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ORIGINAL ARTICLE

Frequency of Postherpetic Neuralgia in Herpes Zoster Patients

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ABSTRACT

Aim: To estimate the incidence ofpostherpetic neuralgia after being infected by herpes zoster virus.
Place and duration of study: This study was conducted in Sharif Medical & Dental College, Lahore from August 2019 to August 2020.
Methodology: A number of 126 patients was included in this research who had history of herpes zoster. Demographic information, medical diagnosis, treatment and symptoms were included in the data collected. Patients with unclear diagnosis regarding herpes zoster were not included in this study. From patient's history, we comprehended the number of patients who developed postherpetic neuralgia after herpes zoster. Severity of pain was judged by the medications prescribed to the patients. Risk factors like age, gender, co-morbidity and localization were also analyzed. We used multivariate logistic regression to analyze potential risk factors. Risk factors were analyzed in order to determine the frequency of postherpetic neuralgia in herpes zoster patients extensively. This gave us a better idea about postherpetic neuralgia occurrence.
Results: Percentage of patients developing postherpetic neuralgia after one month of herpes zoster was 12.7% for age group 50-60. For age group 75-85, this percentage increased up to 26.8%. Neuralgia with severe pain persisted from 9 to 12 months. Mostly patients suffered mild to moderate pain up till 8 months. Patients with ophthalmic localization had 7.6% more chance of developing postherpetic neuralgia than the patients with no localization, after one month of herpes zoster. So, did the patients with co-morbidity.
Conclusion: As the results show, postherpetic neuralgia in herpes zoster patients is a frequently occurring condition. The incidence of postherpetic neuralgia increases with age. As the age increases, so does the chance of postherpetic neuralgia in herpes zoster patients. Ophthalmic localization and co-morbidity, i.e. diabetes mellitus and rheumatoid arthritis, are also related to high prevalence of postherpetic neuralgia. Female population also tend to get more postherpetic neuralgia than male population does.
Keywords: Postherpetic Neuralgia, Herpes Zoster, Incidence, Risk Factors.

INTRODUCTION

Herpes zoster, generally called shingles is common disease occurring in about 2 to 4% people per year.[1] Varicella-zoster virus causes herpes zoster. This is the same virus that causes varicella, also called chickenpox. First, this virus causes varicella and then enters its latent phase, in which it remains dormant in sensory ganglia. After its reactivation from its dormant phase, this virus causes herpes zoster in the respective dermatome.

Herpes zoster's most common complication is postherpetic neuralgia. Herpes zoster is localized sore rash. This heals within a month or two. Another outbreak of this virus results in persistent pain called postherpetic neuralgia. This condition can last up to 1-2 years or more. It is a very painful condition and can impact the lifestyle of patient. Also it can be difficult to treat.[2] Occurrence of postherpetic neuralgia on its own is a very rare condition.[1]

Some writers consider postherpetic neuralgia as the chronic pain after the outbreak of rash while others consider it chronic pain after the healing of rash.[1] In the same way, its classification also varies with different authors. Some authors classify it into acute, subacute and chronic phase.[3] While others, into early and late postherpetic neuralgia.[1]

Acute phase is the initial phase after the breakout of rash, it lasts upto one month. Subacutephase lasts up to 1-4 months and chronic phases persists for more than 4 months. On the other hand, early postherpetic neuralgia occurs 1-6 months after the breakout of rash and late postherpetic neuralgia occurs after 6 months.[1]

Postherpetic neuralgia occurs in almost 30% of all herpes zoster patients.[4] Mostly this risk value increases with age. Patients younger than 50 have 3% chance of developing postherpetic neuralgia while patients over the age of 80 have almost 40% chance of developing this condition. Risk of developing postherpetic neuralgia rapidly increases after the age of 50.[1]

Its treatment includes gabapentin, lidocaine and amitriptyline among many others. Yet, these treatments are limited and not effective in all patients. Treatment and preventive course for postherpetic neuralgia is somehow debatable. Different studies show different results. For example, use of antiviral drugs for prevention of this condition is not clear. Meta-analysis showed that antiviral drugs have no effect on postherpetic neuralgia while a control experimental showed that antiviral drugs do

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decrease the chance of postherpetic neuralgia outbreak.[1] So, overall the treatment strategies are not clear.

According to a study the risk factors of postherpetic neuralgia are old age, fever, extent of herpes zoster infection, ophthalmic localization, impairment of dermatome, diabetes, rheumatoid arthritis, compromised immunity and psychosocial problems.[1]In comparison to males, more females tend to get postherpetic neuralgia.[5,6] Risk factors were analyzed in order to determine the frequency of postherpetic neuralgia in herpes zoster patients extensively. This gave us a better idea about postherpetic neuralgia occurrence.

There are not many studies that have investigated the incidence of postherpetic neuralgia in herpes zoster patients. That is why this study was conducted to estimate the frequency of postherpetic neuralgia in herpes zoster patients.

MATERIAL AND METHODS

Data for this study was collected from August 2019 to August 2020. Only computerized medical records were used. We analyzed data from 126 herpes zoster patients. Demographic information, medical diagnosis, treatment and symptoms were included in the data collected. All patients of herpes zoster diagnosed from Sharif Medical City Hospital, were identified from the database of the hospital. After this, medical records of selected patients were reviewed. Patients with unclear diagnosis regarding herpes zoster were not included in this study. Ethical Committee of the institution approved my research.

In this study, we considered postherpetic neuralgia as any pain that continued for one month at least, after the herpes zoster diagnosis. The patients that complained of pain even after four months were also included in this study. Patients were selected on the basis of diagnosis of postherpetic neuralgia and also the medication prescribed to them. Medication included topical painkillers, opioid pain medication and antidepressants.[5] The total pain spell was measured for as long as the patient complained of pain and painkillers were prescribed. In this study, the longest duration of pain was up to 7 years.[7] Further information regarding risk factors like age, gender, co-morbidity and localization was also collected. Co-morbidity included rheumatoid arthritis, diabetes mellitus and psychological problems during the period of herpes zoster. Data regarding use of painkillers before the diagnosis was also collected.

The duration of postherpetic neuralgia was judged from the time period of prescriptions. Severity of the condition was assessed from the medication prescribed.[5] SPSS was used to analyze data. First, we diduni‌variate analysis of potential risk factors of postherpeticneuralgia. The factors that had P <0.1 in the univariate analysis were then used to build a multivariate regression model. We used this model to judge the influence of each risk factor on the incidence of postherpetic neuralgia. The same risk factors were used for multivariate regression analysis of patients who had pain even after four months of the herpes zoster diagnosis.[1,8]

RESULTS

Initial search of database resulted in 256 patients out of which only 126 were selected at the end. Patients were selected on the basis of diagnosis of postherpetic neuralgia and medication for this condition prescribed to them to confirm the diagnosis. Also the patients with unclear diagnosis regarding herpes zoster were eliminated from the study. 48% of the total patients of herpes zoster were of 55 or more age (Table 1). This shows the influence of age even on the frequency of herpes zoster.

Table 1: Incidence of herpes zoster in different age groups (n=126)

Age (years)	n	Incidence
50 or less	11	2.3
51 –60	15	3.8
61 –70	16	5.4
71 –80	18	6.8
81 - 90	40	9.4

Postherpetic neuralgia was diagnosed in 7% patients after one month of herpes zoster diagnosis and after 4 months in 3% patients. We observed that these percentages were greatly influenced by age (Table 2). It shows that with time the chance of developing postherpetic neuralgia decreases, if the patient had not already developed it.

Table 2: Postherpetic neuralgia percentage 1 and 3 months after the diagnosis of herpes zoster

Age (years)	%age after 1 month	%age after 4 months
50 or less	0.8	0.4
51 – 60	4	0.9
61 – 70	6.8	2.9
71 – 80	11	3.5
81 – 90	19	9.5

Univariate analysis resulted in age, diabetes mellitus, ophthalmic localization, psycho-pharmaceuticals usage being the potential risk factors for the incidence of postherpetic neuralgia. On the other hand, multivariate analysis resulted in only age and ophthalmic localization being the independent factors supporting the risk of postherpetic neuralgia development. Table 3 shows the influence of risk factors on the development of postherpetic neuralgia after one month of diagnosis of herpes zoster.

Table 3: Influence of risk factors on the development of postherpeticneuralgia in herpes zoster patients after 1 month

Factors	Variables	%
Gender	Female	6.8
	Male	6.4
Age group	50 or less	1.7
	60 – 70	8.6
	More than 80	18.4
Ophthalmic localization	Absent	6
	Present	12.8
Co-morbidity	No diabetes	6.2
	Diabetes	13.8
	No use of psycho-pharmaceuticals	6.1
	Use of psycho-pharmaceuticals	11.4

The frequency of postherpetic neuralgia development is more in females than in males (Table 3). This frequency also increases with the age of patient. Ophthalmic localization and co-morbidity also increases the risk of postherpetic neuralgia. Table 4 shows the influence of risk factors on the development of postherpetic neuralgia after four months of diagnosis of herpes zoster.

Table 4: Influence of risk factors on the development of postherpetic neuralgia in herpes zoster patients after 4 months

Factors	Variable	%
Gender	Female	3
	Male	2.4
Age group	50 or less	0.5
	60 – 70	3.3
	More than 80	9.4
Ophthalmic localization	Absent	2.4
	Present	5.9
Co-morbidity	No diabetes	2.3
	Diabetes	6.9
	No use of psycho-pharmaceuticals	2.6
	Use of psycho-pharmaceuticals	3.9

If the patients develop postherpetic neuralgia four months after the onset of rash, the influence of age, localization and co-morbidity is same as that in patients who develop it after one month. These factors increase the frequency of postherpetic neuralgia incidence. After the age of 50, the frequency and severity of pain increased. If the pain was more severe than the duration of postherpetic neuralgia was also long. Patients with mild pain had almost 6.9 months duration of pain, moderate pain lasted up to almost 10.5 months and severe pain lasted up to one year. After one year of diagnosis, almost 11 patients still complained about mild to moderate pain. Most of these patients become pain free within seven years' time period.

Table 5: Follow up of postherpetic neuralgia patients

Gender (age of diagnosis)	Pain at 1 year	Years of follow up
Women		
50	Mild	1
69	Moderate	6.9
70	Mild	5.5
74	Mild	5.7
80	Mild	6.8
84	Mild	6
88	Mild	5.6
90	Mild	6.8
Men		
67	Moderate	7
73	Mild	6.2
82	Mild	6.7

Out of total selected patients almost 33.2% patients developed postherpetic neuralgia at some point after herpes zoster. According to all the above mentioned results women are more likely to get postherpetic neuralgia than men. So are patients of more age and suppressed immunity. The incidence of postherpetic neuralgia are increasing over the time, especially in older patients.[9,10] Studies show rapid increase in postherpetic neuralgia since 1940s[9]. The knowledge about its frequency is very important for its proper management.

DISCUSSION

The results of this study are somehow similar to the result of another study[3]. Out of all the risk factors included in this study, only age and ophthalmic localization independently influenced the incidence of postherpetic neuralgia. Our study was retrospective, this means that the data might be insufficient due to factors like under-reporting or wrong diagnosis. Our investigation was based upon the data collected from database according to the complaints of patients related to pain. So, we depended on the judgment of patients. There could have been some patients, who even though suffered mild pain, but did not consult a doctor. They could have self-treated themselves with some analgesics. Usually people consult doctor when they suffer from severe pain and not when they have mild pain. So, this study may include only those patients who suffered moderate to severe pain. This could describe the difference in results from some other studies. Consequently, we would like it to be clear that our study was based on the clinically presented cases of postherpetic neuralgia. Also the diagnosis of most postherpetic neuralgia patients selected for this study, were mostly based on the judgment of doctors. The presence of herpes zoster or postherpetic neuralgia was not confirmed by any diagnostic tests in many patients. Due to this, it might be possible that the diagnosis were wrong and hence, the data misjudged.

Other factors like discontinuation of treatment, death and relocation might also have reduced the number of postherpetic neuralgia incidence in this study. Another weak point of this study could be that we did not knew exactly the extent of pain and severity of rash the patients had as we judged it on the basis of prescription. This could alter the influence of potential risk factors we analyzed. The number of patients included in this study were also limited. This could be a problem when generalizing the results.

The results of this study supports the results of many previous studies[1,3,5,10]. These studies also reported more incidence of postherpetic neuralgia in old people. Hence, we can support that old age influences the frequency of postherpeticneuralgia. This can be due to the fact that with age the immunity of a person starts declining, making it easy for the virus to infect the person.[11] We also found that the incidence of postherpetic neuralgia is almost null in children. This result supports another study doneto investigate the incidence of postherpetic neuralgia in children. We also observed that the frequency of postherpetic neuralgia is more in immunosuppressed patients i.e. the patients who had diseases like diabetes mellitus. Stress can also increase the incidence of postherpetic neuralgia. We also found the effect of ophthalmic localization of the incidence of postherpetic neuralgia like many other researches[1].

This study also observed the clinical duration of postherpetic neuralgia. It can take up to seven years to clear up. But that is just according to the data we collected. It might last longer than that. We also observed that the frequency of postherpetic neuralgia development is more in females than in males.[6,7,12] This could be an indication that

females immune system responds to the herpes zoster in a different way than males. Furthermore, severity of pain was also measured as mild, moderate and severe. This was based on the prescription of medicines. This helped us in estimating the severity of postherpetic neuralgia. Some other studies estimated the severity by survey[13].

We perceived that the percentage of postherpetic neuralgia patients have not decreased since some study conducted in 1975[14]. This might indicate that the preventive medications i.e. antivirals, used since then may not be working in postherpetic neuralgia patients.[15] The risk of postherpetic neuralgia is increasing almost 4–5% per year.[2] Some countries recommend herpes zoster vaccine in people aged above 50 to prevent zoster and postherpetic neuralgia.[6] Therefore, if herpes zoster and postherpetic neuralgia are to be managed clinically, their incidence, management and risk factors must be clearly understood.

CONCLUSION

As the results show, postherpetic neuralgia in herpes zoster patients is a frequently occurring condition. The incidence of postherpetic neuralgia increases with age. As the age increase so does the chance of postherpetic neuralgia in herpes zoster patients. Ophthalmic localization and co-morbidity, i.e. diabetes mellitus and rheumatoid arthritis, are also related to high prevalence of postherpetic neuralgia. Female population also tend to get more postherpetic neuralgia than male population does.

Conflict of interest: None

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