Trends in Herpes Zoster Infection in Saudi Arabia; A Call for Expanding Access to Shingles Vaccination

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Received: July 2022 Accepted: August 2022; Published: September 1, 2022.
Citation: Saleh F. Alqifari et al. Trends in Herpes Zoster Infection in Saudi Arabia; A Call for Expanding Access to Shingles Vaccination. World Family Medicine. 2022; 20(9): 6-13. DOI:10.5742/MEWFM.2022.9525130

Abstract

Background: Data on Herpes Zoster (HZ) incidence and complications in Saudi Arabia (KSA) are unknown. We aim to evaluate the trends in HZ cases and complications in Saudi Arabia to aid decision makers in optimizing vaccine access.

Methods: A retrospective survey was conducted among patients with history of HZ throughout KSA between June and December 2021. 68 patients were included and data were collected by online questionnaire and telephone interviews.

Results: Females were predominantly affected by HZ. Overall mean age at diagnosis was 39.43±16.50 years. Among all the symptoms; painful blisters were frequently reported in 81% of participants. Symptoms continued for <30 days in two-thirds of the participants, while others remained symptomatic for a longer period. Most females, 40 (59%), were non-pregnant or lactating at time of the infection. Medications used were analgesics, antiviral drug therapy and herbal remedies with 36 (53%) using analgesics alone. The majority of participants, 56 (82%), were not vaccinated against HZ.

Conclusion: HZ is a prevalent condition affecting a wide range of patients including geriatrics. Available vaccine products help in reducing both the incidence of HZ and its complications. With the given efficacy of the vaccine products, vaccine access should be widened across KSA.

Keywords: Herpes Zoster, Healthcare, Vaccination, Shingles, Public Health

Introduction

Herpes zoster (HZ), generally known as shingles, is an extremely contagious dermatomal rash characterized by painful blistering that results from reactivation of the varicella-zoster virus (VZV) (1). Since the rash appears to spread in a belt-like pattern, the name "shingles" is derived from the Latin word "cingulum," which means "belt" or "girdle". VZV is frequently contracted early in childhood and manifests as chickenpox (varicella), after which the virus lies dormant in the dorsal root ganglia (1). The reactivation of the latent VZV has been related to the weakening of immunity that occurs with aging and several immunocompromised states (2). The disease spreads via aerosol and direct skin contact. It manifests as vesicular lesions of the primary infection (chickenpox) and is often characterized by an itchy, painful vesicular rash that commonly starts on the head and face, in addition to fever and malaise (3). Although the pain may last longer, the HZ rash usually lasts 7 to 10 days, with the skin healing entirely in 2 to 4 weeks (4).

HZ is primarily a disease of nerve tissue, but the acute and long-term manifestations require a multidisciplinary management approach. Complications of HZ can be dermatological (e.g., secondary bacterial infection) or neurological (e.g., postherpetic neuralgia (PHN), segmental paresis, stroke or herpes zoster ophthalmicus (HZO); a condition in which the infection involves the first division of the trigeminal nerve). Disseminated zoster occurs mainly in immunocompromised patients and, in the case of visceral location, can lead to pneumonia, encephalitis, with associated cognitive impairment and sensory or motor deficits, and hepatitis with a 5–10% fatality rate (5). Ocular involvement is one of HZ serious complications. It can affect the eyelid leading to blepharoconjunctivitis, the episclera/sclera causing episcleritis/scleritis or it can affect other structures of the eye causing uveitis, retinal necrosis, optic neuritis or oculomotor palsies (6). The most common encountered complication is PHN, which is a very debilitating condition. PHN is defined as persistence pain lasting for 3 months after the onset of the infection which is often accompanied with burning, throbbing, steady or intermittent pain (7). Prevalence of PHN increases with age, and most cases occur above 50 years of age. Even though the disease is usually mild, its complications, particularly PHN, may significantly burden the patient, caregivers, the healthcare system, and employers (8).

Acyclovir, valacyclovir, and famciclovir are three antiviral drug therapies used to manage HZ infection. These modalities help reduce the length and severity of the illness. Analgesic medications can help in reducing the pain, while itching can be relieved with wet compresses, calamine lotion, or colloidal oatmeal baths (7).

For the prevention of HZ infection and its complications, the United States Food and Drug Administration (USFDA) approved two vaccine products, SHINGRIX® and Zostavax®. These products are approved for adults 50 years and older (7).

Zostavax® is a single-dose live attenuated vaccine that has been recommended in older adults as a way to reduce the incidence and duration of HZ infection and PHN. Zostavax® reduced the incidence of HZ infection in those aged 60 years and older and in those aged 70 years and older by 51.3% and 38% respectively, and the incidence of PHN by 66.5% and 66.8% respectively. Serious side effects related to the vaccine were reported in only a few cases including uveitis, sciatica and lumbar radiculopathy (9).

SHINGRIX® is a two-dose recombinant subunit vaccine regimen which was approved by the USFDA in October, 2017 as HZ prophylaxis with an overall efficacy of 97.2% among participants 50 years of age or older. The commonly reported side effect is injection-site reaction with a minority of patients experiencing hypotension with syncope (10).

HZ infection remains a major public health issue worldwide despite the recent advances in its management and prevention. With an estimated one million cases occurring annually in the United States, the incidence ratio is approximately 4 cases per 1,000 with increasing incidence among individuals 60 years and older (10,11). In Saudi Arabia, the incidence of HZ and HZ-related complications remains unknown. A few independent small studies have provided some insight on incidence and outcomes of HZ, but no inclusive data from multiple regions of Saudi Arabia has been reported to date. More importantly, to date, the HZ vaccine in Saudi Arabia is still not available despite the effectiveness of the vaccine products and its availability in many countries. As a result, it is crucial for decision-makers and healthcare practitioners to remain updated on the most recent research on the disease burden of HZ infection, its sequelae, and vaccination.

Our protocol aims to evaluate the current trends in HZ infection and its complications in Saudi Arabia to aid decision-makers in optimizing vaccine access. The reported studies about the incidence, prevalence, and complications of HZ infection in Saudi Arabia are insufficient. Only three studies were conducted in three different healthcare centers.

An observational retrospective cross-sectional study from 963 records of King Fahd Hospital (KFH) dermatology clinic, Albaha region, was conducted between January 2017 and December 2019. It reported HZ infection as the second most common viral skin disease among the study group with a prevalence of (20.8%) among other viral skin infections. The study found 200 HZ cases with males constituting (52.9%) of the sample. The Prevalence of HZ in relation to age was (3.5%) for patients less than 18 years, (35.1%) for patients between 18-36 years, (27.1%) for patients between 37-54 years, and (34.2%) for patients above 54. The study showed that HZ infection increased with age, which is in agreement with other regional and global data. Also, it showed that HZ largely affects males in contrast to females (12).

In King Fahad Hospital of the University in Alkhobar, a retrospective study was conducted at the outpatient clinic of the dermatology department for the period between

January, 2010 and December 2014. A variety of viral skin infections were diagnosed, and HZ comprised (7.7%) of the total skin infection cases with no specific age distribution of the total reported cases. A previous report studying the pattern of skin diseases in the eastern province of Saudi Arabia between 2002-2003 reported that HZ incidence was 6.2%. The increase in incidence could be attributed to increased incidence of diabetes mellitus, use of immunosuppressive drug therapy and increased lifespan of patients who are more prone to HZ (13).

Another retrospective case-control study of HZ infections in patients with systemic lupus erythematosus (SLE) conducted at King Saud University Hospital between 1982 and 2006 found that HZ infections are more common in SLE patients and are associated with significant morbidity. Immunosuppressive therapy and severe lupus symptoms might increase the risk for HZ infection regardless of illness flare or immunosuppressive therapy. Patients with SLE have a higher risk of infection, with 11–23% of all hospitalized patients developing serious infections, and 50% of all SLE patients developing major infections during the course of their condition. Furthermore, HZ is the most common viral infection in SLE patients around the world (14).

Materials and Methods

Study Design

This is a retrospective study of HZ infected cases conducted in Saudi Arabia between June 2021 to December 2021. A total of 68 participants with a history of HZ who completed the study survey were included. Patients with incomplete records were excluded. The survey was conducted via an online questionnaire for (50 Participants) from multiple regions in Saudi Arabia, and through telephone interviews for (18 Participants) whose contact information was obtained from the electronic medical records at MOH hospitals. Informed consent was obtained for all participants. The study protocol was approved by the medical ethical committee in the Al-Qassim region, Saudi Arabia.

Data Collection

The survey contains variables that assist in reporting the HZ prevalence and complications. It includes demographic data: age, gender, age at incidence, history of chickenpox, chickenpox vaccination status, HZ symptoms, duration of HZ symptoms, HZ vaccination status, medication therapy utilized for symptoms management, and history of concomitant pregnancy or lactation.

Data Analysis

Descriptive statistics were utilized to describe variables of interest in the study. Mean and standard deviation were calculated for continuous variables, and frequency was reported for categorical variables.

Results

The study included 68 participants with a mean age of 43.60±16.53 years. Females constituted around 63% of the sample. The mean age of incidence of HZ in this sample was 39.43±16.50 years. Of all participants, 42 (61.8%) had reported a history of previous chickenpox during childhood, 9 (13.23%) of the participants denied being infected at any point in their life, and 17 (25%) of them did not know if they had a history of chickenpox or not. A considerable percentage of the sample 31 (45.6%) didn't know if they were vaccinated against chickenpox, 18 (26.5%) had the vaccine, and 19 (28%) were not vaccinated. Baseline characteristics of participants are illustrated in Table 1.

The spectrum of experienced symptoms of HZ reported by the participants includes painful blisters, fever, fatigue, headache, diarrhea, vomiting, sensitivity to light and rash. A summary of the number of the reported individual symptoms is shown in Figure 1.

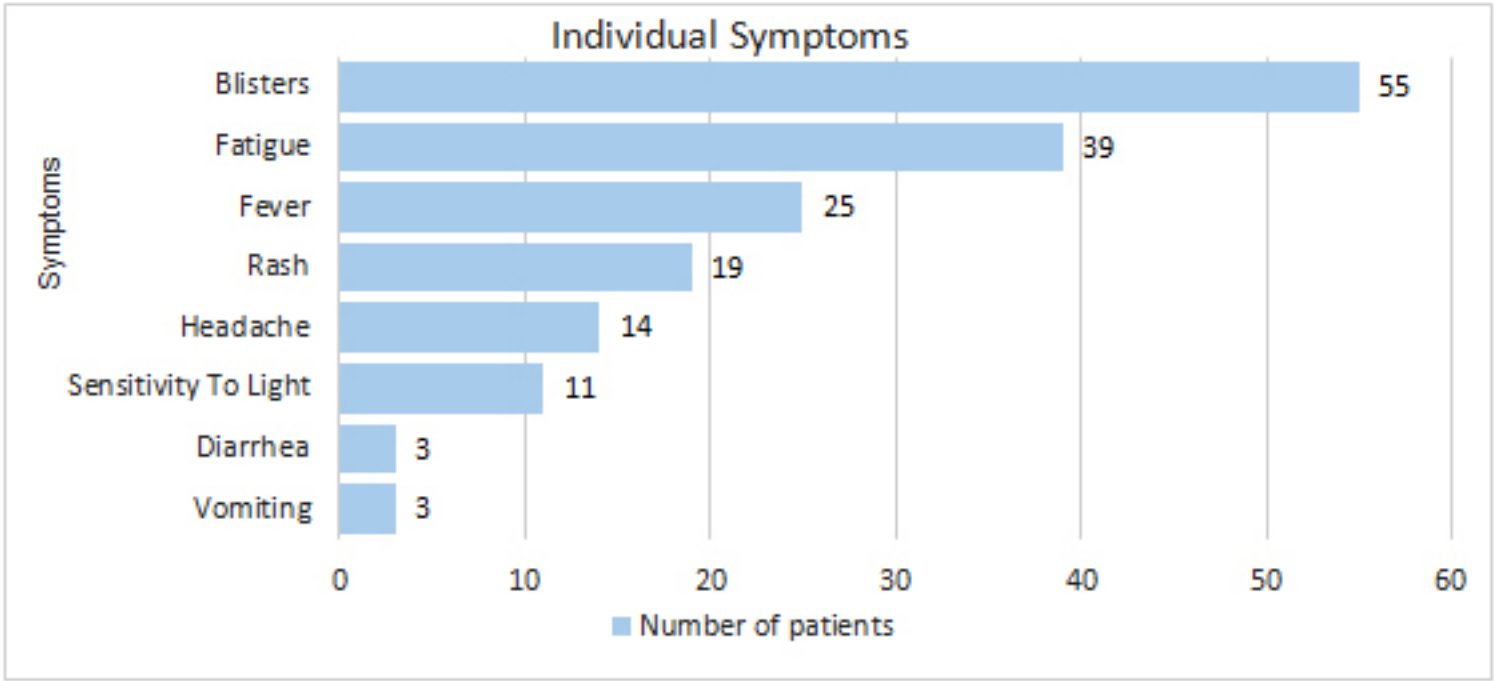
Painful blisters were the most frequently reported symptom in this sample which were experienced in 55 patients as demonstrated in Figure 1, with 13 (19.11%) of the participants having only painful blisters as the presenting symptom, and others had painful blisters along with other groups of symptoms as shown in Figure 2.

The reported symptoms in different age groups were variable according to gender, group of symptoms and duration of the symptoms. A summary is shown in Table 2.

Table 1: Baseline characteristics of participants

Characteristics		Mean ± SD
Age (years)		43.60 ±16.53
Age of incidence		39.43 ±16.50
		N (%)
Gender	Female	43 (63.2%)
	Male	25 (36.8%)
History of chickenpox	Yes	42 (61.8%)
	No	9 (13.23%)
	Don't know	17 (25%)
Chickenpox vaccination status	Yes	18 (26.5%)
	No	19 (28%)
	Don't know	31 (45.6%)
Shingles symptoms duration	Less than 30 days	44 (64.7%)
	1-3 months	21 (30.9%)
	More than 3 months	3 (4.4%)
Shingles vaccination status	Yes	2 (2.9%)
	No	56 (82.4%)
	Don't know	10 (14.7%)
Medication therapy used	Herbal remedies	5 (7.4%)
	Analgesics	9 (13.2%)
	Analgesics+ Antivirals	36 (52.9%)
	Analgesics+ Antivirals+ Herbal remedies	5 (7.4%)
	Antivirals	13 (19.1%)
History of concomitant pregnancy or lactation	No pregnancy or lactation	40 (58.8%)
	Pregnancy only	3 (4.4%)
	Lactation only	2 (2.9%)

Figure 1



Our sample showed an overall variability in the symptom constellations as summarized in Figure 2.

Figure 2: Number of patients for different combination of symptoms.

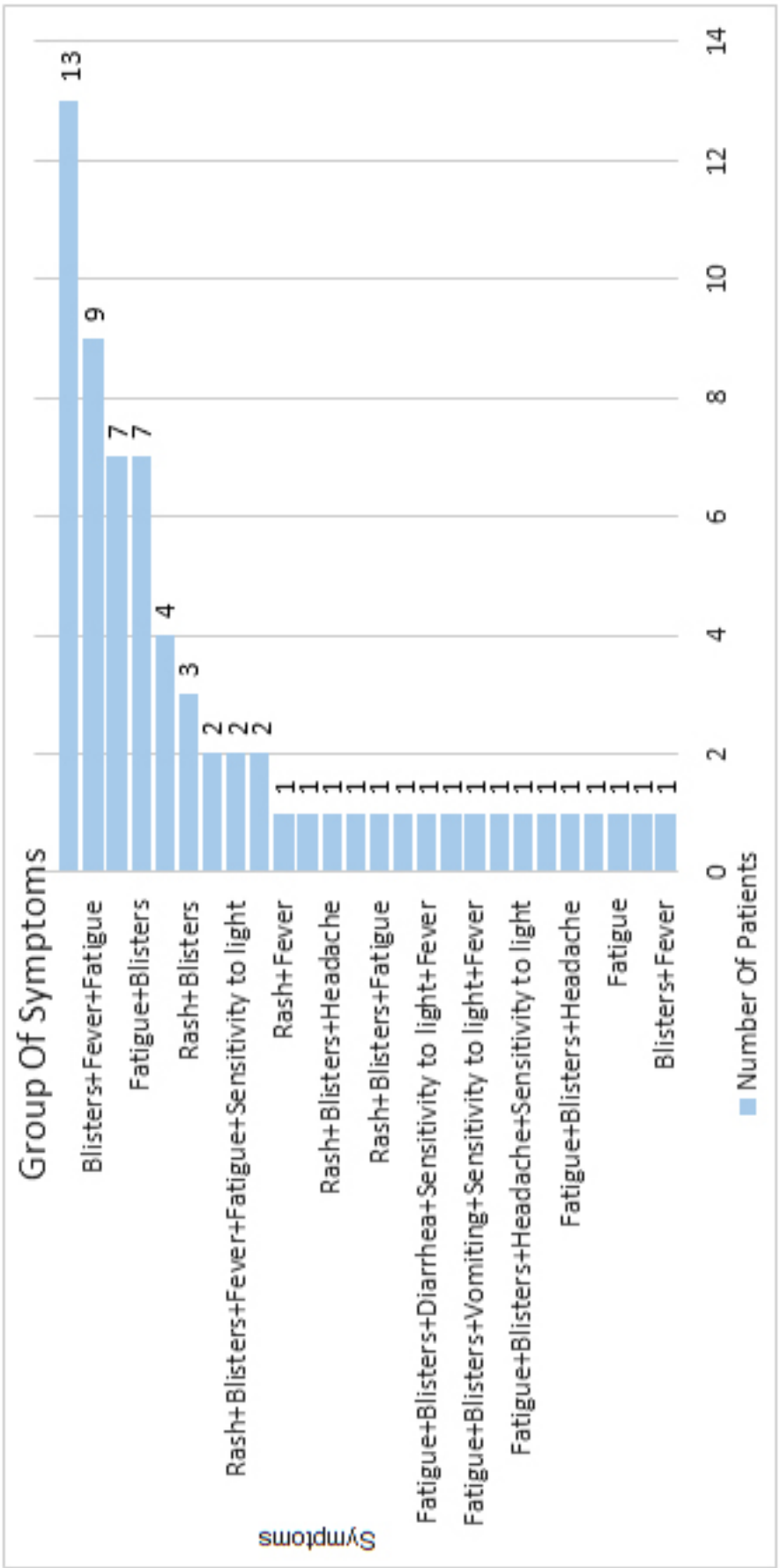


Table 2. Summary of reported symptoms in each age group.

AGE YEARS	GENDER		SYMPTOMS		DURATION OF SYMPTOMS		
	Male	Female	Less than 3	More than 3	≤1 Month	1-3 Months	≥3 Months
≤ 10	1	-	1	-	1	-	-
10-19	2	4	4	2	3	2	1
20-29	2	11	8	5	9	4	-
30-39	6	11	11	6	15	2	-
40-49	6	4	7	3	7	3	-
50-59	4	7	2	9	4	6	1
60-69	4	4	2	6	3	4	1
≥70	-	2	-	2	2	-	-

Discussion

The topic of HZ vaccination and complications has not been explored comprehensively in Saudi Arabia. We lack epidemiological and clinical data as no studies in Saudi Arabia have yet investigated the need for broad vaccine access and its implications. To our knowledge, this is the first comprehensive study to emphasize the current trend of HZ infection implying the need for vaccine access in Saudi Arabia. Unlike earlier hospital-based studies, the present research relies on evaluating HZ cases from multiple regions in Saudi Arabia and analyzes the cases according to a variety of symptoms, duration of symptoms, complications, use of different medications, history of chickenpox and vaccine status, rendering this protocol more representative of HZ characteristics across Saudi Arabia.

We showed that HZ infections predominantly occurred among females with a female-male ratio of 1.72:1. Our result is consistent with a previous systematic literature review of HZ incidence worldwide conducted by van Oorschot et al. in 2021. It estimated that female preponderance is more common than male (15). The finding is in contrast to findings from nearby countries that showed a male to female ratio of 4:1, 2.5:1, and 3:2 in Qatar, Nepal, and Iran, respectively(16–18).

The reason behind gender differences in the incidence of HZ infection remains unknown; a review in this regard attributed this to gender bias at the time of diagnosis as females usually seek medical attention more frequently than males (19). It is also hypothesized that physiological stressors and hormonal changes among females may also have an effect on HZ prevalence (20).

The incidence of HZ is thought to rise with age and to frequently affect the elderly. However, in this report, the maximum incidence was in the age group between 30–39 years (25%), followed by 50-59 years (16%). Minimum incidence was observed in the groups of extreme age, less than 10 years and above 70 years, which was 1.5% and 2.9%, respectively, as shown in Table 2. The findings are consistent with a study by Al-Ghamdi et al. done in the southern Albaha region of Saudi Arabia in 2020, which indicated that HZ primarily affected adults in their 30s and 40s (12).

Similar to a Canadian study by van Oorschot et al, the disease-defining symptoms of rash and painful blisters were reported by nearly all patients (21). As expected, with increase in age, the number and spectrum of symptoms also increased. Patients above the age of 50 had more than three symptoms combined with a longer duration of symptoms. Additionally, only three individuals in our sample had PHN, and two of them were over the age of 50 years, as shown in Table 2.

In our sample, it was evident that the majority of the symptom constellations and complications affected the elderly. Thus, vaccine access is imperative at a national level.

Pregnancy is one of the major causes of HZ reactivation, leading to maternal and fetal complications (22). Additionally, the presentation of HZ resembles other serious pregnancy complications exposing mothers to extensive and expensive evaluations. Furthermore, medications used for the management of the illness's acute flares may carry more risks than benefits for pregnant females (22,23).

The acute phase and complications of HZ such as PHN hinders patients' quality of life and imposes a huge economic burden on the society and healthcare system with drug costs of $127.34 per episode according to a population-based analysis done in Canada (24). This raises the need for a cost-effective vaccine to prevent HZ infections. The cost of SHINGRIX® vaccine is 122 Canadian dollars per dose and Zostavax®

cost is approximately $176.77 (25). Cost-effectiveness of SHINGRIX® was evaluated in Canadians aged 60 years or older(25). In comparison to no vaccination, the SHINGRIX® vaccine would prevent 554,504 HZ infections and 166,196 cases of PHN. This was estimated to be cost effective with 28.36 Canadian dollars per quality-adjusted life year (QALY). This is below the willingness to pay (WTP) threshold used in Canada and also the proposed threshold in Saudi Arabia (26). Comparing SHINGRIX® against Zostavax® resulted in a $2,513 per QALY, which indicates a preference of SHINGRIX® over Zostavax® is more cost-effective. A similar study done in the United States estimated that in comparison to no vaccination, SHINGRIX® would prevent 103,603 HZ infections, 11,197 PHN cases, and 14,455 other complications, at $11,863 US dollars per QALY. Additionally, compared to Zostavax®, SHINGRIX® would prevent 71,638 HZ infections, 6403 PHN cases, and over 10,582 other complications, resulting in net total cost savings of over $US96 million (27).

Anecdotal reports of vaccine product availability in some MOH facilities have been reported on social media. However, to our knowledge, no targeted vaccine campaigns have been released to the public to date.

Study limitations:
Our study was limited as patient's comorbidity such as diabetes and use of immunosuppressant medications were not assessed in the survey. Recall bias is another limitation of this study as participants were asked to self-report previous history of HZ infection.

Conclusions

HZ is a quite common contagious condition affecting a wide range of residents of Saudi Arabia, especially the geriatric group. Health institutions in Saudi Arabia need to address the concerns regarding the burden of this condition, its catastrophic complications, and its preventive tools. Available vaccines against HZ provide a great effectiveness in reducing both the incidence of HZ and its complications. Widening the vaccine access and incorporating the vaccines in the immunization protocols in Saudi Arabia is important to improve population immunity against HZ infection.

Author Contributions: All authors contributed equally. All authors have read and agreed to the published version of the manuscript.
Funding: This research received no external funding.
Institutional Review Board Statement: The study approved by the ethics committee of Buraydah colleges (Protocol code 22-10-1443, date: 30/5/2021)
Informed Consent Statement: Informed consents have been obtained prior to the start of the interview with each participant in this study. All participants received clear information of the purpose of the study, their rights during completing the questionnaire and withdrawal from data collection at any stage. Data confidentiality and all the requirements in completing the questionnaire. Participation was voluntary and only those who provide informed consent were included in the study.
Data Availability Statement: all the provided data of this study are available by contacting the corresponding authors upon request.
Conflicts of Interest: The authors declare no conflict of interest.

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