

A HOSPITAL BASED STUDY ON ASSOCIATION OF HERPES ZOSTER WITH DIABETES MELLITUS

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**ABSTRACT**

Introduction: Herpes zoster (HZ) is a viral infection caused by the varicella zoster virus which presents with both neural and cutaneous manifestations. Diabetes mellitus is an endocrine disorder occurring in people which may result in decreased immunity. Several studies have been done in different parts of the world to look for an association between herpes zoster and diabetes mellitus. This study is done to determine any association between herpes zoster and diabetes mellitus.

Materials and Methods: The study was done on newly diagnosed HZ cases attending the outpatient department of Bir Hospital, Kathmandu. Inclusion criteria include new patients presenting with HZ to the department of dermatology, Bir hospital. Patients who refused to participate in the study, who were below 16 years, suffering from psychiatric illness, lactating and pregnant females, and those taking drugs that can alter blood glucose levels were excluded from the study. The random blood sugar of each patient was done and in patients with raised blood sugar, fasting and postprandial blood sugar were done.

Results: Around 20% of herpes zoster patients were diabetics at presentation, mostly in the age group >65 years in both male and female. Undiagnosed diabetes mellitus was common in HZ patients.

Conclusion: Our study showed a higher incidence of diabetes mellitus in patients with herpes zoster mostly in the age group >65 years. So, elderly patients presenting with herpes zoster should be evaluated for a blood glucose levels.

Keywords: diabetes mellitus; herpes zoster; varicella zoster virus

INTRODUCTION

Herpes zoster (HZ) is the viral infection characterized by unilateral dermatomal rash and pain resulting from reactivation and multiplication of endogenous varicella zoster virus (VZV) that is latent in sensory ganglia due to primary varicella infection.^{1,2}

Herpes zoster and diabetes mellitus, both are common conditions occurring in our part of the world. The average annual incidence of HZ ranges from 2-4/1000 in several studies done in different countries.³⁻⁵ The incidence of HZ was 6.57 per 1000 in a study conducted in a central hospital of Nepal in the year 2007-2008.⁶ Also in another study done in a tertiary hospital in Nepal the annual incidence was 0.55% in the year 2014-2015.⁷ The incidence of HZ increases with increasing age with mean age being ≥60 years.⁸

Diabetes mellitus (DM) is defined as a common metabolic disorder that present as hyperglycemia that gives rise to risk of microvascular damage (retinopathy, nephropathy and neuropathy).⁹ The diagnosis of DM is established when a patient presents with symptoms of hyperglycemia (thirst, polyuria, weight loss, blurry vision) and has a random glucose value of 200mg/dl (11.1mmol/L) or higher.¹⁰

The diagnosis of DM in asymptomatic individual can be established as per the American Diabetic Association (ADA) criteria.¹⁰

The risk factors and potential risk factors for varicella zoster virus reactivation are prior varicella zoster virus (VZV) exposure, age ≥50 years, immunocompromised state, immunosuppressive drugs, human immunodeficiency

virus/acquired immunodeficiency syndrome (HIV/AIDS), bone marrow transplantation or organ transplantation, cancer, chronic steroid therapy, psychologic stress and trauma to name few.¹¹

Early detection of diabetes mellitus can prevent the complications of diabetes and patients with risk factors should be screened for diabetes. There are few studies done which show that HZ is more common in patients with DM.¹²

This study is done to look for association between diabetes mellitus and herpes zoster patient in our set-up.

MATERIALS AND METHODS

It was a case control study which was done on patients of HZ attending outpatient department of Department of Dermatology of Bir hospital, Kathmandu during the period of March 2018 to February 2019. The ethical clearance was taken from the Institutional Review Board of National Academy of Medical Sciences. (Reference no. 1129)

The patients presenting with HZ to the Department of Dermatology, Bir Hospital were included in the study as cases and the age and sex matched patients visiting the Department of Dermatology, Bir hospital with other dermatological condition were included as controls. The cases and controls selected for the study were evaluated for random blood glucose level. In case of abnormal blood glucose level, the patients were advised for fasting and postprandial blood glucose level and managed accordingly by Endocrinology department. The patients refusing to participate in the study, pregnant and lactating women, patients suffering from psychiatric illness, patients below 16 years of age and patients taking drugs that can alter blood glucose level (eg. Steroids, propranolol) were excluded from the study. Both cases and control were explained about the purpose of the study and the methods used. The informed written consent was taken and full confidentiality was assured.

The total number of patients enrolled in the study was 46 cases and 46 controls. The collected data were stored in an electronic database (MS-Excel Sheet). Statistical analyses were performed with appropriate version of SPSS Data based software to get final interpretation.

The criteria for diagnosis of Diabetes mellitus were symptoms of diabetes plus random glucose concentration ≥ 200 mg/dL or fasting plasma glucose ≥ 126 mg/dL or HbA1C $\geq 6.5\%$ or two hour plasma glucose ≥ 200 mg/dL during oral glucose tolerance test.¹³

The disseminated herpes zoster is defined as involvement of 3 or more contiguous dermatome¹⁴ and more than 20 lesions outside the affected dermatome.¹⁵

The results were analyzed using appropriate statistical methods. All the meaningful statistics were worked out. P-value was calculated under the predetermined level of significance (0.05) and Confidence Interval (CI) of 95% was constructed. The results were expressed as percentages, mean \pm standard deviation and median for variables. Appropriate dummy tables were used for data analysis.

RESULTS

The total number of 46 patients who fulfilled the inclusion criteria were included in the study. Age and sex matched individuals presenting to the Department of Dermatology and Venereology for conditions other than herpes zoster were selected as control for the study.

Out of all patients included in the study, the minimum age was 18 years while the maximum age was 87 years with the mean age 50.17 ± 20.16 . Out of 46 cases, 21 (46%) were female and 25 (54%) were male patients with herpes zoster enrolled in the study. The male to female ratio was 1.19:1 (Table 1).

Table 1: Distribution according to age and gender

Age group(years)	Male (%)	Female (%)	Total (%)
16-25	5 (10.87%)	2(4.35%)	7(15.22%)
26-35	3(6.52%)	3(6.52%)	6(13.04%)
36-45	1(2.17%)	5(10.87%)	6(13.04%)
46-55	4(8.70%)	3(6.52%)	7(15.22%)
56-65	5(10.87%)	5(10.87%)	10(21.74%)
>65	7(15.22%)	3(6.52%)	10(21.74%)
Total	25(54.35%)	21(45.65%)	46(100%)

The most commonly affected dermatome in both males and females was thoracic dermatome which was seen in 19(41.31%) patients. It was followed by the cervical and herpes zoster ophthalmicus which was seen in 8 (17.39%) and 7 (15.22%) patients respectively. The frequency of involvement of lumbar dermatome was more in females as compared to males (Table 2).

Table 2: Frequency distribution according to dermatome involvement in patients with herpes zoster

Dermatome	Male (%)	Female (%)	Total (%)
Herpes Zoster (V1)	4(8.70%)	3(6.52%)	7(15.22%)
HZ Maxillary (V2)	0(0.0%)	1(2.17%)	1(2.17%)
Cervical	6(13.04%)	2(4.35%)	8(17.39%)
Thoracic	12(26.09%)	7(15.22%)	19(41.31%)
Lumbar	2(4.35%)	8(17.39%)	10(21.74%)
Sacral	1(2.17%)	0(0.0%)	1(2.17%)
Total	25(54.35%)	21(45.65%)	46(100%)

The severity of herpes zoster was assessed by whether the disease is localized or disseminated. The localized

herpes zoster was seen in 23 male patients and 21 female patients. The disseminated disease was seen in 2 male patients but none of the female patient had disseminated disease (Table 3).

Table 3: Frequency distribution of severity of herpes zoster

Severity	Males (%)	Females (%)	Total (%)
Localized	23(50.0%)	21(45.65%)	44(95.65%)
Disseminated	2(4.35%)	0(0.0%)	2(4.35%)
Total	25(54.35%)	21(45.65%)	46(100%)

Out of 46 patients, 36(78.26%) were euglycemics and 10 (21.74%) were diabetics. Similarly, in controls 39(84.78%) were euglycemics and 7(15.22%) were diabetics. In both cases and controls, none of the patients were diabetics and all diabetics are seen in age group >45 years. There were 7(15.22%) diabetics in age group >65 years in cases of herpes zoster.(Table 4).

Table 4: Comparison of prevalence of Diabetes mellitus in different age groups in cases and controls

Age Groups (Years)	Cases		Controls	
	Euglycemic	Diabetic	Euglycemic	Diabetic
16-25	7(15.22%)	0(0.0%)	7(15.22%)	0(0.0%)
26-35	6(13.04%)	0(0.0%)	6(13.04%)	0(0.0%)
36-45	6(13.04%)	0(0.0%)	6(13.04%)	0(0.0%)
46-55	6(13.04%)	1(2.17%)	5(10.87%)	2(4.35%)
56-65	8(17.39%)	2(4.35%)	7(15.22%)	3(6.52%)
>65	3(6.52%)	7(15.22%)	8(17.39%)	2(4.35%)
Total	36(78.26%)	10(21.74%)	39(84.78%)	7(15.22%)

There was not much difference in the mean blood sugar level in males of most of the age group except age group > 65 years where blood sugar was seen to be more in cases than in control group. There was not much difference in the mean blood sugar in age groups 16-25 years and 26-35 years. There was some difference in the age groups 36-45 years and >65 years with increased blood sugar level in cases. The blood sugar level in age group 46-55 years and 56-65 years was more in controls. (Table 5).

Table 5: Comparison of mean blood sugar level in cases and control in males and females

Age group	Cases		Control	
	Males	Females	Males	Females
16-25	85.4	89.5	89.8	90.5
26-35	88.3	88	98	98.3
36-45	63	126.8	94	92
46-55	95.5	82.7	118.8	155.3
56-65	126.8	98.2	109.6	180.4
>65	147.3	175.7	147.3	129.3

On comparing the blood sugar level of cases and those of controls, in this study the males had mean blood sugar level of 112.08 ± 44.77 mg% in cases and 105.20 ± 30.62 mg% in controls. Among females mean blood sugar level was 111.57 ± 53.42 mg% in cases and 128.19 ± 88.54 mg% in controls (Table 5).

Table 5: Comparison of mean blood sugar level between cases and controls

Gender	Male		Female	
	Case	Control	Case	Control
Mean blood glucose level(mg%)	112.08 ± 44.77	105.20 ± 30.62	111.57 ± 53.42	128.19 ± 88.54
p-value	0.634		0.466	

While comparing the prevalence of diabetes in study groups, it was found that 10 cases out of 46 had diabetes while only 7 out of 46 in control group had diabetes. The p-value is 0.5921 which was not significant (Table 6). Thus, there was no association between diabetes mellitus and herpes zoster.

Table 6: Prevalence of diabetes mellitus in cases and controls

Diabetes Mellitus	Case	Control	P-Value
Yes	10 (21.74%)	7 (15.22%)	p-value= 0.5921
No	36(78.26%)	39 (84.78%)	
Total	46 (100%)	46 (100%)	

DISCUSSIONS

A total of 92 patients were included in the study, out of which males (54.35%) were found to be affected more than females (45.65%) with a ratio of 1.19:1. The result of this study was in accordance with the result of a study done by Pezer M. et al which showed incidence of herpes zoster in male to be 29 (52.7%) and in female 26 (47.3%) showing preponderance of males with the ratio of 1.12: 1.¹⁶ However, the incidence of herpes zoster was found to be higher in females (59.4%) as compared to males (40.65%) in a study done in UK by Forbes HJ. et al.¹⁷ With the above results it was observed that the incidence was higher in females than in males, in the studies conducted in developed countries as compared to the studies done in developing countries. This could be due to less health access to females as compared to males in developing countries.

Herpes zoster can occur at any age but the incidence increases with the increasing age. Our study had 43.48% cases of the age >56 years. The incidences were high both in males and females in older age group. In a study done by Yawn BP et al in USA, showed the mean age at HZ diagnosis was 59.4 years, with 49% patients aged 60 years or older which is consistent to our study. In our

study patients younger than 16 years were not included so incidence in children could not be determined.

The dermatomal involvement in our study showed thoracic dermatome involvement in 41.3%. The cervical and herpes zoster ophthalmicus followed dermatomal involvement with 17.4% and 15.2% respectively. The least affected dermatome was sacral dermatome. The findings were consistent with the study done in Telangana, India which showed thoracic dermatome was most commonly involved 106 (44.2%) followed by cranial 59 (24.6%), cervical 30 (12.5%), lumbar 22 (9.2%) and sacral 15 (6.2%) dermatome.¹⁸ In contrast to our study, the ophthalmic zoster was seen only in 3% cases in a study done by Goh and Khoo.¹⁹

The severity of herpes zoster can be categorized into localized or disseminated disease according to involvement of dermatomes or dissemination of lesions outside dermatome. The occurrence of localized disease was seen in 95.6% of patients and disseminated disease in 4.4% of patients in our study. Out of 2 patients with disseminated herpes zoster, 1(2.17%) had immunosuppression due to HIV. The results of our study correspond to the results of a study done by Ragozzino MW et al with the disseminated herpes zoster cases occurring in 2% and localized cases in 98%.²⁰

In our study, the mean blood glucose level in different age groups was calculated in cases and controls which showed not much difference in the age groups 13-25, 26-35 and 36-45 years. The mean blood glucose level in the age groups 46-55 and 56-65 years showed a higher levels in controls compared to cases. The reason behind this could be because our sample size is small and even a single data can affect the result significantly. Lastly, the mean blood glucose in the age groups > 65 years was seen to be higher in cases.

The mean blood glucose levels in male cases was 112.08±44.77mg% and in controls was 105.20±30.62 mg% with p-value of 0.634 which was not statistically significant. Similarly, the mean blood glucose in female cases was 111.57±53.42mg% and in controls was 128.19±88.546mg% with p-value of 0.466. Thus, the finding was statistically non-significant.

The main objective of this study was to assess if there is any association between herpes zoster and diabetes mellitus. There were 10 (21.74%) cases of herpes zoster with diabetes while 7(15.22%) of control were diabetics while 36 (78.26%) of cases and 39 (84.78%) of control were euglycemic at presentation in our study (p-value=0.5921). This result showed no statistically significant association between herpes zoster and diabetes mellitus. However, Pezer M et al conducted a study which showed

significant difference in the prevalence of diabetes mellitus between the herpes zoster and control group (p= 0.017)¹⁶ which is different from our study.

The number of patients included in the study was small. The study is based on only one centre, so multicentric study should be done. Further research is needed to test this hypothesis.

CONCLUSION

Diabetes mellitus was common in patients with herpes zoster as compared to non herpetic patients but the difference was not statistically significant. Diabetes mellitus was observed in higher frequency in Herpes zoster patients of older age groups (>55 years). We therefore, recommend that HZ can be considered as a criterion for screening of undiagnosed DM in elderly people.

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