ejpmr, 2017,4(04), 666-675

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

AN EPIDEMIOLOGICAL ANALYSIS OF HERPES ZOSTER AMONG DIFFERENT AGE GROUPS

[1]Elsam Koshy, MD, [2]Hanaasha Kumar, MD and [3]Wu Jianbo*, PhD

[1,2,3]Department of Dermatology, Zhongnan Hospital of Wuhan University, Wuhan, China.

***Corresponding Author: Wu Jianbo**
Department of Dermatology, Zhongnan Hospital of Wuhan University, Wuhan, China.

Article Received on 17/02/2017 **Article Revised on 10/03/2017** **Article Accepted on 31/03/2017**

ABSTRACT

Introduction: Herpes zoster occurs due to the reactivation of the varicella zoster virus following a primary infection with varicella virus. Its incidence is high among the elderly and immunocompromised patients. Early management with antivirals can reduce severity and complications with herpes zoster. Vaccination for individuals above 60 years can help reduce incidence of herpes zoster. **Objective:** To analyze the epidemiology of Herpes zoster among different age and gender by comparing their Total hospital stay and Numeric rating scale score on admission and on discharge. **Materials and Methods:** A retrospective analysis was conducted in 60 patients with herpes zoster infection treated in Zhongnan hospital of Wuhan University, Wuhan, China. All patients were divided into three groups. Group I (n=20) include patients aged <30 years, Group II (n=20) include patients aged 30-60 years and Group III (n=20) include patients aged ≥60 years. A univariate analysis with multiple comparison was performed with total hospital stay, duration at presentation, Numeric rating scale on admission and on discharge. The male and female incidence was performed using chi square test. An independent t test was used to analyze total hospital stay and duration at presentation of both males and females. **Results:** Among the 60 cases, the total male and female involvement was shown to be non significant (p=0.63). The total hospital stay among Group I and Group II were significant (p=0.047 and p=0.011) and the duration at presentation among Group I was also significant (p=0.02). Thoracic dermatome was involved in 31.6% patients among all age groups. Hypertension was the most common underlying disease with 20% involved among all age groups. **Conclusion:** Herpes zoster is not a gender specific disease. Treatment with ganciclovir can reduce hospital stay only in patients less than 30 years and patients aged 30-60 years. Thoracic dermatome was most commonly involved in all patients. Ganciclovir is safe and has shown no adverse effects in any patients. Gabapentin is effective in managing pain with a good prognosis in all patients among all age groups. Combination therapy with antivirals, analgesics and neurotropic agents can reduce pain, promotes fast healing and decrease complications.

KEYWORDS: Herpes zoster (HZ); Varicella zoster virus (VZV); Post herpetic neuralgia (PHN).

INTRODUCTION

Herpes zoster (HZ) also known as shingles occurs from the reactivation of the varicella zoster virus (VZV) in the sensory dorsal root ganglia or the cranial sensory ganglia after a primary infection with VZV.[1] The disease is characterized by painful vesicular unilateral erythematous rash along the affected dermatome. Pain, itch, fever, headache, myalgia are common symptoms.[2] About 20-30 % of population has a life time risk of developing HZ. The incidence of HZ increases with age with an increased incidence in patients aged ≥50 years and those with immunocompromised status.[3] HZ can affect single or multiple dermatomes and can sometimes lead to cutaneous, visceral, ocular or neurological complications. Post herpetic neuralgia (PHN) is the most common and serious complication of HZ.[4] Recurrence of HZ is noted in 10-20% patients and the recurrence can occur most commonly in the previously involved dermatome.[5]

Diagnosis of HZ can usually be made clinically due to characteristic appearance of the rash. But in case of atypical HZ, direct fluorescent antibody assay (DFA) and polymerase chain reaction assay (PCR) are helpful in identifying the zoster virus due to its high sensitivity and specificity.[3,6] Treatment for HZ includes antivirals, corticosteroids and analgesics. Antivirals are recommended to be given within 72 hours of onset of rash to reduce pain and risk of HZ associated complications.[6] Corticosteroids along with antivirals are beneficial in managing ocular complications and ramsay hunt syndrome (RHS).[7,8] Analgesics such as acetaminophen, NSAIDS, opiods, tricyclic antidepressants and anticonvulsants can help reduce acute zoster pain but they are not effective in reducing PHN.[9] Pregabalin and gabapentin are preferred agents for managing PHN.[10,11] Administration of HZ vaccination in individuals aged ≥ 60 years is

recommended to prevent zoster infection, its recurrence and to reduce its complications.[12]

The purpose of our study was to analyze the epidemiology of HZ among different age and gender, the dermatomal distribution, incidence of underlying disease and efficacy of ganciclovir in treating HZ.

METHODS AND MATERIALS

Study population

The study included 60 patients (n=60) suffering from HZ, who were all under treatment in the inpatient department of dermatology in Zhongnan Hospital of Wuhan University, Wuhan, China between January 2015 to August 2016. Patients among all age groups were included in the study. Among the 60 patients, 29 patients were males and 31 patients were females. All the patients were divided into 3 groups respectively. Group I (n=20) include patients aged <30 years, Group II (n=20) include patients aged 30-60 years and Group III (n=20) include (iv) patients aged >60 years. Baseline characteristics of all patients are shown in Table 1.

Treatment Methods

All the patients were treated with antiviral agent ganciclovir. Among the 60 patients, 21 patients who developed severe pain were given gabapentin along with ganciclovir. One of the patient with pain was given pregabalin, an alternative to gabapentin. Additional agents used were prednisolone, intravenous vitamin B6, vitamin C, Cobamamide, deproteinised calf blood serum and mecobalamin. Analgesics such as ibuprofen, codein and diclofenac were also given for those patients with pain.

Exclusion Criteria

(i) Pregnant women.
(ii) Patients not treated with ganciclovir.
(iii) Patients seeking medical care after the complete remission of rash.

Table: 1 Baseline characteristics of all patients

Characteristics	Group I <30 years (n=20)	Group II 30-60 years (n=20)	Group III > 60 years (n=20)
Sex (M:F)	8:12	10:10	11:09
Age (y)			
mean±SD	22.8 ± 5.06	46.45 ± 9.27	71.3 ± 8.31
Duration at presentation			
mean±SD	4.6±1.5	6.25±2.6	5.7±2.2
Total Hospital Stay			
mean±SD	6.9 ± 1.8	8.4 ± 2.16	8.85 ± 2.91
NRS on admission			
mean±SD	1.65 ± 1.309	2.2 ± 1.473	2.0 ± 1.376
NRS on discharge			
mean±SD	0.25 ± 0.55	0.5 ± 0.61	0.4 ± 0.5
Treatment			
Ganciclovir	12	13	14
Ganciclovir + Gabapentin/Pregabalin	8	7	6

Statistical Analysis

SPSS version 21.0 statistical software were used to analyze the epidemiology of HZ among different age groups. Least significant difference (LSD) for multiple comparisons was used to analyze the total hospital stay, duration at presentation, NRS score on admission and NRS score on discharge among all age groups. Chi square test was used to calculate the male and female incidence rate among all age groups and to calculate the dermatomal involvement incidence among male and female. An independent t-test was used to analyze the total hospital stay and duration at presentation of males and females. A p value < 0.05 was considered statistically significant. The baseline characteristics of all patients are expressed in mean and standard deviation (SD).

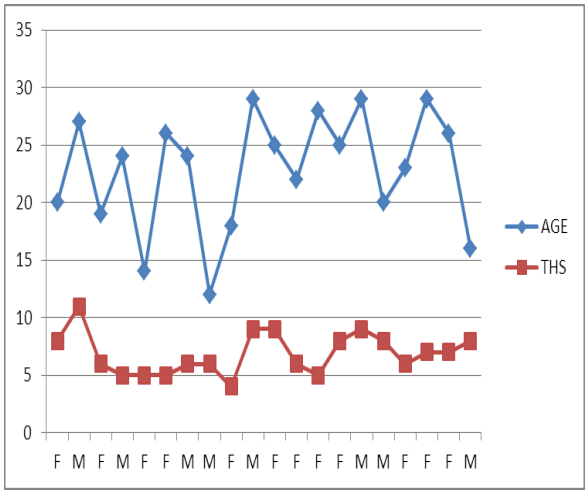
RESULTS

Sixty cases of HZ were recorded from January 2015 to August 2016. The mean age in all groups was 23 years (22.8±5.06), 46 years (46.45±9.27) and 71 years (71.3±8.31). Table 2 and 3 illustrates the results obtained after analysis under SPSS. The results were obtained through univariate analysis (chi-square test or fisher's exact test).

Evaluation of gender association in the incidence of HZ

In group I, 8 patients (n=8) were males and 12 (n=12) were females. In group II, 10 patients were males (n=10) and 10 patients were females (n=10). In group III, 11 patients were males (n=11) and 9 patients were females (n=9). No statistical significance was observed for gender in the incidence of HZ in all age groups (p=0.63).

No statistical significance was observed for duration at presentation among male and female (p=0.733). Total average hospital stay among male and female gender in group I was 8 days and 6 days. In group II, average stay for both men and women was 8 days. In group III average stay for both men and women was 9 days. No statistical significance was observed for male and female in total hospital stay (p=0.225). The overall hospital stay for both gender found to be equal in all age groups which is shown in Figure 1, 2 and 3. This support our analysis that herpes zoster is not a gender specific disease.



*THS: Total hospital stay

Figure 1: Gender difference for total hospital stay in Group I

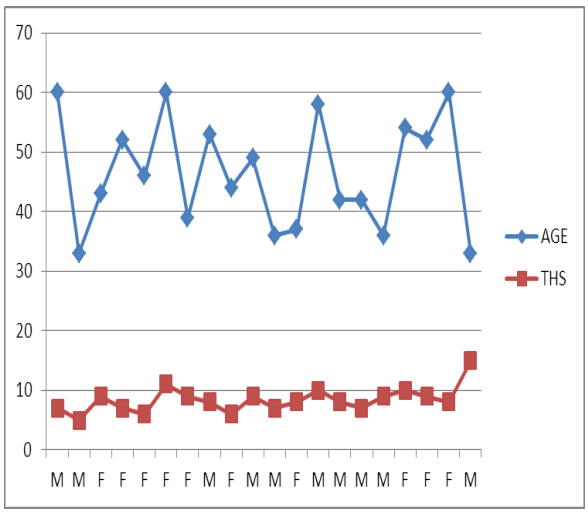


Figure 2: Gender difference for total hospital stay in group II

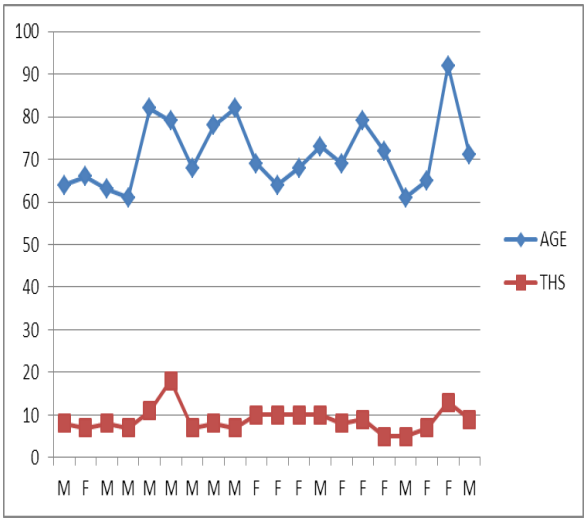


Figure 3: Gender difference for total hospital stay in group III

Evaluation of the efficacy of ganciclovir in reducing hospital stay and NRS scores

Ganciclovir was used as an antiviral agent in all age group patients. The mean duration at presentation of HZ for all patient's were 5 days (4.6±1.5) in group I, 6 days (6.25±2.6) in group II and 6 days (5.7±2.2) in group III. The mean total hospital stay among all age groups was 7 days (6.9 ± 1.8), 8 days (8.4 ± 2.16) and 9 days (8.85 ± 2.91). The mean NRS score on admission in all age groups was "2" (1.65 ± 1.309, 2.2 ± 1.473 and 2.0 ± 1.376). The mean NRS score on discharge among all age groups was "0" (0.25 ± 0.55, 0.5 ± 0.61 and 0.4 ± 0.5). A significant result were obtained for group I and group II on terms of hospital stay showing a p value of 0.047 and 0.011. Group III showed a p value of 0.545 which was not considered statistically significant. None of the groups showed significant results for NRS on admission and NRS on discharge.

Table 2: Univariate analysis results (chi-square test or Fisher's exact test)

Total Hospital Stay	**Average days**	**P value**
Group I	7	0.047
Group II	8	0.011
Group III	9	0.545
NRS on admission	**Average score**	
Group I	2	0.215
Group II	2	0.428
Group III	2	0.65

NRS on discharge	Average score	
Group I	0	0.16
Group II	0	0.396
Group III	0	0.571
Duration at presentation	**Average days**	
Group I	5	0.02
Group II	6	0.117
Group III	6	0.43

Table 3: Univariate analysis result for gender

Gender	P value
Total population	
M/F	0.63
Total Hospital Stay	
M/F	0.225
Duration at presentation	
M/F	0.733
Dermatomal involvement	
M/F	0.636

Pain was seen in 44 patients (73%). Gabapentin was used to manage pain in most of the patients in all age groups (n=21). Pregabalin was used in one patient in group III (n=1). Supportive treatments given were corticosteroids in 3 patients in group I, 2 patients in group II and 3 patients in group III, intravenous vitamin B12 was given for 18 patients in group I, 17 patients in group II and 15 patients in group III, intravenous vitamin C was given for 3 patients in group I and not used for any patients in group II and III, intravenous deproteinised calf blood serum was given equally in all age groups (n=18 patients), mouse nerve growth factor injection was given for one patient in group I, 2 patients in group II and 4 patients in group III, calcium gluconate injection was given for 3 patients in group I and one patient in group II. It was not used for any patients in group III. Other analgesics such as ibuprofen, codein and diclofenac were used in 3 patients in group I, 6 patients in group II and 6 patients in group III. Antihistamines were used for 3 patients in group I and one patient in group III. It was not used in any patients in group II. Results of treatment are shown in table 4.

Table 4: Supportive treatment given

Other Treatment	Group I	Group II	Group III	Total (%)
Corticosteroids	3	2	3	13.3
Vitamin B1	17	17	14	80
Vitamin B12	18	17	15	83.3
Vitamin C	3	0	0	5
Deproteinised calf blood serum	18	18	18	90
Mouse nerve growth factor	1	2	4	11.6
Calcium gluconate	3	1	0	6.6
Analgesics	3	6	6	25
Antihistamines	3	0	1	6.6
Thymopolypeptide	1	1	3	8.3

Evaluation of Dermatomal involvement

Thoracic dermatome was mostly involved in all age groups (31.6%) followed by trigeminal (23.3%), lumbar (15%), lumbosacral (11.6%), sacral (8.3%) and cervicothoracic (5%). Cervical, cervicolumbar and thoracolumbar were least involved in all age groups (1.6%). Dermatomal involvement of HZ in the total population is shown in Table 5 and Figure 4.

Thoracic involvement was high for group II (40%). Trigeminal involvement was equal for group I (25%) and group II (25%) with a less involvement in group III (20%). A high lumbar (20%) and lumbosacral (20%) involvement was seen in group III compared to others. Sacral involvement was high for group I (15%) and not seen in any patients in group III. Cervicothoracic involvement was seen only in group I (5%) and group III (10%). Cervical (5%) and cervicolumbar (5%) involvement was noticed only in group I. Thoracolumbar (5%) involvement was noticed only in group II. None of the patients in group III had cervical, cervicolumbar or thoracolumbar involvement. Thoracic involvement was high for both males (31%) and females (29%) in all age groups. A non significant value (p=0.636) was obtained for dermatomal involvement among male and females.

Table 5: Dermatomal involvement of HZ in different age groups

Segments involved	Group I < 30 years n (%)	Group II 30 - 60 years n (%)	Group III > 60 years n (%)	Male n (%)	Female n (%)	Total n (%)
Cervical	1 (5)	0 (0)	0 (0)	0 (0)	1 (3.2)	1 (1.6)
Lumbar	2 (10)	3 (15)	4 (20)	3 (10.3)	6 (19.3)	9 (15)
Sacral	3 (15)	2 (10)	0 (0)	2 (6.8)	3 (9.6)	5 (8.3)
Thoracic	5 (25)	8 (40)	6 (30)	9 (31)	10 (32.2)	19 (31.6)
Trigeminal	5 (25)	5 (25)	4 (20)	8 (27.5)	6 (19.3)	14 (23.3)
Lumbosacral	2 (10)	1 (5)	4 (20)	5 (17.2)	2 (6.4)	7 (11.6)
Cervicothoracic	1 (5)	0 (0)	2 (10)	2 (6.8)	1 (3.2)	3 (5)
Thoracolumbar	0 (0)	1 (5)	0 (0)	0 (0)	1 (3.2)	1 (1.6)
Cervicolumbar	1 (5)	0 (0)	0 (0)	0 (0)	1 (3.2)	1 (1.6)
Total	20	20	20	29	31	60

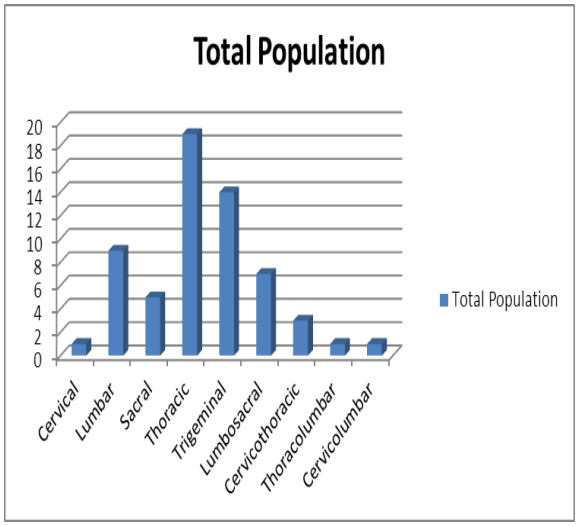


Figure 4: Dermatomal involvement of HZ in total population

Evaluation of underlying diseases

Underlying diseases was high in age group >60 years. Hypertension (HTN) was the most common disease seen with 11 patients (55%) in group III and one patient (5%) in group II. Diabetes mellitus (DM) was seen in 2 patients (10%) in group III. Other diseases seen in patients in group III include dyslipidemia (15%), TB (10%), COPD (5%), chronic heart disease (10%), chronic kidney disease (15%), anemia (5%), SLE (5%), stroke (15%), Ca. lung (5%), Ca. prostate (5%),Ca. breast (5%), gastritis (5%) and vitiligo (5%). In group II, chronic kidney disease (5%) was seen followed by dyslipidemia (10%) rheumatoid arthritis (5%), hyperthyroidism (5%), T cell lymphoma (5%) and duodenal ulcer (5%). History of any underlying disease was less noticed in group I. Gout (10%), atopic dermatitis (5%), chronic urticaria (5%) and verucca vulgaris (5%) was seen in group I. Underlying disease in patients with HZ is shown in Table 6.

Blood transfusion was done in two of our patient with hemorrhagic duodenal ulcer and CKD in Group II. Two patients have undergone chemotherapy for T cell lymphoma and breast carcinoma from Group II and Group III. Thyroid nodule surgery and tonsillectomy was performed on two patients in Group II. One of our patient in Group II with renal disease have undergone renal transplantation 3 years ago and is still on immunosuppression therapy. Three of our patients from Group II and Group III had a previous history of HZ. Among the three patients, two of them developed HZ within 10 years after the first episode and one patient of 61 years age had previous history of HZ in his third decade of life.

Table 6: Underlying diseases at the onset of HZ

Diseases	Group I < 30 years n (%)	Group II 30 - 60 years n (%)	Group III > 60 years n (%)
Hypertension	0 (0)	1 (5)	11 (55)
Diabetes Mellitus	0 (0)	0 (0)	2 (10)
Dyslipidemia	0 (0)	2 (10)	3 (15)
Tuberculosis	0 (0)	0 (0)	2 (10)
Chronic obstructive pulmonary disease	0 (0)	0 (0)	1 (5)
Coronary heart disease	0 (0)	0 (0)	2 (10)
Chronic kidney disease	0 (0)	1 (5)	3 (15)
Rheumatoid arthritis	0 (0)	1 (5)	0 (0)
Hyperthyroidism	0 (0)	1 (5)	0 (0)
T cell lymphoma	0 (0)	1 (5)	0 (0)
Anemia	0 (0)	0 (0)	1 (5)

SLE	0 (0)	0 (0)	1 (5)
Stroke	0 (0)	0 (0)	3 (15)
CA. Lung	0 (0)	0 (0)	1 (5)
CA. Prostate	0 (0)	0 (0)	1 (5)
CA. Breast	0 (0)	0 (0)	1 (5)
Gastritis	0 (0)	0 (0)	1 (5)
Duodenal ulcer	0 (0)	1 (5)	0 (0)
Gout	2 (10)	0 (0)	0 (0)
Atopic dermatitis	1 (5)	0 (0)	0 (0)
Chronic Urticaria	1 (5)	0 (0)	0 (0)
Veruca Vulgaris	1 (5)	0 (0)	0 (0)
Vitiligo	0 (0)	0 (0)	1(5)

DISCUSSION

Herpes zoster is a major health burden affecting individuals of any age with a higher incidence among individuals aged ≥ 50 years, those with immunocompromised status and in those under immunosuppressant drugs. The risk factors and complications associated with HZ are also higher among this group of individuals. The characteristic presentation of lesion in our study was unilateral painful erythematous, papulovesicular rash, clustered blisters with a red base and edematous plaques. In our study both male and female were equally affected and no significant result was shown for gender. This was supported by several other studies.[13-15] The average total hospital stay for all age groups was also shown to be similar which again supports our study that HZ is not a gender specific disease. Acyclovir, ganciclovir, famcyclovir and valacyclovir are several antiviral agents used for the treatment of HZ since ages. In our study all patients was treated with ganciclovir from the first day of hospital admission. A significant result for treatment with ganciclovir was obtained for reducing total hospital stay among patients in group I (p= 0.047) and group II (p= 0.011). Patients in group III did not show a reduction in hospital stay with treatment with ganciclovir and the results of analysis was not statistically significant among this age group (p=0.545).

Ganciclovir is an acyclic nucleoside and it is structurally similar to acyclovir. The side effects associated with ganciclovir is similar to acyclovir. Clinicians are recommended to monitor any symptoms of neurotoxicity in patients treated with ganciclovir.[16] In our study, none of the patients developed any side effects to ganciclovir. Forty two patients have shown a good prognosis with ganciclovir therapy and 18 patients has shown a favourable prognosis. However, patients with a favourable prognosis were asked to return to the outpatient department if they develop PHN. Two studies from China have reported a good efficacy for ganciclovir in treating severe HZ and HZ neuralgia with few or no adverse effects.[17,18] In our study, supportive therapy with corticosteroids, vitamin B, vitamin C, deproteinised calf blood serum injection, mouse nerve growth factors, calcium gluconate, antihistamines and thymopolypeptides were given to all patients. Analgesics such as diclofenac, ibuprofen and codeine were also given to patients with mild to moderate pain along with gabapentin. A study by Schencking et al reported that the addition of a supportive intravenous vitamin C to patients with HZ has shown a positive effect for the reduction of pain and other HZ symptoms such as impaired concentration and fatigue. It also showed a reduction in the development of PHN.[19] Addition of a local subcutaneous injection of methylcobalamin (MeB12) to patients with HZ has shown an increased efficacy in reducing the pain and discomfort associated with sub-acute herpetic neuralgia (SHN).[20] Neurotrophic vitamins such as vitamin B1 and B12 have a special affinity towards neural tissues. They help in maintaining the nervous system, promote myelination and transportation of the axonal cytoskeleton and also promote regeneration of the peripheral nerves.[21] A study by Shurong et al reported that combination therapy with mouse nerve growth factor and cobamamide for acute herpetic neuralgia has shown good effect in reducing pain compared to monotherapy with these agents.[22] Nerve growth factor is usually produced in the body after a skin injury and is required in the peripheral nervous system (PNS) for the development and maintenance of the sympathetic neurons.[23] In patients with HZ neuralgia, treatment with mouse nerve growth factor can promote wound healing and reduce pain by regenerating the damaged neurons. The anti-inflammatory action of corticosteroids helps to reduce the nerve damage and thereby cause relief of pain. A meta-analysis comparing 5 clinical studies showed that corticosteroids can reduce pain only in acute herpetic neuralgia and it cannot prevent PHN.[24] In our study corticosteroids was given for 3 patients in group I, 2 patients in group II and 3 patients in group III. Among the 8 patients, 6 patients with acute herpetic neuralgia were given prednisolone, 1 patient in group III with trigeminal involvement of HZ was given methylprednisolone and 1 patient in group I with edematous lesion was prescribed dexamethasone ointment. Long term corticosteroid management was not prescribed for any patients in our study. Antihistamines such as desloratadine, chlorpheniramine and citrizine were given to manage itch. All patients have shown improved response to itch with antihistamine therapy.

Pain was the most common symptom seen in all age groups (73%) followed by fever (52%) and itch (12%). Numeric rating score (NRS) was used to calculate pain in

all patients. A score of '0' was considered as no pain, a score of 1-3 was considered as mild pain, a score of 4-6 was considered as moderate pain and a score of 7-10 was considered as severe pain. The pain was described has stabbing and aching pain by most of the patients. The presence of pain and itch along a dermatome is a sign for the onset of HZ infection and this should be an alert for the practitioner.[15] One of our patient in group II developed PHN. Similarly, one patient each in group I, II and III were suspected to develop PHN. Ramsay Hunt Syndrome (RHS) was noticed in one patient in group II. The patient developed pain and blisters on left side of face and ear followed by fever, itch, blurred vision and facial palsy to the left side. The patient with RHS was treated with a combination of ganciclovir and steroid and has shown a good prognosis. Antiviral and steroid combination therapy is the recommended choice for RHS than steroid monotherapy.[25,26] The patient who developed PHN and the 3 patients who were suspected to develop PHN also showed a good prognosis to ganciclovir and gabapentin therapy and have left hospital with a complete remission of pain and rash.

Our study has noticed a total increased incidence of HZ on the thoracic dermatome (30%) in all age groups followed by trigeminal involvement (23.3%). Group I has shown a similar incidence of thoracic (25%) and trigeminal (25%) dermatomal involvement. Both males and females have shown a high involvement of the thoracic dermatome compared to others. The high incidence of thoracic dermatome involvement observed.[15,27,28] Trigeminal, lumbosacral and cervicothoracic involvement was higher among males than females. Lumbar and sacral involvement was higher for females than males. Cervical, thoracolumbar and cervicolumbar involvement was also observed only in females.

Our study has observed an association of underlying diseases at the onset of HZ most commonly among patients in group III. Hypertension was the most common disease seen with 5% in group II and 55% in group III. None of the patient in group I had hypertension. Dyslipidemia, CKD and stroke was seen in equal number of patients in group III (15%). Ten percent of the patients in group II had dyslipidemia and 5% had CKD. Diabetes mellitus (10%), TB (10%) and CHD (10%) was seen in group III. None of the patients in group I and II had DM, TB and CHD. Other conditions observed in group III were COPD (5%), SLE (5%), anemia (5%), Ca. lung (5%), Ca. prostate (5%), Ca breast (5%), gastritis (5%) and vitiligo (5%). Few diseases were noted in group I such as gout (10%), atopic dermatitis (5%), chronic urticaria (5%) and verucca vulgaris (5%). Other diseases observed in group II were RA (5%), hyperthyroidism (5%), T cell lymphoma (5%) and duodenal ulcer (5%). A study by A. Hata et al reported that lung cancer, breast cancer, esophageal cancer, gastric cancer, colorectal cancer, gyneacological cancers, brain tumor, malignant lymphomas, SLE, RA, DM, HTN, CKD and disk hernia are all risk factors for HZ. The study has shown that the reason behind the increased risk of HZ in patients with underlying disease can be due to the decline in VZV cell mediated immunity that occur with conditions that affects the immune system.[29] Results of two studies performed in Germany and Spain have shown a high incidence of HZ hospitalization in patients with RA treated with TNF antagonist. The immunosuppressive effect of TNF antagonist and glucocorticoids used in the management of several autoimmune diseases can lead to HZ.[30-32] Long standing DM can cause decline in the cell mediated immunity thereby increasing the risk of widespread infection such as HZ. The neuronal stress occurring in DM patients due to an impaired diabetic micro-vascular network can lead to viral reactivation and cause HZ.[33] In our study, one of the patient aged 61 in group III with a 3 year history of COPD and a previous history of HZ during his 3rd decade of life had a recurrent episode of HZ which can be due to the decline in his cell mediated immunity due to COPD. This was supported by Yang et al showing an increased incidence of HZ among patients with COPD. The study also reported an increased risk of HZ infection among patients using inhaled or oral corticosteroids for the management of COPD.[34] Steroids can reduce cell mediated immunity by reducing the synthesis of inflammatory cytokines, decreasing the action of antigen presenting cells and by declining the T cell activation.[35]

Stroke was noted in 3 patients in group III. No previous studies have shown stroke has a cause for developing HZ. But patients can develop stroke after an HZ attack. One of the participant in our study had a previous history of HZ ten years ago and had later developed stroke. A study by Schink et al have reported the risk of developing stroke after an attack of HZ with an increased incidence during the 3rd and 4th week of HZ onset. The study has observed a 1.3 fold increased incidence of any variant of stroke within the first 3 months of HZ attack.[36] A meta-analysis comparing 6 cohort studies has also reported the association of stroke after an HZ infection.[37] The other 2 patients with stroke had also a history of other associated diseases such as CKD, HTN and DLP. The decline of cell mediated immunity with age or due to these diseases can be the cause of HZ in these patients. The mechanism behind HZ infection and stroke has been researched. The reactivated VZV can cause damage to the cerebral arteries leading to VZV vasculopathy. The VZV infection in the arteries can cause occlusion and ischemia of the vessels later leading to aneurysm and hemorrhage. Similarly, occurrence of PHN following a HZ infection can also increase the risk of stroke.[36-38] Cardiovascular events have also been associated with HZ incidence. Herpes zoster can increase the risk of CVS diseases within 5 years of HZ onset. However, the risk of CVS disease following an HZ infection is less when compared to that with HTN, DM and DLP.[39] A retrospective cohort study performed in UK has shown that patients are at risk for developing

stroke, transient ischemic attacks (TIA) and myocardial infarction following a HZ infection.[40] The reactivation of VZV can infect the sympathetic and autonomic ganglia that innervate the heart thereby leading to CVS diseases. Interleukin (IL)-6 and cytokines has shown to be higher in patients with HZ and PHN. Cytokines, LDL and inflammatory cells are also responsible for the formation of atherosclerosis. As a result, patients with HZ can also develop atherosclerosis due to the action of IL-6 and cytokines.[39, 41] Herpes zoster infection is high among elderly cancer patients compared to general population with a higher complication for those with hematological cancer than solid cancer. A 1.7 fold increased risk of hematological cancer was noted among patients hospitalized for HZ even after a 10 year follow up. Hence, hospitalization for HZ can be marker for long term risk of cancer.[42, 43] Our study has observed one patient with hematological cancer (T cell lymphoma) in group II and 3 cases of solid cancer (Ca. lung, Ca. breast and Ca. prostate) in group III. Previous history of solid cancers was shown to be higher in our study. Chemotherapy, radiotherapy, organ transplantation, HIV, stress, recent weight loss and psychiatric illness are all risk factors for HZ infection.[44-46] In our study, 2 patients have undergone chemotherapy for cancers and one patient has undergone renal transplantation. Trauma, smoking, diet, tonsillectomy, exposure to pesticides or herbicides are not risk factors for HZ.[45] Smoking and alcohol use can cause a decline in the immune function. But more studies are required to confirm its effects in causing HZ.

A recurrent history of HZ was noted in 3 of our patients with 2 of them developed second episode of HZ within 10 years of first attack and one patient developed second episode approximately 35 years after first attack. Herpes zoster is not a once in a life time disease for most of the patient. A recurrent episode of HZ is most commonly seen among individuals who had a severe and long lasting painful first episode HZ history. According to Yawn et al, due to the high recurrence rate of HZ infection a HZ vaccination is recommended for all patients who had a previous HZ incidence to prevent a HZ recurrent episode.[47] Vaccination is recommended for all patients above 60 years of age and at high risk for the development of HZ infection to reduce incidence of HZ as well as to prevent severe neuropathic complications.[12,40] The vaccine is contraindicated for immunocompromised patients, pregnant women and patients who are allergic to vaccine components.[12]

In conclusion, HZ is a health burden affecting individuals of any age with a higher risk of complications and associated diseases among patients aged ≥60 years and those with immunocompromised status. The similar incidence of HZ among males and females, the total hospital stay among males and females and the high involvement of the thoracic dermatome among both males and females can prove that HZ is not a gender specific disease. Treatment with ganciclovir can reduce hospital stay among young patients (<30 years) and middle aged patients (30-60 years). Elderly patients (>60 years) require more hospital stay due to their weak immune system and other associated underlying diseases which makes HZ more severe. Treatment of HZ should not be limited to just one agent. Combination therapy with antivirals, analgesics and neurotropic agents reduces pain, promotes fast healing and decrease complications. Ganciclovir therapy was safe and had no adverse effects in any patients in all age groups. Gabapentin is effective for managing pain showing a good prognosis in patients among all age groups. Other supportive therapy with vitamin C, Vitamin B1 and B12, mouse nerve growth factor, calf blood serum, and corticosteroids can help regeneration of the damaged neurons and promote wound healing thereby preventing complications.

ACKNOWLEDGEMENT

Author would like to thank Dr. Ligi Isac and Dr. Saramba M.I for their support in reviewing the article for submission.

REFERENCES

1. Johnson RW, Wasner G, Saddier P, Baron R. Herpes zoster and postherpetic neuralgia optimizing management in the elderly patient. Drugs Aging, 2008; 25(12): 991-1006.
2. Roxas M. Herpes zoster and postherpetic neuralgia: diagnosis and therapeutic considerations. Altern Med Rev, 2006; 11(2): 102-13.
3. Jeon YH. Herpes zoster and postherpetic neuralgia: Practical consideration for prevention and treatment. Korean J Pain, 2015; 28(3): 177-84.
4. Lingaraj MM. Clinical study of herpes zoster. J of Evolution of Med and Dent Sci, 2015; 4(72): 12485-92.
5. Tunsuriyawong S, Puavilai S. Herpes zoster, clinical course and associated diseases: A 5-year retrospective study at Ramathibodi hospital. J Med Assoc Thai, 2005; 88(5): 678-81.
6. Sampathkumar P, Drage LA, Martin DP. Herpes zoster (shingles) and postherpetic neuralgia. Mayo Clin Proc, 2009; 84: 274-80.
7. Worme M, Chada R, Lavallee L. An unexpected case of Ramsay hunt syndrome: case report and literature review. BMC Research Notes, 2013; 6: 337.
8. Shaikh S, Ta CN. Evaluation and Management of Herpes Zoster Ophthalmicus. American Family Physician, 2002; 66(9): 1723-30.
9. Strommen GL, Pucino F, Tight RR, Beck CL. Human Infection with Herpes Zoster: Etiology, Pathophysiology, Diagnosis, Clinical Course, and Treatment. Pharmacotherapy, 1988; 8(1): 52-68.
10. Beydoun A. Postherpetic Neuralgia: role of gabapentin and other treatment modalities. Epilepsia, 1999; 40: S51-6.
11. Wang BC, Liu D, Furnback WE, Bifa F, Dong P, Xie L, et al. The cost-effectiveness of pregabalin versus gabapentin for peripheral neuropathic pain

(pNeP) and postherpetic neuralgia (PHN) in China. Pain Ther, 2016; 5: 81-91.
12. Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep, 2008; 57: 1-30.
13. Di Legami V, Gianino M, Ciofi degli Atti M, Massari M, Migliardi A, Tomba GS, et al. Epidemiology and costs of herpes zoster: background data to estimate the impact of vaccination. Vaccine, 2007; 25(43): 7598-604.
14. Chidiac C, Bruxelle J, Daures JP, Hoang-Xuan T, Morel P, Leplege A, et al. Characteristics of patients with herpes zoster on presentation to practitioners in France. Clin Infect Dis, 2001; 33(1): 62-9.
15. Goh C-L, Khoo L. A retrospective study of the clinical presentation and outcome of herpes zoster in a tertiary dermatology outpatient referral clinic. Int J Dermatol, 1997; 36: 667-72.
16. Ernest ME, Franey RJ. Acyclovir and Ganciclovir induced neurotoxicity. Ann Pharmacother, 1998; 32(1): 111-3.
17. Sen Y, Guo-shu L, Wen-ming Z. Clinical evaluation of ganciclovir and acyclovir in the treatment of Herpes Zoster. The Chinese journal of dermatovenerology, 2002: 02.
18. Dong-mei J, Hai-hui S, Ying Z. An open multicenter clinical trial of ganciclovir of the treatment of Herpes zoster. The Chinese journal of dermatovenerology, 2006: 09.
19. Schencking M, Vollbracht C, Weiss G, Lebert J, Biller A, Goyvaerts B, et al. Intravenous Vitamin C in the treatment of shingles: Results of a multicenter prospective cohort study. Med Sci Monit, 2012; 18(4): CR215-24.
20. Xu G, Lv Z-W, Feng Y, Tang W-Z, Xu G(X). A single-center randomized controlled trial of local methylcobalamin injection for subacute herpetic neuralgia. Pain Med, 2013; 14(6): 884-94.
21. Okada K, Tanaka H, Temporin K, Okamoto M, Kuroda Y, Moritomo H, et al. Methylcobalamin increases Erk1/2 and Akt activities through the methylation cycle and promotes nerve regeneration in a rat sciatic nerve injury model. Exp Neurol, 2010; 222(2): 191-203.
22. Shurong W, Bei Z. Curative effects of mouse nerve growth factor combined with cobamamide on neuralgia of acute herpes zoster. Medical journal of national defending forces in southwest China, 2014: 08.
23. Kawamoto K, Matsuda H. Nerve growth factor and wound healing. Prog Brain Res, 2004; 146: 369-84.
24. Chen N, Yang M, He L, Zhang D, Zhou M, Zhu C. Corticosteroids for preventing postherpetic neuralgia. Cochrane Database Syst Rev, 2010; (12): CD005582.
25. R da Costa Monsanto, Bittencourt AG, Neto NJB, Almeida Beilke SC, Moura Lorenzetti FT, Salomone R. Treatment and prognosis of facial palsy on ramsay hunt syndrome: Results based on a review of the literature. Int Arch Otorhinolaryngol, 2016; 20(4): 394-400.
26. Park YM, Kim DR, Park JY, Kim SK, Kim SY, Kim JS, et al. A case of ramsay hunt syndrome diagnosed after kidney transplantation. Kidney Res Clin Pract, 2015; 34(4): 241-4.
27. Dubey A, Jaisankar T, Thappa D. Clinical and morphological characteristics of herpes zoster in south India. Indian J Dermatol, 2005; 50(4): 203-7.
28. Latheef ENA, Pavithran K. Herpes zoster a clinical study in 205 patients. Indian J Dermatol, 2011; 56(5): 529-32.
29. Hata A, Kuniyoshi M, Ohkusa Y. Risk of Herpes zoster in patients with underlying diseases: A retrospective hospital-based cohort study. Infection, 2011; 39(6): 537-44.
30. Gracia-Doval I, Perez-Zafrilla B, Descalzo MA, Rosello R, Hernandez MV, Gomez-Reino JJ, et al. Incidence and risk of hospitalisation due to shingles and chickenpox in patients with rheumatic diseases treated with TNF antagonists. Ann Rheum Dis, 2010; 69(10): 1751-5.
31. Stangfeld A, Listing J, Herzer P, Liebhaber A, Rockwitz K, Richter C, et al. Risk of herpes zoster in patients with rheumatoid arthritis treated with anti–TNF-alpha agents. JAMA, 2009; 301(7): 737-44.
32. Gupta G, Lautenbach E, Lewis JD. Incidence and risk factors for herpes zoster among patients with inflammatory bowel disease. Clin Gastroenterol Hepatol, 2006; 4(12): 1483-90.
33. Heymann AD, Chodick G, Karpati T, Kamer L, Kremer E, Green MS, et al. Diabetes as a risk factor for herpes zoster infection: Results of a population-based study in Israel. Infection, 2008; 36(3): 226-30.
34. Yang YW, Chen YH, Wang KH, Wang CY, Lin HW. Risk of herpes zoster among patients with chronic obstructive pulmonary disease: a population-based study. CMAJ, 2011; 183(5): E275-80.
35. Holt PG, Thomas JA. Steroids inhibit uptakes and/or processing but not presentation of antigen by airway dentritic cells. Immunology, 1997; 91: 145-50.
36. Schink T, Behr S, Thone K, Bricout H, Garbe E. Risk of stroke after herpes zoster - evidence from a German self-controlled case-series study. PLoS One, 2016; 11(11): e0166554.
37. Yang SY, Li HX, Yi XH, Han GL, Zong Q, Wang MX, et al. Risk of stroke in patients with herpes zoster: A systematic review and meta-analysis. J Stroke and Cerebrovasc Dis, 2017; 26(2): 301-7.
38. Nagel MA, Gilden D. The relationship between herpes zoster and stroke. Curr Neurol Neurosci Rep, 2015; 15(4): 16.
39. Wu P-Y, Lin C-L, Sung F-C, Chou T-C, Lee Y-T. Increased risk of cardiovascular events in patients with herpes zoster: A population-based study. J Med Virol, 2014; 86(5): 772-7.
40. Breuer J, Pacou M, Gautier A, Brown MM. Herpes zoster as a risk factor for stroke and TIA: A

retrospective cohort study in the UK. Neurology, 2014; 83(2): e27-33.
41. Zhu S-M, Liu Y-M, An E-D, Chen Q-L. Influence of systemic immune and cytokine responses during the acute phase of zoster on the development of postherpetic neuralgia. J Zhejiang Univ Sci B, 2009; 10(8): 625-30.
42. Yenikomshian MA, Guignard AP, Haguinet F, LaCasce AS, Skarin AT, Trahey A, et al. The epidemiology of herpes zoster and its complications in Medicare cancer patients. BMC Infect Dis, 2015; 15: 106.
43. Sorensen HT, Olsen JH, Jepsen P, Johnsen SP, Schonheyder HC, Mellemkjaer L. The risk and prognosis of cancer after hospitalization for herpes zoster: a population-based follow-up study. Br J Cancer, 2004; 91(7): 1275-9.
44. Insinga RP, Itzler RF, Pellissier JM. Acute/Subacute Herpes Zoster. Pharmacoeconomics, 2007; 25(2): 155-69.
45. Marin M, Harpaz R, Zhang J, Wollan PC, Bialek SR, Yawn BP. Risk factors for herpes zoster among adults. Open Forum Infect Dis, 2016; 3(3): ofw119.
46. Yang YW, Chen YH, Lin HW. Risk of herpes zoster among patients with psychiatric diseases: a population-based study. J Eur Acad Dermatol Venereol, 2011; 25(4): 447-53.
47. Yawn BP, Wollan PC, Kurland MJ, St Sauver JL, Saddier P. Herpes zoster recurrences more frequent than previously reported. Mayo Clin Proc, 2011; 86(2): 88-93.