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Study of cases of herpes zoster in tertiary care hospital

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Abstract
Background: Herpes Zoster (HZ) is a viral disease caused by reactivation of varicella zoster virus (VZV) characterised by distinctive prodromal pain followed by herpetiform vesicular eruptions. Immunocomprised state like elderly age, diabetes, HIV infection, immunosuppressive drugs are known predisposing factors.
Objectives: The study was conducted to know the clinicoepidemiological profile of the cases of HZ attending to tertiary care centre.
Materials and Methods: Clinical profile of patients with HZ was noted on predesigned proforma. Detailed investigation was performed and data was analysed by tabulation, mean, standard deviation on Statistical Package for the Social Sciences verion 20.
Results: Total 190 cases of HZ were enrolled. There were 126 males and 64 females with sex ratio of 2:1. 59% had definite history of chicken pox. Eleven cases were HIV positive, 02 were diagnosed HIV infection while evaluating herpes zoster. 91% cases had prodrome before eruptions. Thoracic dermatome was most commonly involved followed by trigeminal. Post herpetic neuralgia (PHN) was present in 41 (27%) cases.
Conclusion: Herpes zoster constituted 0.84% of total dermatology OPD in six months reflects sizable burden of herpes zoster in tertiary care centre. There was higher incidence of PHN (27%) on prolonged follow up, however, involvement of thoracic dermatome and association with diabetes mellitus is consistent with other studies.

Keywords: Herpes zoster, varicella zoster, clinical, epidemiological profile, complication, systemic association

Introduction

Herpes Zoster (HZ) or shingles is a viral disease caused by endogenous reactivation of an infection by the varicella-zoster virus (VZV). Following primary infection of varicella, the virus persists asymptomatically in the sensory cranial nerves ganglia and spinal dorsal root ganglia. As cellular immunity to VZV decreases with age or because of immunosuppression, the virus reactivates and travels along the sensory nerves to the skin, causing the distinctive prodromal pain followed by eruption of the papulovesicular rash. Clinically, the disease is characterized by eruption of grouped vesicles on eryhtematous base, eryhtematous papules distributed in a particular dermatolme[1]. Shingles incidence increases with age, especially after the age of 50 and is more common in immunocompromised persons and among children with a history of intrauterine varicella or varicella occurring within the first year of life; the latter have increased risk of developing shingles at an earlier age [2]. Vaccination against HZ virus is the mainstay of prevention of HZ infection3. Many treatment modalities are available for HZ infection as well as for post-herpetic neuralgia (PHN). Nevertheless, approximately 22% of patients with herpes zoster still suffer from PHN[4]. Wider use of varicella vaccination leads to reduced prevalence of varicella, thereby resulting in reduced chances of periodic re-exposure to varicella. This in turn can reduce natural boosting of immunity and lead to an increased incidence of HZ [6]. Even though, HZ is a common condition without any serious consequences, its incidence and pattern of occurrence in the era of HIV infection, use of newer *immunosupressives* agents and associated systemic conditions requires constant relook. This study was undertaken to look into clinicoepidemiological profile of this disease in busy tertiary care set up where dermatology load is high along with heavy cross referral from other specialities.

Aim and objectives

To study the clinic epidemiological profile of cases of HZ in a tertiary care centre with emphasis on precipitating factors, immunocompromised status, any association with HIV infection or any systemic disease. Also to know the rate of PHN and disease burden in a tertiary care centre.

Materials and Methods

This was a prospective study conducted between Jan to Jun 2019

in, a tertiary care centre of north India. All consecutive cases of herpes zoster attending skin outpatient department and referred from other departments were enrolled into the study after taking the informed consent. Ethical clearance was taken from the hospital ethical committee. Diagnosis of HZ was clinical. Whenever doubt existed Tzanc smear was done to confirm the diagnosis. Patient who were less than 10 year of age or unwilling for follow up were excluded from the study. All patients were followed for at least three months to maximum of six months. Data was filled up in the predesigned proforma. Details like age, sex, duration of HZ, precipitating factor, recurrence, family history, and detailed clinical examination including morphology, the segment of involvement, duration between neuralgia and eruptions, or any complication were noted. A set of laboratory investigation including complete blood count (CBC), blood sugar, renal function test (RFT), urine analysis, enzyme-linked immunosorbent assay (ELISA) for HIV antibody was done in all cases. All patients were treated with Acyclovir if the reported within 72 hr of ons*et al*ong with supportive therapies. Follow up was planned fortnightly for one month and monthly for next five months. During follow up course of disease, resolution time and complications including PHN were assessed. Opinion from other specialties such as ophthalmology and general medicine was sought whenever necessary. Detailed data was endorsed in excel sheet for analysis. Mean, average, percentage, standard deviation were calculated on collected data using window 10 operating system of computer.

Results

203 cases reported in OPD between Jan to June, 2019. 13 patients could not report for follow-up so excluded from the study. Total 190 cases were anlalysed for study, out of which 126 were males and 64 were females with male to female ratio of 2:1. This constituted 0.84% of total dermatology OPD cases of that duration. Age group was ranging from 10-90 years with mean age 43.2 yrs (SD 12.4). 101 patients (53%) were below 50 years and 89 (47%) were above 50 years and 7.3% cases were below 20 years of age. The age and sex distribution is given in table 1.

Table 1: Age and sex distribution of Herpes Zoster

Age group	Male	Female	Total no. of cases	Percentage
10-20	8	6	14	7.3
21-30	11	7	18	9.4
31-40	20	12	32	16.8
41-50	24	13	37	19.4
51-60	27	15	42	22.1
61-70	21	7	28	14.7
71-80	16	4	18	9.4
81-90	01	-	1	0.5

Mean age of males was 50.3 (SD 12.3) and females was 48.2 (SD 10.2). One twenty cases (63%) were seen in summer season from Apr to June. Out of 190 cases, 112 (59%) had definite history of chicken pox in childhood. The remaining 78 cases (41%) either had no history of chicken pox at all or did not remember it. Sixty six patients (34%) had comorbidities in the form of diabetes mellitus(35), hypertension(28), carcinomas(9), coronary artery disease (CAD-8), chronic kidney disease (CKD-2), skin diseases(6), pulmonary Koch (2), rheumatoid arthritis (RA-1), idiopathic thrombocytopenic purpura (ITP-1), ankylosing spondylitis(1), squamous cell carcinoma (SCC-1). Eighteen patients (9%) had precipitating factors in the form of extreme physical exertion, history of fever and surgery in the recent past. Forty three patients (22%) had some form of immune suppression in the form of DM, steroid or immunosuppressive intake. Eleven patients had HIV infection (08 males and 03 females) and two had pulmonary tuberculosis. Two patients were diagnosed HIV positive while screening. Recurrence was seen in four cases (2.1%) and family history was present in five cases (2.6%). Eleven (5.7%) cases had significant constitutional symptoms including high grade fever, headaches, body ache and joint pains as prodrome or concurrently with eruption. Five cases had sore throat with dry cough. Persistent hiccup as uncommon complaint in HZ was seen in 01 patient involving thoracic dermatome. Segment wise distribution is given in table 2.

Table2: Dermatomal distribution of Herpes Zoster

Region	Sex M F	Side R L	Number of cases	Percentage
Cranial	24 04	16 12	28	14.7
Cervical	8 10	8 10	18	9.4
Thoracic	56 34	48 42	90	47.3
Lumbar	12 07	10 9	19	10
Sacral	05 03	5 3	08	4.2
Cervico- Thoracic	03 01	2 2	04	2.1
Thoraco-Lumbar	03 02	3 2	05	2.6
Lumbo- Sacral	05 01	4 2	06	3.1
Multidermatomal	02 01	2 1	03	1.5

Thoracic dermatome was most affected (n-90; 47.3%) followed by trigeminal (n-28; 14.7%). 17 patients (8.9%) had herpes zoster ophthalmicus of which 04 had corneal involvement. Three had mutidermatomal involvement, two were HIV positive. Ninety eight had right sided lesions, ninety two left sided. 91% patients had segmental neuralgia during the course of disease in the form of pricking, burning, shooting, deep boring pain, interfering with sleep in few cases. Pain was more evident in old age. Vesicular eruption was preceded by pain in 169 (90%) cases. Eruptions were seen within 02 days of pain in 70% patients. They followed classical progression of erythematous papule or macule, vesiculation (1-2 days), pustulation (1-7 days) and crusting over 10-15 days. Period of resolution ranged from 8 to 15 days. In immunocompromised individuals it prolonged upto 20 days. Twenty one (11%) patients were admitted. There were two cases of HIV infection who were found positive on screening. Hospital stay varied between 07-16 days with average of 09 days. Fifty one patients (26%) out of 190 had developed complications. They were secondary bacterial infection (12 cases), severe ulceration (03 cases), keloid (02 cases), scarring (02Cases), motor weakness

(01 case), trigeminal neuralgia (01 case), and eye involvement (04 cases). 56% cases of PHN had coexisting above mentioned complications. PHN occurred in 41 cases (22%) of whom were 23 males and 18 females. Among them 33 (80%) were above 60 years of age. Mainly it was either continuous deep nagging, intermittent pricking or lancinating with allodynia. Interference with sleep was seen in 20% of cases. It led to constant fatigue and interference with daily activities in patients over 70 years, more in females. Thoracic segment was most commonly involved followed by trigeminal nerve in PHN. Extension of pain beyond dermatome was not seen. On follow up it persisted upto 06 months in 29 cases (70%) of total PHN cases. Total 23 out of them were above 60 years of age. Clinical images of involvement different dermatomes are depicted in figure 1a, b, c and d.

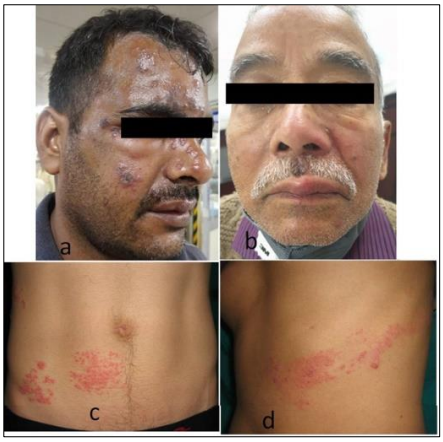

Fig 1a, 1b, 1c and 1d: Clinical images of different morphological forms of herpes zoster; 1a illustrating herpes zoster ophthalmicus right side. 1b illustrates herpes zoster involving maxillary branch of trigeminal nerve; 1c and 1d demonstrates herpes zoster involving T11 right and T7 dermatomes respectively.

Complication which were seen in the cases of HZ are illustrated in figure 2 a, b, c and d.

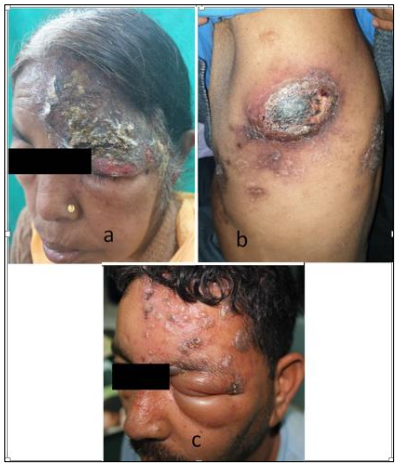

Fig 2a, 2b, 2c: Clinical images illustrating different complication of herpes zoster. 1a illustrates severe necrosis of skin following herpes zoster ophthalmicus; 1b illustrates abscess and scarring following herpes zoster of T6 dermatome left side; 1c demonstrates severe edema of both the eyelids of left side. This patient had corneal ulceration which is not seen in the image.

Discussion

HZ constitute sizable burden i.e 0.84% of total dermatology cases in tertiary care centre. This study of 190 cases revealed that the majority of the patients affected were adults, (47%) above 50 years of age and (53%) below 50 years of age. This is in similar to study by Abdul Lateen EN, Pavithran K [7], Pavithran K [8], Sehgal VN [9] *et al*, Chandrika C, Tharini GK [10].but in contrast there are many other studies [11-15]. This data suggests that HZ is not just a disease in elderly. A study of Brisson [14] *et al* showed that mass childhood vaccination increases incidence of HZ between 30-50 years and increased incidence relatively in younger group in a study conducted in China was due to urbanisation [16]. Similar conclusion cannot be drawn from our study as it was not population based study.Males were almost double the number of female cases. It may be because this hospital primarily caters security personnel or their dependents with mandatory reporting to hospital. This is in contrast to western studies [17, 18]. Where both are equally affected or female affected more[15]. Though male preponderance have been seen in few studies from India, Nepal and Pakistan [10, 19, and 20]. Higher female incidence as per literature is probably because of difference in immune response to latent virus [21, 22].

Family history as a possible risk factor recently reported by Lai YC[23] was seen in 2.6% cases. Even though, HZ does not occur following VZV exposure, physical and mental stress, surgical history and fever episode in recent past maybe predisposing factors. Trauma and physical exertion are a factor for male preponderance in Indian setup [7, 23-25]. Immune suppression in form of steroid intake (17 cases), malignancies, diabetes mellitus and HIV as provoking factor was seen commonly (40% cases). Depressed cellular immunity in these conditions could be a possible factor for development of HZ [26]. It was also associated with extensive involvement and complication as per available literature [27]. Increased incidence in the summers in this study can be explained to reactivation of latent infection on exposure to varicella virus as chicken pox also is common in summers [20]. It contradicts reports of herpes zoster risk reduction through exposure to chicken pox patients. This exogenous boosting hypothesis states that re-exposure to circulating VZV can inhibit viral reactivation and consequently also herpes zoster in VZV-immune individuals which is also the basis for varicella zoster vaccination [28]. However, other studies documented no significant seasonal variation for herpes zoster [15, 29].

Constitutional symptoms were seen in 25% cases as per older Indian studies [8,18] but in contrast to high incidence study conducted in south India in 2011 [7,10]. In accordance to the previous literature reports [23, 30, 31], pain followed by vesicular eruption was seen in most of the cases (90%). Incidence of prodrome was higher in contrast to other studies[7]. Prodrome was more evident after 60 years of age. Rash was more severe in cases above 50 years of age in accordance with previous reports [30, 32]. Eleven cases were asymptomatic with mild discomfort, and 4% had neuralgia without vesicular eruptions zoster sine herpetic as noticed in the study by Wollega U [34]. Persistent hiccups preceding HZ in accordance with Reddy *ET al*l was seen in one patient [35].In our study thoracic segment was most commonly involved followed by cranial nerve involvement [10, 31, 36]. The pattern of dermatomal involvement was slightly different from

Previous Indian studies with maximum cranial or lumbar involvement [11, 12, 19]. Among the cranial nerves, trigeminal nerve was involved in 28 patients and one patient had Ramsay-Hunt syndrome. 17 patients had herpes zoster ophthalmicus, of which 04 had corneal involvement, less as in literature with 20-70% eye involvement in HZO [37]. No case of disseminated HZ characterised by 20 vesicles away from primary or adjacent dermatome was seen during this period. Herpes Zoster myelitis (HZM), segmental zoster paresis and acute urinary retention as reported neurological complications were not seen in our study [38-40]. PHN was observed in 27% cases, 89% of whom were more than 60 years of age.

Female predilection with 60% cases as seen in previous studies [29, 41]. It was considered after 03 months of persistent neuralgia past diagnosis of HZ. Incidence is higher compared to older studies and literature [8, 42, 43]. Gauthier *et al*. reported that 19.5% of herpes zoster patients develop PHN1 (pain persisting at least 1 month after rash onset) and 13.7% develop PHN3 (pain persisting at least 3 months after rash onset) [41].

Increased incidence in our study may be due to long term 06 months follow up and with the increased life expectancy. In our study PHN was affecting thoracic dermatome as compared to ophthalmic in a study by Jung BF [44] *et al*. It was more common in cases with initial greater acute pain severity as observed by Jung BF [44]. Some patients had temporary cessation of pain return after few weeks in accordance with few studies in past[45]. Extension of pain beyond dermatome as reported in a study was not seen in our cases [46]. Single case of HZO developed trigeminal neuralgia as reported in two studies [47, 48].

Herpes Zoster was presenting features in two HIV patients out of 11 cases. Herpes zoster is associated with HIV diagnosis, included in stage II marker of WHO staging [49]. Decline in CD4+ cells and increased CD8+ cells in HIV patients leads to higher incidence of HZ in HIV cases [49].

Patients who have risk behaviors of HIV infection should receive regular surveillance for undiagnosed HIV infection when they present with herpes zoster [51, 52]. Multidermatomal involvement with secondary infection was seen in two patients. Recurrence seen in two cases but unusual morphologies as quoted in previous studies [32, 53] was not seen.

Diabetes and HTN was freshly detected in 03 cases each indicating herpes zoster as an indicator of existing disease. Few studies document association between diabetes and HZ [54]. Further research needed in this regard. Unlike other studies no cerebrvascular accident, myocardial infarction noted. Increased risk of this has been noted following 3-12 months of HZ in few population based studies [55].

Conclusion

Herpes zoster constituted 0.84% of total dermatology OPD in six months reflects sizable burden of herpes zoster in tertiary care centre. Presence of this disesase in relatively young population or in male may be due to composition of dependent clientele. There was higher incidence of PHN (27%) on prolonged follow up, however, involvement of thoracic dermatome and association with diabetes mellitus is consistent with other studies.

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