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ORIGINAL ARTICLE

Herpes Zoster Post Covid-19 Vaccination

JAVERIA HAFEEZ[1], SAKINA SADIQ MALIK[2], UZMA BASHIR[3], AYESHA HAFEEZ[4], AQSA NAHEED[5], TEHSEEN NAVEED[6]
[1]*Assistant Professor & Consultant Dermatologist CMH Rawalpindi*
[2]*Assistant Professor & Consultant Dermatologist PEMH Rawalpindi*
[3]*Consultant Dermatologist PEMH Rawalpindi*
[4]*Associate Professor & Consultant Chemical Pathologist, CMH Multan*
[5]*Associate Professor of Dermatology, HITEC-IMS (Heavy Industry Taxilla Institute of Medical Sciences), Taxilla*
[6]*Assistant Professor of Dermatology, CMH Peshawar*
Correspondence to Dr. Javeria Hafeez, E-mail: javerianauman@gmail.com Cell: 0321-5133013

ABSTRACT

Aim: To find out association of herpes zoster and changes in disease course like incidence of post-herpetic neuralgia with Covid-19 vaccination.
Study design: Cross-sectional, observational study.
Place and duration of study: Outpatient Department of Dermatology, CMH and PEMH Rawalpindi from 1st January 2021 to 30th September 2021.
Methodology: Seventy three patients presenting with herpes zoster selected by convenience sampling after their verbal and written consent. Demographics, Covid-19 vaccination history, type of vaccination, dermatome effected, co-morbids and presence of post herpetic neuralgia were recorded in them.
Results: Mean age of participants was 48.09±15.73 years with 50 (68.5%) were males and 23 (31.5%) were females. 33 (45.2%) were vaccinated and 36 (49.3%) were non-vaccinated against covid-19. Maximum patients were vaccinated with Sinopharm i.e. 19(57.6%).8 (24.2%) patients developed the lesions after first dose and 25(75.8%) after 2nd dose of vaccination.
Conclusion: Herpes zoster risk is increased with covid-19 vaccination.
Key words: Herpes Zoster, Covid-19 vaccination.

INTRODUCTION

After first reported infection from Wuhan (China) in December 2019, a novel virus was identified which is responsible for the present Covid pandemic and was named Severe Acute Respiratory Corona Virus 2 (SARS-Cov-2) by WHO. In an effort to reduce the virus transmission and hence reducing the mortality and morbidity associated with this deadly disease two types of vaccines are being used i.e. mRNA vaccines and viral vector vaccines.[1] At least 13 of such vaccines have been developed.[2] The Pfizer BNT-162b2) vaccine was listed for WHO Emergency Use Listing (EUL) on 31 December 2020; SII/Covishield and AstraZeneca/AZD1222 vaccines on 16 February; Ad26.COV 2.S developed by Johnson & Johnson on 12 March 2021; Moderna (mRNA 1273) on 30 April 2021; Sinopharm was listed on 7 May 2021 and the Sinovac-Corona Vaccine was given EUL on 1st June 2021[3].

Functional exhaustion of cytotoxic lymphocytes i.e. Natural Killer cells and cytotoxic T lymphocytes is correlated with Covid-19 infection, hence breaking anti-viral immunity.[4] This can lead to reactivation of different viruses like herpes-virus 6 ,7 and Epstein Bar virus.[5] Such effects can also be predicted with covid-19 vaccination.

There are few case reports indicating increased risk of herpes zoster reactivation in Covid effected patients and now case reports are showing herpes zoster reactivation even after covid-19 vaccination.[6,7] Herpes Zoster has reported concurrently or after COVID-19 onset. However it may precede the onset of illness and may act as an indicator of latent COVID-19 infection. This should raise the suspicion of COVID-19 diagnosis in patients with asymptomatic HZ.[8]

Worldwide 399 cases of Herpes zoster reactivation have been reported post covid-19 vaccination.[9] After having varicella, the virus of Varicella Zoster remains latent in dorsal root ganglia of spine and trigeminal ganglia .On reactivation it causes a painful vesicular rash in sensory dermatomes of dorsal root ganglia or 1st, 2nd or 3rd branches of fifth nerve usually.

The purpose of this study is to find the association of herpes zoster with covid-19 vaccination and its effect on different aspects of disease.

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MATERIALS AND METHODS

It was a cross-sectional observational study. Study was conducted in the Outpatient Department of Dermatology in CMH Rawalpindi and PEMH Rawalpindi over a period of 09 months from 1st January 2021 to 30th September 2021, after permission from IRB CMH Rawalpindi: Ref. no.197/9/21 of IRC/ERB certificate dated 22/9/21. All the patients reporting to outpatient dermatology department with herpes zoster like presentation were examined and questioned by consultant dermatologists and were included in the study only after their written consent. Thorough history taking, clinical examination alongwith Tzanck smear testing was done for establishing the diagnosis of herpes zoster. Their records can be counterchecked from the computer database of hospital management system (HMS). History of recent covid-19 infection and vaccination against Covid-19 was also taken. Co-morbids were investigated. Treatment in the form of oral acyclovir for 5-7 days and pain killers were given. Weekly follow up for 4 weeks were done for each patient and they were asked to report to the consultant in case of post herpetic neuralgia even after 4 weeks. Data was recorded with three consultants simultaneously to avoid any error. Quantitative data was analyzed by SPSS version 21. Inferential statistics were calculated using chi-square and T-tests depending on the numerical or categorical nature of variables being compared.

RESULTS

There were 50(68.5%) males and 23(31.5%) females with mean age 48±15.7 years. Thirteen patients (17.8%) had Trigeminal herpes zoster, 21(28.8%) had cervical dermatome involvement, 28(38.4%) had thoracic dermatome involvement, 8(11%) had lumbar and 3(4.1%) had sacral dermatome involvement. 45 (61.64%) had uni-dermatome involvement, 22(30.1%) had zoster duplex, 5(6.84%) had three dermatomes involved and only 1(1.36%) had disseminated zoster. All patients recovered in 7-14 days without any complications. Thirty three herpes zoster patients (45.2%) were vaccinated against covid-19, 36 (49.3%) were un-vaccinated and 4(5.5%) recovered from Covid-19 in the last 4 weeks. Minimum days of onset of Herpes zoster post vaccination was 2 days and maximum 123 days with mean of 40.3±27.2 days (Table 1).

Twelve patients (16.4%) had diabetes, 3(4.1%) had cancer or were having chemotherapy, 5(96.8%) were having immuno-

suppressants for medical reasons and 53(72.6%) did not have any of these comorbidities. Forty patients (54.8%) developed post herpetic neuralgia i.e. pain in the affected area after 4 weeks of onset of herpes zoster (Table 2).

Mean age of Covid-19 vaccinated patients developing Herpes zoster was 57±13.9 years that of un-vaccinated herpes zoster patients was 40.5±12.9 years and that of Herpes zoster patients who had covid-19 recently was 43±18.2 years. ANOVA showed significant (P=0.00) between groups. Robust test of equality of means showed significance (0.004) by Welch test and 0.009 by Brown Forsyth test. Cross-tabulation of vaccine types with doses of vaccine in patients with herpes zoster rash showed *p*-value of 0.047 which was significant (Fig. 1). Chi-square testing of vaccination type with post herpetic neuralgia showed a *p*-value of 0.231 (Fig. 2).

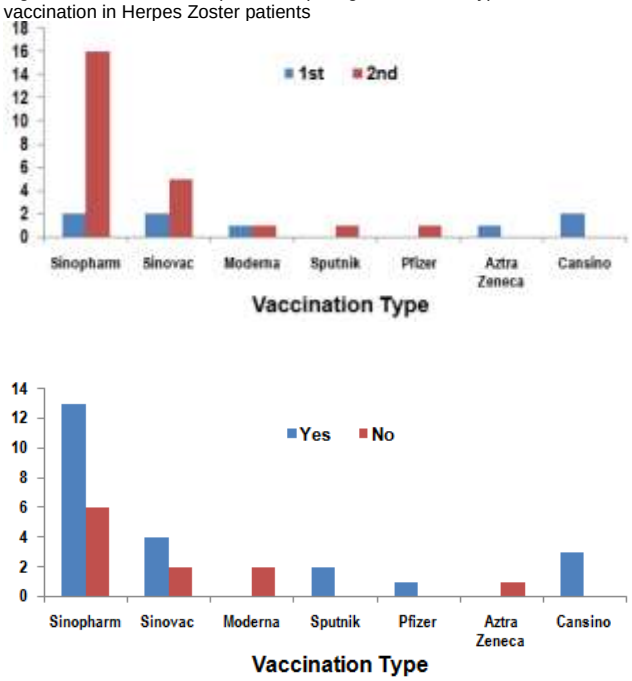
Table 1: Descriptive statistics of patients developing herpes-zoster post covid-19 vaccination (n=100)

Variable	No.	%
Name of Covid-19 vaccination		
Sinopharm	19	57.6
Sinovac	7	21.2
Moderna	2	6.1
Sputnik	1	3
Pfizer	1	3
Aztra Zeneca	1	3
Cansino	2	6.1
Dose of Vaccination		
1st	8	24.2
2nd	25	75.8

Table 2: Comparison of Covid-19 vaccination status with age, gender, co-morbids and dermatome involvement

Variable	Covid-19 Vaccinated	Un-vaccinated	Recently recovered from Covid-19	*P*-value
Post Herpetic neuralgia (n=40)	22 (55%)	16 (40%)	2 (5%)	0.176
Gender				
Male	19 (26%)	29 (39.7%)	2 (2.73%)	0.087
Female	14 (19%)	7 (9.58%)	2 (2.73%)	
Comorbids				
Diabetes	4	6	2	0.149
Cancer/Chemotherapy	-	3	-	
Immuno suppressants	1	4	-	
Nil	28	23	2	
Dermatome involved				
Trigeminal	9	4	-	0.130
Cervical	11	8	2	
Thoracic	9	18	1	
Lumbar	3	5	-	
Sacral	1	1	1	

Fig. 1: Results of Chi-square comparing vaccination type with doses of vaccination in Herpes Zoster patients



DISCUSSION

Different studies have shown reactivation of varicella zoster virus after vaccination for yellow fever, hepatitis A, rabies and influenza.[10] Recently case reports and case series have shown VZV reactivation post covid-19 vaccination, post covid-19 recovery and even as a harbinger of present covid-19 infection.[8] Mechanism is not clear but this may be attributed to innate or cell mediated immune defense failures due to host immune response diversion to vaccination or infection.[10] In a review article Iwanga et al[9] in Aug 2021 has reviewed 20 articles and identified 399 cases of Herpes zoster post covid-19 vaccination proving that vaccine related herpes zoster has been reported world-wide including Spain, Turkey, Portugal, USA, Israel , Greece, India, Italy, Finland, Lebanon ,Taiwan and Holland. Maximum number of post Covid-19 HZ was reported by Barda et al[11] from Israel. We have reported 33 such cases in our study, making it a pilot study in this aspect from Pakistan.

Mean age was 58.9 years with range of 21-94 years in the review article. 54 were females and 46 were male and in 299 cases gender was not reported[9]. While the mean age in our study was 57±13.9 years in the present study which is comparable to other studies. 26% of vaccinated patients developing Herpes zoster were male and 19% were female in our study which is contrary to the statistics in the narrative review. But if in 299 cases in which gender was not mentioned were taken into account, the results would have been different.

In review of 20 articles of VZV (Varicella Zoster Virus) reactivation post covid-19 vaccination 12 cases involved Trigeminal nerve, 11 cervical dermatomes, 24 Thoracic dermatomes and 7 in lumbosacral dermatome. So thoracic was the most common dermatome involved. In our study cervical dermatome was the most common dermatome involved in covid-19 vaccinated population i.e. in 11 cases, followed by trigeminal and thoracic with 9 cases each, 3 involving lumbar dermatome and 1 involving sacral dermatome. In un-vaccinated population Thoracic dermatome in 18 cases was the most common dermatome involved followed by cervical in 8 cases, Lumbar in 5, Trigeminal in 4 and sacral in 1 case respectively[10].

In our study maximum number of Herpes Zoster cases were reported after Sinopharm (N=19), followed by Sinovac[7], Moderna (2), Cansino (2) and 1 case each with Sputnik, Pfizer and Aztra Zeneca. In a review of article published in 2021 reporting Herpes zoster following Covid-19 vaccination, maximum cases i.e. 351

were reported with Pfizer, 28 with Moderna, 14 with Aztra Zeneca and 6 with other vaccination types. In this study 77 cases occurred after 1st dose of vaccine, 32 after 2nd dose and in 290 cases it was not clear whether they occurred after 1st or 2nd dose or after Single dose vaccination. Maximum number of days was 24 and minimum was 01 with mean of 6.75 for herpes zoster post covid-19 vaccination dose.[9] Results are different from our study in which 8 cases occurred after 1st or single dose vaccination and 25 after 2nd dose. Maximum gap in number of days post vaccination for occurrence of Herpes zoster was 123 days in our study and minimum was 2 days with mean of 40.3 days.

Female gender, family history, auto immune diseases like rheumatoid arthritis and systemic lupus erythematosus, asthma, diabetes and chronic obstructive airway disease are established risk factors for reactivation of VZV.[12] In a study carried out in Israel Over weight BMI 25-30 (32%), smoking (18%), followed by Obesity BMI: 30-40 (15%), Hypertension (11%), Diabetes (7%), Asthma (5%), Heart disease (4%), CKD (4%) Immunosuppression (2%), Cancer(1%) were the risk factors associated in VZV reactivation post covid-19 vaccination.[11] In our study 4 patients with VZV reactivation post covid-19 vaccination had diabetes, 1 had immunosuppression and 28 had no risk factors compared to 6 patients having diabetes in the unvaccinated group, 3 having cancer or chemotherapy and 4 having immunosuppression. In patients developing VZV reactivation post Covid-19 infection, 2 had diabetes. We did not look for obesity, hypertension and smoking in our patients.

One of the most troublesome complication of Herpes zoster is neuropathic pain occurring within 3 months of viral reactivation called post-herpetic neuralgia with prevalence of 6-8% in 1st year post herpes zoster.[13] 55% of Covid-19 vaccinated people in our study developing VZV reactivation developed post herpetic neuralgia compared to 40% in non-vaccinated and 5% in covid-19 recovery group. Which shows a positive trend in vaccinated population but the results cannot be generalized with this small population size.

CONCLUSION

Covid-19 vaccination can be related to VZV reactivation and that too with an increased incidence of post zoster neuralgia as compared to the un-vaccinated population. But multi-center study with a large population size covering all the vaccinated individual data is required for establishing a positive association and a causal relationship.

Conflict of interest: Nil

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