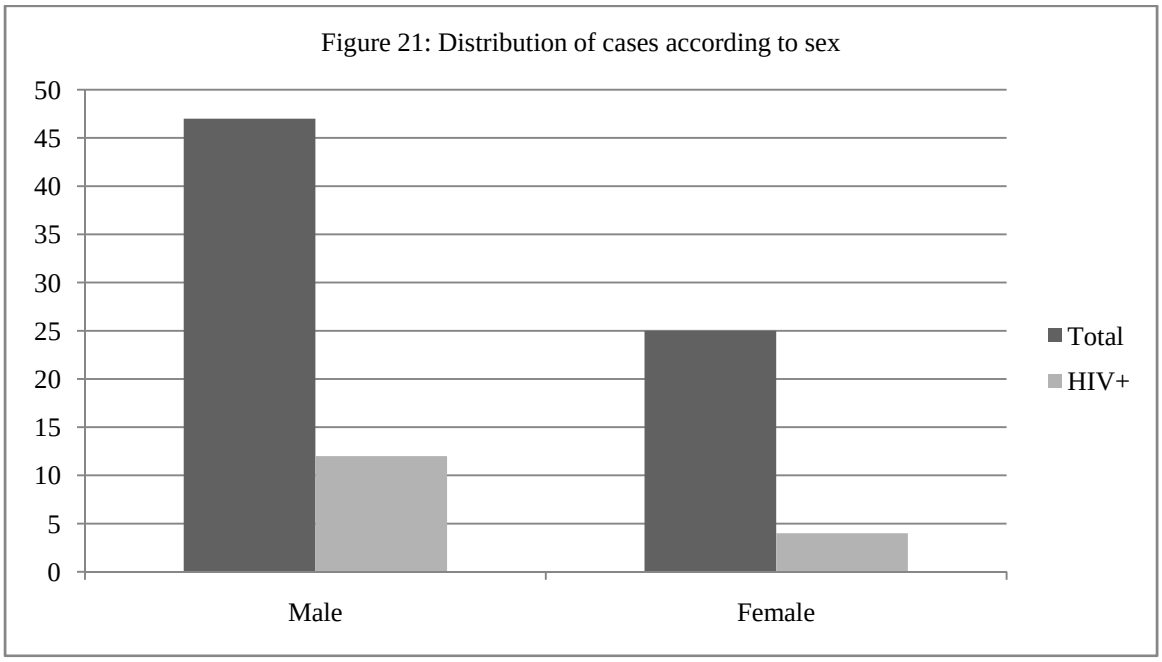


Sex distribution

In the present study, there were 47 males and 25 females affected with herpes zoster, giving a M:F ratio of 1.88:1. Four women out of 25 were HIV seropositive (16%) and 12 out of 47 men were HIV seropositive (25.53%).

Table 5: Distribution of cases according to sex

Sex	Number of patients	Number of HIV+	% in group
Male	47	12	25.53
Female	25	4	16



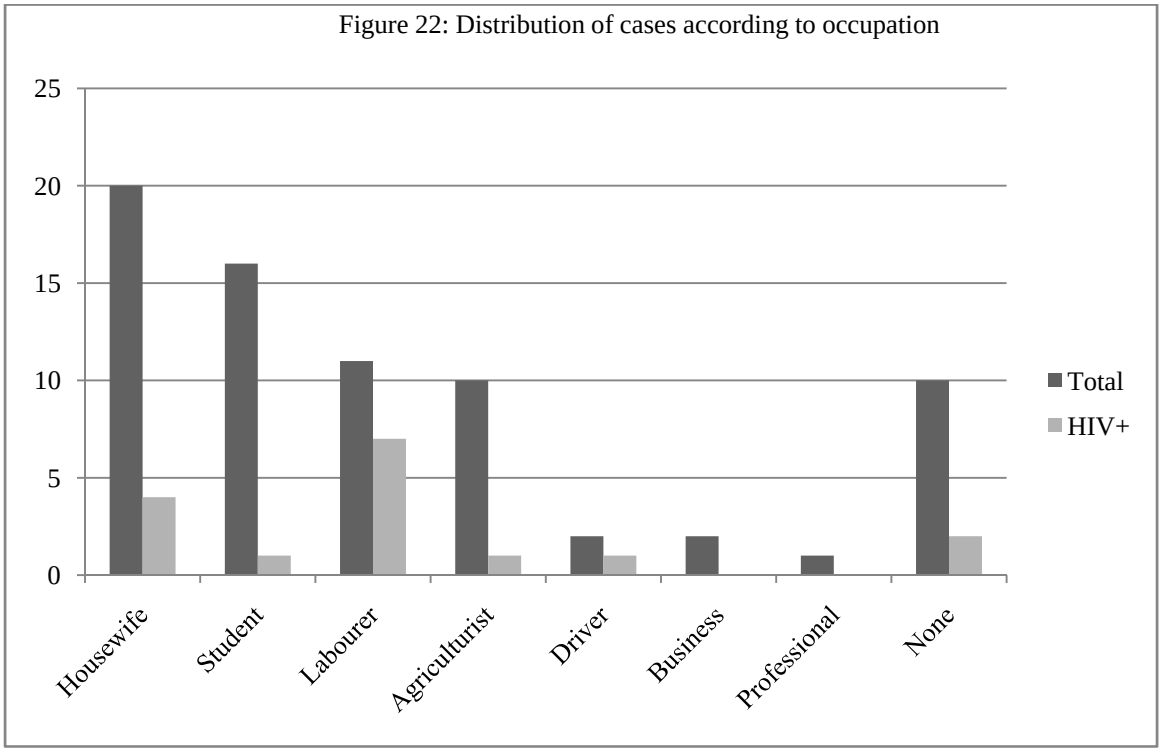
Distribution of patients based on occupation

In the present study, the maximum numbers of patients were housewives (27.78%) and students (22.22%). Labourers (15.28%) and Agriculturists (13.89%) constituted the next common categories. Maximum HIV seropositivity was noted in the labourer group, 7(63.64%) out of 11 were affected. The next common group to be affected was the housewife group, 4 of whom were affected.

Table 6: Distribution of cases according to occupation

Occupation	**Number of cases**	**% of total**	**HIV+**	**% in group**
Business	2	2.78	0	0
Driver	2	2.78	1	50
Professional	1	1.39	0	0
Agriculturist	10	13.89	1	10
Housewife	20	27.78	4	20
Labourer	11	15.28	7	63.64
Student	16	22.22	1	6.25
None	10	13.89	2	20

Figure 22: Distribution of cases according to occupation



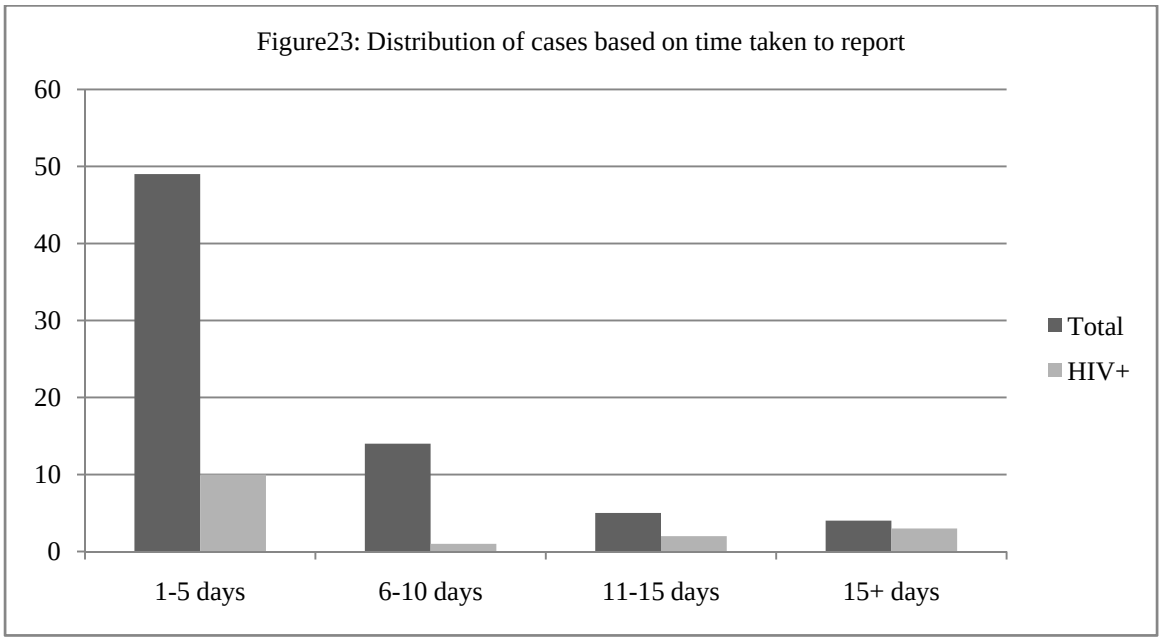
Time taken to report to the hospital

In the present study, the majority of the patients reported within 5 days of onset of their lesions, 49 (68.06%) out of 72 having done so. HIV seropositivity was noted in 20.41% of that group. Fewer patients reported after 10 days of onset of lesions, 5 were in the 11-15 days group and 4 in the 15+ days group. A high proportion of HIV seropositivity was noted in them, 40% for the 11-15 days group and 75% for the 15+ days group.

Table 7: Distribution of cases based on time taken to report

Reporting time	Number of patients	% of total	HIV+	% in the group
1-5 days	49	68.06	10	20.41
6-10 days	14	19.44	1	7.14
11-15 days	5	6.94	2	40
15+ days	4	5.56	3	75

Figure23: Distribution of cases based on time taken to report



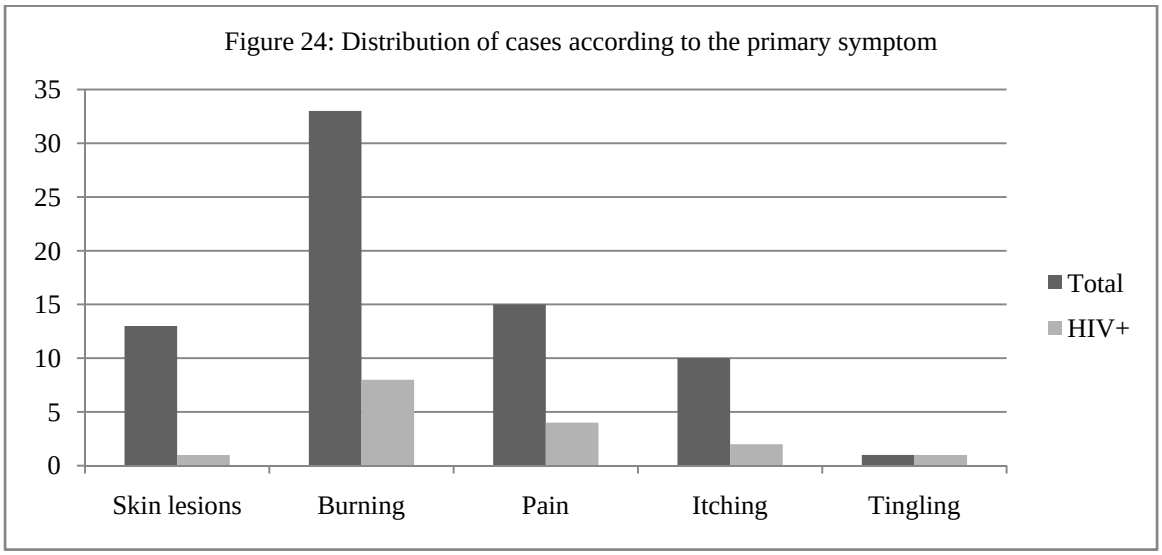
Primary symptom

In the present study, a burning sensation was the most common symptom that appeared first in the patient (45.83%). Among them, 24.24% patients were HIV seropositive. Pain was the first symptom in 15 patients, four of whom were HIV seropositive. Skin lesions appeared first in 13 patients, and only one of them was HIV seropositive. Tingling was the first symptom in one HIV seropositive patient.

Table 8: Distribution of cases according to the primary symptom

First symptom	Total number of patients	% of total	HIV+	% in group
Skin lesions	13	18.06	1	7.69
Burning sensation	33	45.83	8	24.24
Pain	15	20.83	4	26.67
Itching	10	13.89	2	20
Tingling	1	1.39	1	100

Figure 24: Distribution of cases according to the primary symptom



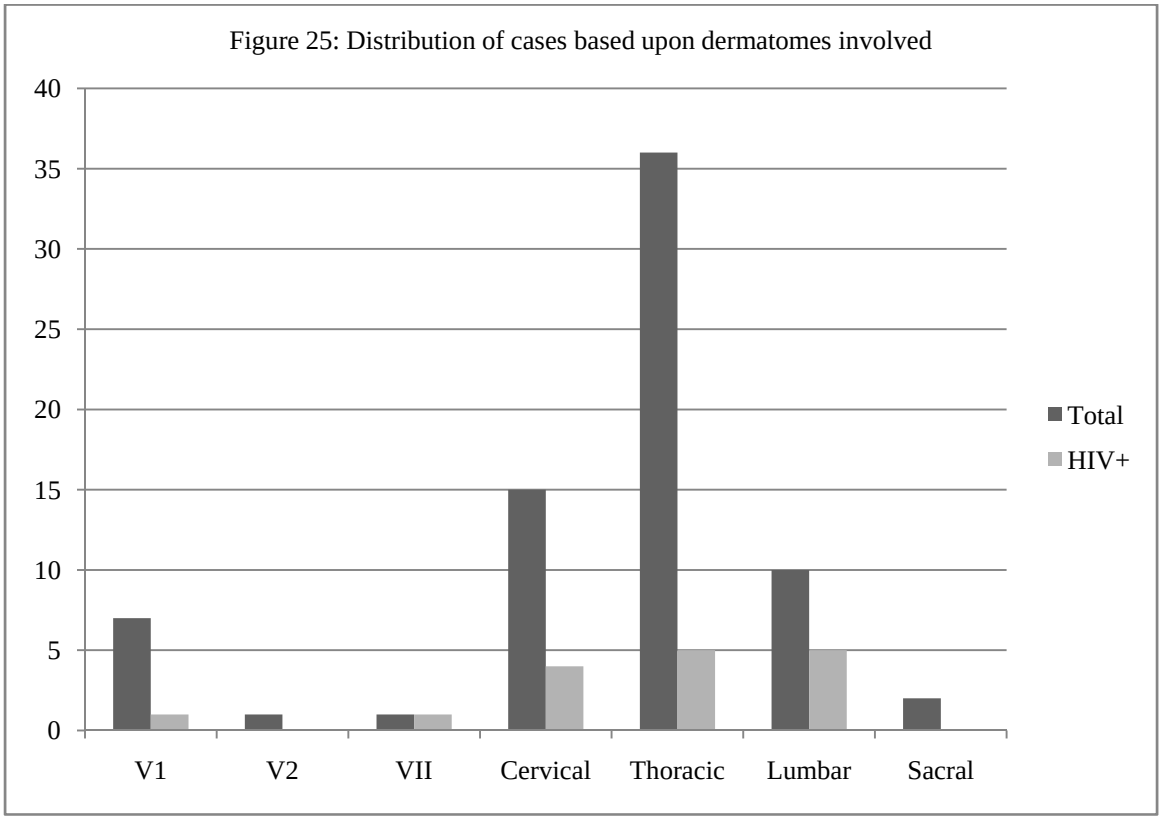
Type of dermatomes involved

In the present study, most of the patients had thoracic dermatome involvement (50%). Five out of those 36 patients were HIV seropositive (13.89%). The next dermatome groups commonly involved were the Cervical (20.83%) followed by the Lumbar (13.89%) group. HIV seropositivity was 26.67% in the cervical dermatome group and 50% in the lumbar dermatome group. Among the cranial nerve dermatomes affected, the ophthalmic branch of trigeminal nerve (V1) was the commonest to be involved. One out of the seven cases of ophthalmic herpes zoster was HIV seropositive. A single case of maxillary branch of trigeminal nerve zoster was present in this study. An HIV seropositive case of Ramsay Hunt syndrome was also present. Two cases of sacral dermatome involvement were present, none of whom were seropositive for HIV.

Table 9: Distribution of cases based upon dermatomes involved

Dermatome group	**Number of cases**	**% of total**	**HIV+**	**% in group**
Cranial nerves				
V 1	7	9.72	1	14.29
V 2	1	1.39	0	0
VII	1	1.39	1	100
Cervical	15	20.83	4	26.67
Thoracic	36	50	5	13.89
Lumbar	10	13.89	5	50
Sacral	2	2.78	0	0

Figure 25: Distribution of cases based upon dermatomes involved



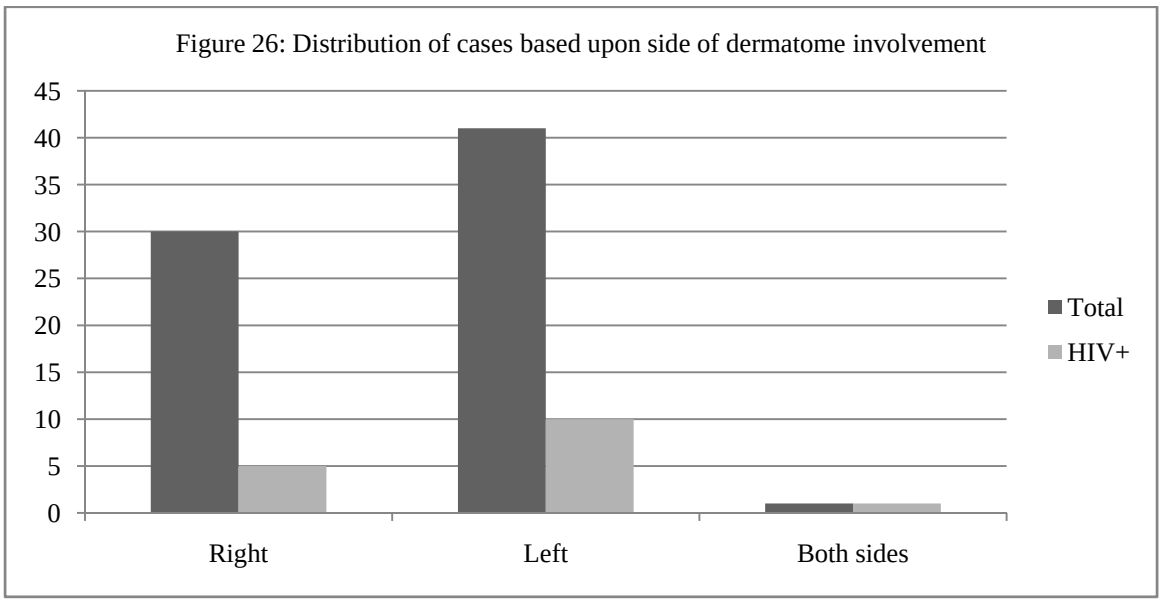
Side of dermatome involvement

In the present study, the left side of the body (56.94%) was more commonly involved than the right side (41.67%). Ten of the 41 left sided herpes zoster cases were HIV seropositive, and 5 of the 30 right sided herpes zoster cases were HIV seropositive. One case of herpes zoster had bilateral dermatomal distribution of lesions and was HIV seropositive.

Table 10: Distribution of cases based upon side of dermatome involvement

Side	Number of cases	% of total	HIV+	% in group
Right	30	41.67	5	16.67
Left	41	56.94	10	24.39
Both sides	1	1.39	1	100

Figure 26: Distribution of cases based upon side of dermatome involvement



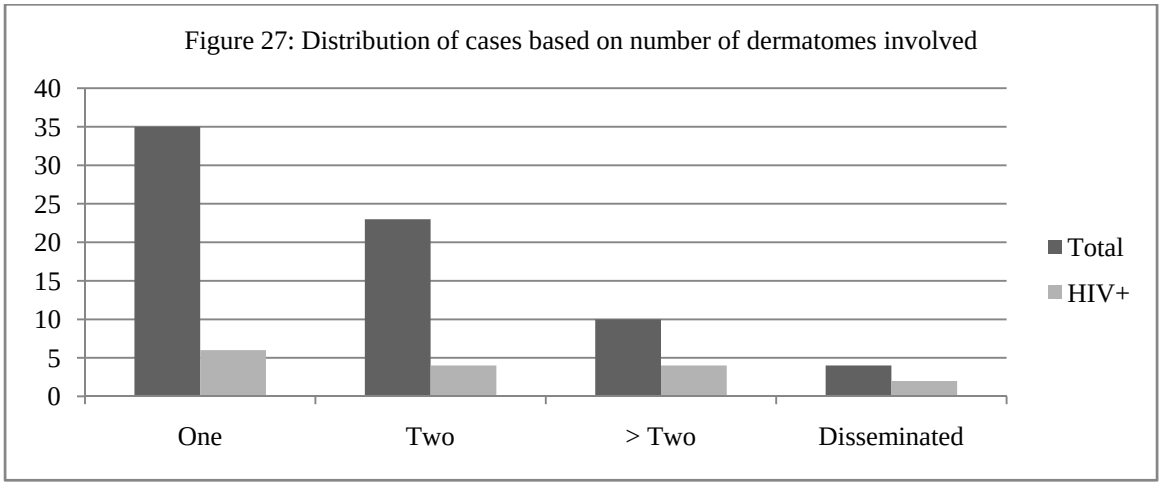
Number of dermatomes involved

In the present study, most of the patients had only one dermatome involved (48.61%). HIV seropositivity was noted in 17.14% of them. Two dermatomes were involved in 31.94% patients and HIV seropositivity was noted in 17.39% of those people. Four out of the ten people who had more than two dermatomes involved were seropositive for HIV. Disseminated herpes zoster was present in 4 patients, and HIV seropositivity was noted in 2 of them.

Table 11: Distribution of cases based on number of dermatomes involved

Number of dermatomes	Number of patients	% of total	HIV+	% in group
One	35	48.61	6	17.14
Two	23	31.94	4	17.39
> Two	10	13.89	4	40
Disseminated	4	5.56	2	50

Figure 27: Distribution of cases based on number of dermatomes involved



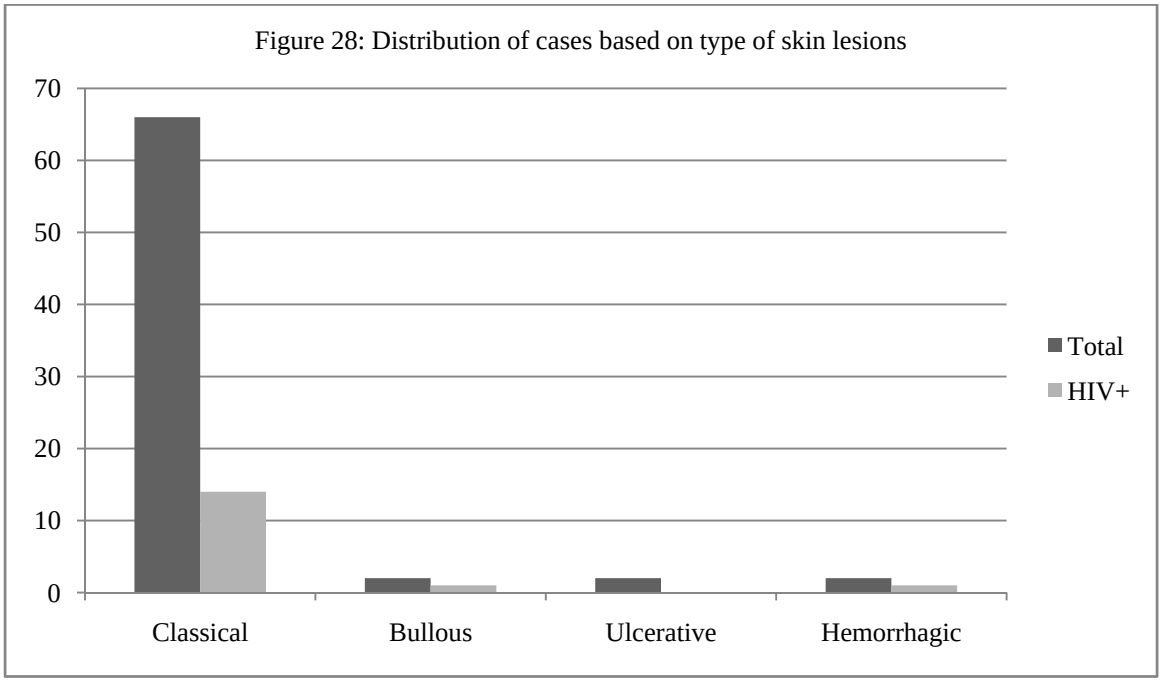
Type of skin lesions

In the present study, most of the patients (91.67%) had classical vesicular type of herpes zoster. In that group, 14 out of 66 were HIV seropositive (21.21%). Two patients each had bullous, ulcerative and hemorrhagic skin lesions. HIV seropositivity was noted in one patient each of herpes zoster with bullous and hemorrhagic skin lesions.

Table 12: Distribution of cases based on type of skin lesions

Type of lesion	Number of patients	% of total	HIV+	% in group
Classical	66	91.67	14	21.21
Bullous	2	2.78	1	50
Ulcerative	2	2.78	0	0
Hemorrhagic	2	2.78	1	50

Figure 28: Distribution of cases based on type of skin lesions



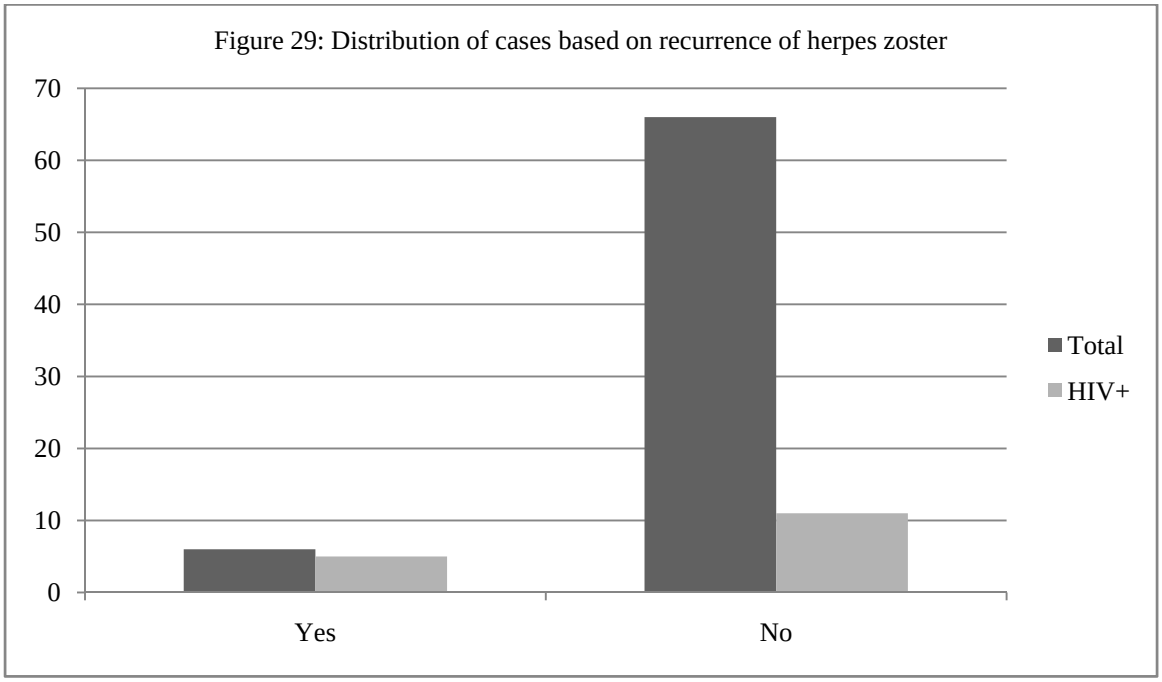
Recurrence of herpes zoster

In the present study, six patients had a recurrence of herpes zoster. Five of those patients were seropositive for HIV (83.33%).

Table 13: Distribution of cases based on recurrence of herpes zoster

Recurrence	Number of patients	% of total	HIV+	% in group
Yes	6	8.33	5	83.33
No	66	91.67	11	16.67

Figure 29: Distribution of cases based on recurrence of herpes zoster



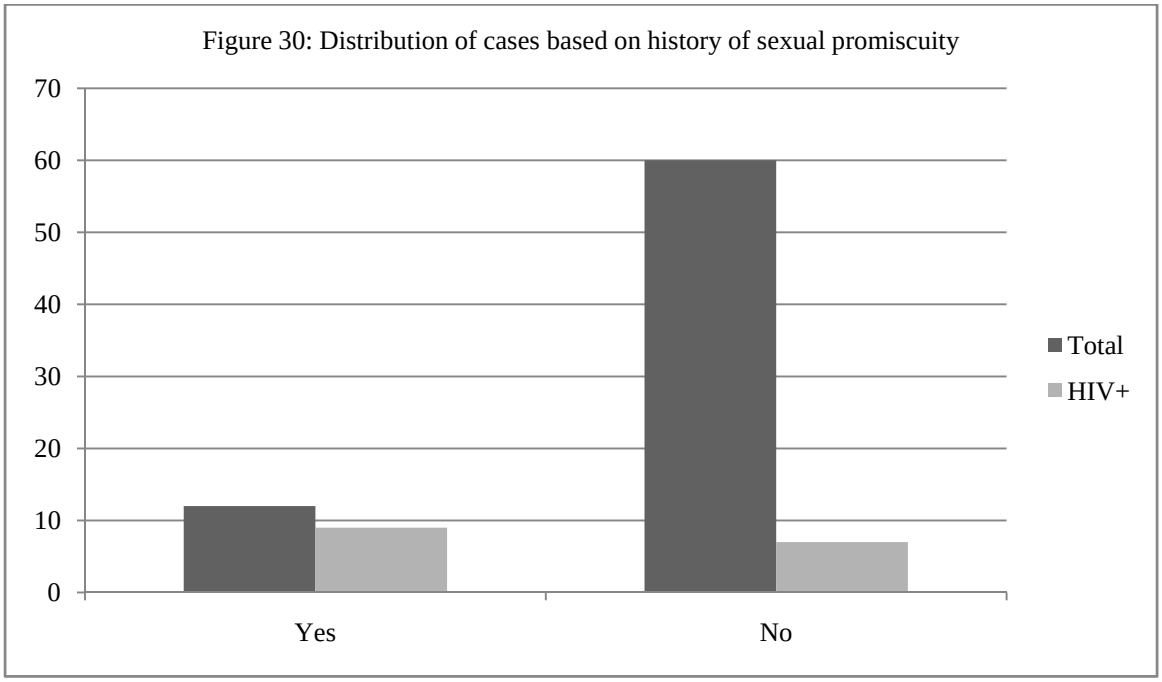
History of high-risk sexual behaviour

In the present study, 12 patients had a history of sexual promiscuity (16.67%). Nine of them were seropositive for HIV (75%). Among the patients who did not give any history of high-risk sexual behaviour, seven were HIV seropositive (11.67%).

Table 14: Distribution of cases based on history of sexual promiscuity

Sexual Promiscuity	Number of cases	% of total	HIV+	% in group
Yes	12	16.67	9	75
No	60	83.33	7	11.67

Figure 30: Distribution of cases based on history of sexual promiscuity



Other associated diseases

In the present study, there were many conditions possibly associated with the development of herpes zoster in the patients. Diabetes mellitus (9.72%), Hypertension (6.94%) and Tuberculosis (6.94%) were the top three associations. HIV seropositivity was 80% among herpes zoster patients who had tuberculosis, whereas those who had diabetes and hypertension were not HIV seropositive. Trauma and operative procedures predisposed to herpes zoster in three patients, and oral steroid intake caused herpes zoster in two patients. None of them were seropositive for HIV. Three HIV seropositive patients had relatives already infected with HIV. Other associations are listed below.

Table 15: Distribution of cases based on associated conditions

Associated disease	Number of patients	% of total	HIV+	% in group
Tuberculosis	5	6.94	4	80
Diabetes Mellitus	7	9.72	0	0
Hypertension	5	6.94	0	0
Hepatitis	3	4.17	1	33.33
Nephrotic syndrome	1	1.39	1	100
Ulcerative colitis	1	1.39	0	0
Hypothyroidism	1	1.39	0	0
Vitiligo	1	1.39	0	0
Operation and trauma	3	4.17	0	0
Steroid intake	2	2.78	0	0
Chemotherapy	1	1.39	0	0
HIV relative	3	4.17	3	100
Pregnancy	1	1.39	0	0
Menarche	1	1.39	0	0
Furunculosis	1	1.39	1	100
Candidiasis	1	1.39	1	100
None	37	51.39	5	13.51

Discussion

Frequency of herpes zoster

The present study was conducted over a period of 12 months from December 2006 to November 2007 in the OPD of Dermatology, Venereology and Leprosy in KLES Dr. Prabhakar Kore Hospital and MRC, Belgaum. A total number of 13,308 skin patients were treated during this period, of which 72 were herpes zoster cases. So the frequency of herpes zoster among the OPD cases was 0.54 %.

The incidence of herpes zoster ranges from 0.24% to 0.6% in various studies.[3,4,9,17] So the frequency of herpes zoster in our study correlates with the above studies.

However, it must be stated that this is a hospital-based study and so the above number does not reflect the true incidence of herpes zoster in the community. The term 'frequency' is preferred over 'incidence'. There is a misconception regarding herpes zoster that there is no specific cure for it and local remedies available in villages thereby prompt people not to access hospitals. These may be possible causes for a lower frequency of herpes zoster in hospital based studies.

HIV seropositivity rate

The HIV seropositivity rates widely vary from 9.5% to 92% in various studies that have been conducted in the last 20 years. Our study correlates closely to a similar study conducted in Mumbai.[84]

The high HIV seropositivity rate in African studies perhaps reflects the high incidence of HIV in that part of the world.

Table 16: HIV seropositivity rates of herpes zoster in different studies including present study

Author	Year	Place	Number of herpes zoster cases	% HIV positive
Van de Perre et al [79]	1989	Kigali	131	92
Colebunders R et al [80]	1988	Zaire	146	91
Dehne KL et al [81]	1992	Karol	182	89
Vasconcellos MR et al [82]	1990	Sao Paulo	66	10.6
Varsha D et al [83]	1998	Mumbai	74	47.3
Desylva et al [84]	1998	Mumbai	120	22.5
Kar PK et al [2]	2003	Bangalore	115	9.5
Laxmisha C et al [85]	2004	Pondicherry	40	35
Onunu AN et al [86]	2004	Nigeria	52	69.2
Dubey AK et al [5]	2005	Pondicherry	46	13.04
Present study	**2007**	**Belgaum**	**72**	**22.22**

Month wise distribution

Herpes zoster occurs sporadically throughout the year without seasonal prevalence.[1] No seasonal variation was noted in some studies,[4,9,17] and an increased incidence was noted in the months of March, April, August, September and December in a few studies.[3,23,24]

The present study showed maximum cases in March, September, January and December, thus correlating partially with previous studies. However, this is a one year study and so true seasonal variation cannot be studied.

Age distribution

It is observed in various Indian studies that the majority of herpes zoster cases occur in the 2nd to 4th decades of life.[3,4,5] The present study also had most cases between the ages of 20 and 40 years, thus correlating well with the above studies. The mean age of the present study was 41.17 years, which closely correlates to the mean age of 37.65 years in another Indian study.[5]

Compared to previous studies, recent ones have showed an increased incidence of herpes zoster in younger populations. This may be due to the increasing prevalence of HIV infection, which mainly affects these age groups.

Sex distribution

Herpes zoster affects both sexes and all races with equal frequency.[21] Many international studies have noted an equal sex incidence.[18,19,20,22] There are a few Indian studies which have noted a higher incidence of herpes zoster in males, with male to female ratios ranging from 1.74:1 to 3:1.[3,4,5,23,24]

The present study gives a M:F ratio of 1.88:1, which correlates with earlier studies. This may perhaps be because fewer women seek medical attention compared to males.

Distribution of patients based on occupation

In a recent Indian study, the maximum number of patients were labourers (24.29%) followed by farmers (20.56%), students (13.08%), housewives (12.14%), drivers (4.67%) and others (25.26%).[5]

In the present study, the maximum numbers of patients were housewives (27.78%) and students (22.22%). Labourers (15.28%) and Agriculturists (13.89%) constituted the next common categories.

Most of the patients attending this hospital are urban people. So in the present study, herpes zoster was found mainly in this group of people.

Time taken to report to the hospital

In the present study, the majority of the patients reported within 5 days of onset of their lesions, 49 (68.06%) out of 72 having done so.

One Indian study reported that 75% of patients sought medical advice within 3-5 days of the eruption, while the remaining 25% reported within 10 days of the eruption.[3] Another Indian study reported that the average duration at presentation was 3.25 days. Majority of the cases (90 cases, 84.1%) presented between 0-5 days, followed by 16 cases (14.9%) between 5-10 days and one case between 10-15 days.[5]

In the present study, fewer patients presented to the OPD early as compared to the other studies mentioned above. This is perhaps because of the lower educational standards and popular misconception that herpes zoster is caused by a snake and drawing an eagle at the advancing end with raw mud will stop its progression.

Primary symptom

In the present study, burning sensation was the most common symptom that appeared first in patients (45.83%). Among them, 24.24% patients were HIV seropositive. Pain

was the first symptom in 15 patients, four of whom were HIV seropositive. Skin lesions appeared first in 13 patients, and only one of them was HIV seropositive.

A recent study of 107 cases of herpes zoster found that pain was the presenting complaint in 97 (90.65%) cases. The most common prodromal symptom seen was paresthesia in 25 (23.30%) cases followed by itching in 21 (19.62%) cases.[5]

The present study shows that burning sensation is the commonest primary symptom and pain was the next commonest. This does not correlate with other studies and perhaps is because patient symptoms are of a subjective nature. Moreover, pain and burning can be easily confused with each other.

Type of dermatomes involved

In the present study, most of the patients had thoracic dermatome involvement (50%). The next dermatome groups commonly involved were the Cervical (20.83%) followed by the Lumbar (13.89%) group. Cranial nerve involvement was seen in 12.5% of patients.

Table 17: Distribution of dermatomal involvement in various studies

Study	**Year**	**Cranial (%)**	**Cervical (%)**	**Thoracic (%)**	**Lumbosacral (%)**
Hope-Simpson [9]	1965	15	14.6	53.6	16.8
Nigam P et al [24]	1972	7.4	13.3	73	5.7
Sehgal et al [4]	1976	8.8	20	52.5	18.8
Chaudhary SD et al [3]	1987	11.3	19.5	55.2	13.9
Das AL et al [87]	1997	9.7	14.5	67.8	8
Dubey AK et al [5]	2005	10.28	15.8	54.81	13.08
Present study	**2007**	**12.5**	**20.83**	**50**	**16.67**

The figures of the present study agree with most of the above studies and suggest that thoracic segments were the commonest dermatomes to get involved in herpes zoster.

Side of dermatome involvement

In the present study, the left side of the body (56.94%) was more commonly involved than the right side (41.67%).

A recent Indian study reported 57% of herpes zoster lesions occurred on the right side of the body and 41.12% on the left side of the body.[5]

Other studies did not notice any appreciable differences between the right side and left side involvement.[3,9]

The present study does not correlate with any of the previous studies.

Number of dermatomes involved

In the present study, most of the patients had only one dermatome involved (48.61%). HIV seropositivity was noted in 17.14% of them. Two dermatomes were involved in 31.94% patients and HIV seropositivity was noted in 17.39% of those people. Four out of the ten people who had more than two dermatomes involved were seropositive for HIV. Disseminated herpes zoster was present in 4 patients, and HIV seropositivity was noted in 2 of them.

It has been observed that herpes zoster occurring in HIV is most often unidermatomal but may be multidermatomal or disseminated.[88] Another study has reported that dermatomal distribution of herpes zoster is similar among HIV seropositives and HIV seronegatives.[75]

A study on 115 men of 21-55 years of age suffering from herpes zoster found that 11 (9.5%) were HIV positive. More than one dermatome was involved in 7 (63.6%) HIV positive and in 2 (1.9%) HIV negative cases. Two HIV positive cases had multiple cranial nerve involvement and one had generalized herpes zoster.[2]

The present study correlates with the above study concerning the fact that increasing incidence of HIV seropositivity is noted as the number of dermatomes involved increases. Disseminated herpes zoster can present even in HIV seronegative patients, especially so when there are other causes of severe immunosuppression.

Type of skin lesions

Herpes zoster occurring in HIV disease is most often unidermatomal, but it may be multidermatomal, recurrent within the same dermatome or disseminated. The eruption may be bullous, hemorrhagic, necrotic, hyperkeratotic, ulcerated and be accompanied by severe pain. Lesions may persist for months, either in localized or disseminated form.[22,87,88]

It was noted that 32.2% of HIV seropositive herpes zoster patients had bullous, confluent and necrotic lesions.[87]

In the present study, most of the patients (91.67%) had classical vesicular type of herpes zoster. In that group, 14 out of 66 were HIV seropositive (21.21%). Two patients each had bullous, ulcerative and hemorrhagic skin lesions. HIV seropositivity was noted in one patient each of herpes zoster with bullous and hemorrhagic skin lesions.

It can be appreciated that even HIV seronegative patients can develop bullous and hemorrhagic skin lesions especially if they are elderly and debilitated or if they are having other causes of profound immunosuppression, such as chemotherapy.

Recurrence of herpes zoster

In the present study, six patients had a recurrence of herpes zoster. Five of those patients were seropositive for HIV (83.33%).

A recent Indian study noted recurrent herpes zoster exclusively in HIV seropositive patients.[85] Another Indian study has reported that recurrence was not found in any of the HIV seropositive patients.[87]

The present study shows that HIV seropositivity is present in a high number of patients who suffer from a recurrent attack of herpes zoster.

History of high-risk sexual behaviour

In the present study, 12 patients had a history of sexual promiscuity (16.67%). Nine of them were seropositive for HIV (75%).

Various studies have reported that the occurrence of herpes zoster in populations at risk for HIV infection is highly predictive of HIV seropositivity.[72,80]

The present study correlates well with the above studies considering the fact that 75% of the sexually promiscuous herpes zoster patients were seropositive for HIV.

Other associated diseases

In the present study, there were many conditions possibly associated with the development of herpes zoster. Diabetes mellitus (9.72%), Hypertension (6.94%) and Tuberculosis (6.94%) were the top three associations. HIV seropositivity was 80% among herpes zoster patients who had tuberculosis, whereas those who had diabetes and hypertension were not HIV seropositive. Trauma and operative procedures predisposed to herpes zoster in three patients, and oral steroid intake caused herpes zoster in two patients. None of them were seropositive for HIV.

Other conditions associated with herpes zoster in the present study included pregnancy, menarche, hypothyroidism, nephrotic syndrome, etc.

An Indian study had 8% cases of tuberculosis among herpes zoster patients who were seropositive for HIV.[87] The present study correlates with the aforementioned fact.

Conclusion

The present study shows that a high proportion of patients with herpes zoster are seropositive for HIV. Herpes zoster commonly occurs in young adults, with burning sensation and pain as common presenting symptoms.

The thoracic dermatome is most commonly affected. Multidermatomal, recurrent and disseminated herpes zoster is more common among HIV seropositive patients. The occurrence of bullae, hemorrhagic lesions and ulceration is present in complicated or atypical herpes zoster and such patients are more likely to be seropositive for HIV. These observations augment the prevailing concept that HIV infection complicates the natural course of herpes zoster, and that patients with such atypical or complicated lesions should prompt the treating clinician to screen the patient for HIV infection.

Occurrence of herpes zoster in young adults who give history of high-risk sexual behaviour need to be tested for HIV infection. Herpes zoster can thus serve as a clinical marker of HIV seropositivity.

Summary

The present study is a one-year time bound observational study from December 2006 to November 2007. The source of data for the study includes all cases of herpes zoster attending the dermatology OPD and referred cases from other departments, at KLES Dr. Prabhakar Kore Hospital and MRC, Belgaum.

The objectives of the study were to determine the HIV seropositivity rate among patients suffering from herpes zoster and to study the various clinical presentations, the common sites, extent of involvement, risk factors and demographic characteristics of herpes zoster.

1. In the study, 72 patients were clinically diagnosed to have herpes zoster out of 13,308 patients who attended the OPD. The frequency of herpes zoster in our hospital is 0.54%.
2. The HIV seropositivity ratio was 22.22%.
3. The maximum number of cases came in the month of March (15.28%), followed by September (12.50%), January and December (11.11% each).
4. The youngest patient was 12 years and the oldest was 83 years old.
5. The youngest HIV seropositive patient was 12 years and the oldest was 64 years old.
6. The mean age of the study population was 41.17 years.
7. The maximum number of cases were seen in the 21-30 years age group (25%) followed by 31-40 years age group (19.44%) and 51-60 years age group (18.06%). Most of the HIV seropositive patients were from the 21-30 and 31-40 years age group, accounting for five cases each.

8. There were 47 males and 25 females affected with herpes zoster, giving a M:F ratio of 1.88:1. Four women out of 25 were HIV seropositive (16%) and 12 out of 47 men were HIV seropositive (25.53%).
9. The maximum number of patients were housewives (27.78%) and students (22.22%).
10. The majority of the patients reported within 5 days of onset of their lesions, 49 (68.06%) out of 72 having done so. HIV seropositivity was noted in 20.41% of that group.
11. Burning sensation was the most common symptom that appeared first in the patients (45.83%). Among them, 24.24% patients were HIV seropositive.
12. Most of the patients had thoracic dermatome involvement (50%). Five out of those 36 patients were HIV seropositive (13.89%).
13. HIV seropositivity was 26.67% in the cervical dermatome group and 50% in the lumbar dermatome group.
14. The ophthalmic branch of trigeminal nerve (V1) was the commonest cranial nerve involved. One out of the seven cases of ophthalmic herpes zoster was HIV seropositive.
15. There was one HIV seropositive case of Ramsay Hunt syndrome.
16. The left side of the body (56.94%) was more commonly involved than the right side (41.67%).
17. One case of herpes zoster had bilateral dermatomal distribution of lesions and was HIV seropositive.
18. Most of the patients had only one dermatome involved (48.61%).

19. Two dermatomes were involved in 31.94% patients and HIV seropositivity was noted in 17.39% of those people. Four out of the ten people who had more than two dermatomes involved were seropositive for HIV. Disseminated herpes zoster was present in 4 patients, and HIV seropositivity was noted in 2 of them.
20. Most of the patients (91.67%) had classical vesicular type of herpes zoster.
21. Two patients each had bullous, ulcerative and hemorrhagic skin lesions. HIV seropositivity was noted in one patient each of herpes zoster with bullous and hemorrhagic skin lesions.
22. Six patients had a recurrence of herpes zoster. Five of those patients were seropositive for HIV (83.33%).
23. 12 patients had a history of sexual promiscuity (16.67%). Nine of them were seropositive for HIV (75%).
24. Diabetes mellitus (9.72%), Hypertension (6.94%) and Tuberculosis (6.94%) were the top three associations. HIV seropositivity was 80% among herpes zoster patients who had tuberculosis.

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Annexures

Annexure I – Proforma

Annexure II – Consent form

Annexure III – Master chart with key

Annexure I

PROFORMA

A study of HIV seropositivity among herpes zoster patients

Case number					**Date**
Name					
Age					
Sex	Male □	Female □			
Address					
Presenting complaints	Burning□	Itching□	Pain□	Blisters□	Duration
History of present illness	Burning□	Itching□	Pain□	Redness□	
	Blisters□	Pustules□	Bleeding□	Duration	
Location of lesions	Face□	Upper limb□	Lower limb□	Trunk□	
Other symptoms	Arthralgia□	Myalgia□	Headache□	Watering from eyes□	
	Difficulty in chewing□		Difficulty in micturition / defecation□		
History of exposure	Present□	Absent□			
Exposure	Multiple□	Single□			
History of blood transfusion	Present□	Absent□			
History of drug abuse	Present□	Absent□			
History of treatment for any other illnesses	Present□	Absent□			
Past History	Herpes Zoster□		Chicken Pox□		HIV□
	DM□	Htn□	TB□	Asthma□	Cancer□
Family history	Married□	Single□			
Family history of herpes zoster	Present□	Absent□			
Family history of chickenpox	Present□	Absent□			
Personal History					
Diet	Veg□	Mixed□			
Appetite	Normal□	Decreased□	Increased□		
Sleep	Normal□	Disturbed□			
Bowel and Bladder Habits	Regular□	Irregular□			
Habits	Smoking□	Alcohol□	Tobacco□		

Examination

General Physical Examination

Build	Poor□	Moderate□	Well□		
Nourishment	Poor□	Moderate□	Well□		
Lymphadenopathy□	Pallor□	Icterus□	Cyanosis□	Clubbing□	Pedal edema□
Vital signs	Pulse	BP	Weight	Temp	RR

Mucocutaneous Examination

Primary lesions	Grouped-	Papules□	Vesicles□	Bullae□	Pustules□
Secondary lesions	Erosions□	Excoriations□		Crusts□	Ulcers□
	Hemorrhagic lesions□				
Sites of distribution	Cranial□	Cervical□	Thoracic□	Lumbar□	Sacral□
Distribution	Unilateral□		Unidermatomal□		Disseminated□
	Bilateral□		Multidermatomal□		
Mucosal involvement	Present□	Absent□			
Ocular involvement	Periorbital edema□		Conjunctivitis□		Keratitis□
	Scleritis□	Iridocyclitis□	Extra ocular muscle palsy□		
Genital involvement	Ulcer□	Erosion□	Discharge□	Warts□	Scar□
Other skin conditions	Present□	Absent□			

Systemic Examination

CVS
RS
Per Abdomen
CNS

Investigations

Blood	Hb	TC	DC
	ESR	RBS	
Urine routine			
Tzanck smear			
HIV 1&2 by ELISA	Reactive□	Non Reactive□	

Signature of investigator **Signature of guide**

Annexure II

INFORMED CONSENT FORM

A study of HIV seropositivity among herpes zoster patients

Purpose of the Study:

The purpose of this study is to study the various clinical presentations of herpes zoster, common sites of involvement, risk factors and demographic characteristics. We will also be studying the importance of underlying HIV infection on herpes zoster. You are being asked to participate in this research because you have been clinically diagnosed as suffering from the disease, herpes zoster. All patients attending the outpatient department, who are diagnosed to have this disease, will be requested to participate in this study during the period of one year. This study will be conducted by Dr. Suneil Pravin Gandhi of the J N Medical College, Belgaum.

Procedure and Treatment:

Should you choose to participate, you will be asked to give a detailed history of your disease, undergo a physical examination, and consent to a few routine blood and urine investigations. You will undergo a Tzanck test. In addition to this, you will agree to undertake an HIV test.

Risks and Benefits:

You may undergo a slight degree of discomfort during the process of investigations, which may include a slight amount of pain and bleeding. However, all necessary steps and precautions will be taken to ensure your safety. The result of you taking part in this research would help health care providers towards a better understanding of this disease, and thus we will be able to provide improved patient care.

Alternatives:

If you decide not to participate in this study, you will still be receiving the usual standard care for your disease.

Privacy and confidentiality:

Your privacy will be respected and all information collected about you during the course of this study will be kept confidential. Your identity will remain undisclosed.

Institutional Policy:

The J N Medical College will provide, within the limitations of the laws of the State of Karnataka, facilities and medical attention to patients who suffer injuries as a result of participating in it's projects. In the event you believe that you have suffered any physical injury as the result of your participation in this study, you may contact Dr. Suneil Pravin

Gandhi, Telephone No. 9886123355 or Dr. B Siddaramappa, Telephone No. 9341100796. In the event of an emergency, you should contact KLES Hospital and MRC on Telephone No. 95 831 2473777.

Financial Incentives:

You shall not be receiving any payment or any financial incentives for participating in this study.

Authorization to publish results:

The results of this study may be published for scientific purpose or presented to a scientific group. Your identity, however, will be maintained confidential at all times.

Voluntary participation:

Your participation in this study is voluntary. Your decision whether or not to participate will neither affect the care of your current disease, nor your future relations with the doctor or the hospital. You are free to discontinue participation in this study at any time and for any reason. In case you need further information regarding your rights as a study participant, you may please contact Dr. V D Patil, Principal and Chairman of the Ethical Committee, J N Medical College, Belgaum on telephone no. 95 831 2473777.

Statement of Consent:

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me and I may ask questions at any time.

Participant's name:

Signature or left thumb print of participant:

Witness' name:

Signature of witness:

Signature of Doctor:

Date:

If the participants are Minors (under 18), the parents sign the form, rather than the participants.

Sl. No.	Date	Age	Sex	Occupation	Duration	First Symptom	Chickenpox Hx	Dermatome(s)	Side	Type of lesions	Number of dermatomes	Sexual Promiscuity	Other Factors	Recurrence	HIV
1	22.11.06	81	M	NONE	3	PAIN	NO	S1,S2	L	CLASSICAL	2	NO	NO	NO	NO
2	27.11.06	55	F	HWIFE	3	PAIN	YES	C4	L	CLASSICAL	1	NO	NO	NO	NO
3	02.12.06	30	M	LAB	4	BURNING	YES	T5	L	CLASSICAL	1	YES	NO	YES	YES
4	04.12.06	30	M	LAB	6	BURNING	NO	C5,C6,C7,C8,T1	R	BULLOUS	5	YES	TB	NO	YES
5	18.12.06	47	M	FARMER	3	PAIN	NO	T3,T4	L	CLASSICAL	2	NO	NO	NO	NO
6	18.12.06	30	M	LAB	4	PAIN	YES	C3	L	CLASSICAL	1	YES	NO	NO	YES
7	20.12.06	22	M	STUDENT	6	BURNING	YES	T4,T5,T6,T7,T8	R	CLASSICAL	5	NO	HEPATITIS	NO	NO
8	21.12.06	12	M	STUDENT	3	ITCHING	NO	L2,L3	L	CLASSICAL	2	NO	HIV RELATIVE	NO	YES
9	27.12.06	64	M	LAB	1	BLISTERS	NO	L1,L2,L3	R	CLASSICAL	3	YES	TB	NO	YES
10	29.12.06	62	M	FARMER	4	BURNING	NO	V1	R	CLASSICAL	1	NO	NO	NO	NO
11	04.01.07	21	F	HWIFE	4	BURNING	NO	T5	R	CLASSICAL	1	NO	NO	NO	NO
12	06.01.07	83	M	NONE	7	BURNING	NO	V1	L	CLASSICAL	1	NO	NO	NO	NO
13	08.01.07	39	F	HWIFE	14	PAIN	YES	L2,L3	R	HEMORRHAGIC	DISSEMINATED	NO	HIV RELATIVE	NO	YES
14	08.01.07	35	F	HWIFE	1	BURNING	YES	L3	L	CLASSICAL	1	NO	NO	NO	YES
15	10.01.07	42	M	FARMER	2	BURNING	YES	T3,T4	R	CLASSICAL	2	YES	HEPATITIS, HSV	YES	YES
16	20.01.07	13	M	STUDENT	4	ITCHING	YES	T5	R	CLASSICAL	1	NO	STEROIDS	NO	NO
17	22.01.07	44	F	HWIFE	7	PAIN	NO	T12	R	CLASSICAL	1	NO	HTN	NO	NO
18	31.01.07	76	M	NONE	12	BURNING	NO	T6,T7	R	HEMORRHAGIC	DISSEMINATED	NO	NO	NO	NO
19	06.02.07	42	M	FARMER	10	BLISTERS	NO	V1	R	CLASSICAL	1	YES	NO	NO	NO
20	13.02.07	22	F	HWIFE	5	BLISTERS	YES	T7	R	CLASSICAL	1	NO	PREGNANCY	NO	NO
21	20.02.07	21	M	STUDENT	5	ITCHING	YES	T11,T12	L	CLASSICAL	2	NO	DRUG ALLERGY	NO	NO
22	22.02.07	36	M	LAB	2	ITCHING	YES	C2	L	CLASSICAL	1	YES	TB	NO	YES
23	23.02.07	60	F	HWIFE	3	PAIN	NO	T1,T2	L	CLASSICAL	2	NO	NO	NO	NO
24	03.03.07	52	F	HWIFE	1	BLISTERS	NO	T7	R	CLASSICAL	1	NO	DM	NO	NO
25	04.03.07	32	M	DRIVER	20	BURNING	YES	V2	R	ULCERATIVE	DISSEMINATED	YES	CANDIDIASIS, FP	NO	YES
26	05.03.07	56	M	LAB	6	ITCHING	NO	T10	L	CLASSICAL	1	NO	NO	NO	NO
27	12.03.07	38	M	BUSINESS	2	BURNING	YES	T10	L	CLASSICAL	1	NO	NO	YES	NO
28	16.03.07	24	M	DRIVER	3	BURNING	YES	L3,L4	L	CLASSICAL	2	YES	NO	NO	NO
29	17.03.07	25	M	STUDENT	2	PAIN	YES	T9	L	CLASSICAL	1	NO	NO	NO	NO
30	17.03.07	35	M	FARMER	5	BURNING	YES	V1	L	CLASSICAL	1	NO	NO	NO	NO
31	24.03.07	45	F	HWIFE	10	BURNING	NO	T4,T5,T6	R	BULLOUS	DISSEMINATED	NO	CHEMO	NO	NO
32	26.03.07	60	F	HWIFE	14	PAIN	NO	V1	L	CLASSICAL	1	NO	DM, HTN	NO	NO
33	30.03.07	72	M	NONE	9	BURNING	NO	C3,C4	R	CLASSICAL	2	NO	HTN	NO	NO
34	30.03.07	60	F	HWIFE	7	ITCHING	NO	T2	L	CLASSICAL	1	NO	NO	NO	NO
35	17.04.07	30	F	HWIFE	20	TINGLING	NO	C6	L	CLASSICAL	1	NO	HIV RELATIVE	YES	YES
36	20.04.07	37	M	ENGINEER	4	PAIN	NO	C6	R	CLASSICAL	1	NO	NO	NO	NO
37	25.04.07	20	M	FARMER	2	BLISTERS	YES	L2,L3,L4	L	CLASSICAL	3	NO	TRAUMA	NO	NO
38	11.05.07	22	F	STUDENT	3	BLISTERS	YES	C4	L	CLASSICAL	1	NO	NO	NO	NO
39	19.05.07	35	M	LAB	1	BLISTERS	YES	L1,L2,L3	L	CLASSICAL	3	NO	OPERATION	NO	NO
40	21.05.07	12	F	STUDENT	7	BURNING	YES	S1,S2,S3	L	CLASSICAL	3	NO	MENARCHE	NO	NO
41	07.06.07	54	M	FARMER	3	BLISTERS	NO	C2,C3	L	CLASSICAL	2	NO	OPERATION	NO	NO
42	19.06.07	24	M	STUDENT	7	BURNING	YES	T3,T4	L	CLASSICAL	2	NO	NO	NO	NO
43	05.07.07	55	F	HWIFE	3	BLISTERS	NO	T6	L	CLASSICAL	1	NO	TB, DM	NO	NO
44	13.07.07	60	M	NONE	2	ITCHING	NO	T6,T7	L	CLASSICAL	2	NO	DM	NO	NO
45	25.07.07	13	F	STUDENT	3	BURNING	YES	T3	L	CLASSICAL	1	NO	NO	NO	NO
46	29.07.07	49	F	HWIFE	2	BLISTERS	YES	V1	R	CLASSICAL	1	NO	DM, HTN	NO	NO

Sl. No.	Date	Age	Sex	Occupation	Duration	First Symptom	Chickenpox Hx	Dermatome(s)	Side	Type of lesions	Number of dermatomes	Sexual Promiscuity	Other Factors	Recurrence	HIV
47	30.07.07	45	M	LAB	15	PAIN	YES	T8,T9	L	CLASSICAL	2	YES	FURUNCULOSIS	YES	YES
48	07.08.07	35	F	HWIFE	10	BURNING	YES	L2,L3	L	CLASSICAL	2	NO	NO	NO	NO
49	08.08.07	25	M	STUDENT	3	ITCHING	YES	V2	R	CLASSICAL	1	NO	NO	NO	NO
50	10.08.07	23	M	STUDENT	4	BURNING	YES	T1,T2	L	CLASSICAL	2	NO	ULC COLITIS	NO	NO
51	27.08.07	72	M	NONE	12	BURNING	NO	T3,T4	R	CLASSICAL	2	NO	NO	NO	NO
52	31.08.07	30	M	LAB	5	PAIN	YES	L2,L3,L4	L	CLASSICAL	3	YES	NO	NO	YES
53	11.09.07	24	F	STUDENT	2	BLISTERS	YES	L1	L	CLASSICAL	1	NO	NO	NO	NO
54	12.09.07	67	M	NONE	4	BURNING	YES	C3,C4	R	CLASSICAL	2	NO	CHR ECZEMA	NO	NO
55	18.09.07	31	F	HWIFE	3	BURNING	YES	T9,T10,L3,L4	BOTH	CLASSICAL	4	NO	TB, HEPATITIS	NO	YES
56	18.09.07	23	F	STUDENT	21	PAIN	YES	T7,T8	L	CLASSICAL	2	NO	HYPOTHYROIDISM	NO	NO
57	18.09.07	61	M	NONE	4	BURNING	NO	V1	L	ULCERATIVE	1	NO	NEPH SYNDROME	NO	YES
58	22.09.07	72	M	NONE	2	BLISTERS	NO	T12	L	CLASSICAL	1	NO	DM, BPH	NO	NO
59	24.09.07	55	F	HWIFE	2	BURNING	NO	C7,C8,T1	L	CLASSICAL	3	NO	DM, EPILEPSY	NO	NO
60	26.09.07	64	M	NONE	17	BURNING	YES	T3,T4	L	CLASSICAL	2	NO	NO	YES	YES
61	27.09.07	53	M	FARMER	2	BLISTERS	NO	C6,C7	R	CLASSICAL	2	NO	NO	NO	NO
62	09.10.07	19	M	STUDENT	7	PAIN	YES	T4	R	CLASSICAL	1	NO	NO	NO	NO
63	15.10.07	40	F	HWIFE	3	BURNING	YES	C5,C6	R	CLASSICAL	2	NO	VITILIGO, HSV	NO	NO
64	16.10.07	50	F	HWIFE	1	BURNING	NO	C4,C5,C6,C7	L	CLASSICAL	4	NO	HTN, STEROIDS	NO	NO
65	22.10.07	40	M	LAB	2	BURNING	YES	T8	R	CLASSICAL	1	YES	T CRURIS	NO	NO
66	26.10.07	48	M	FARMER	4	BURNING	NO	T5	L	CLASSICAL	1	NO	NO	NO	NO
67	27.10.07	33	M	LAB	7	ITCHING	YES	T5,T6	R	CLASSICAL	2	NO	NO	NO	NO
68	27.10.07	18	M	STUDENT	3	BURNING	YES	C3	R	CLASSICAL	1	NO	NO	NO	NO
69	30.10.07	53	M	BUSINESS	3	BURNING	YES	T3,T4	R	CLASSICAL	2	NO	NO	NO	NO
70	03.11.07	31	F	HWIFE	3	PAIN	YES	T3,T4	L	CLASSICAL	2	NO	NO	NO	NO
71	21.11.07	52	M	FARMER	3	ITCHING	YES	T11	R	CLASSICAL	1	NO	NO	NO	NO
72	27.11.07	23	M	STUDENT	4	BURNING	YES	T3	R	CLASSICAL	1	NO	NO	NO	NO

Key to Master Chart

M – Male	TB – Tuberculosis	ULC COLITIS – Ulcerative colitis
F – Female	DM – Diabetes Mellitus	CHR ECZEMA – Chronic eczema
HWIFE – Housewife	HTN – Hypertension	NEPH SYNDROME – Nephrotic syndrome
LAB – Labourer	HSV – Herpes simplex virus infection	BPH – Benign prostatic hyperplasia
L – Left side	STEROIDS – Oral steroid intake	T CRURIS – Tinea cruris
R – Right side	FP – Facial Palsy	