

Original article

Epidemiological Features and Risk Factors of Herpes Zoster in Western Libya: A Retrospective Study

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Abstract

Herpes zoster (HZ) is caused by reactivation of varicella zoster virus (VZV). The virus remains latent in dorsal root ganglia and can reactivate, especially in the elderly. However, epidemiology of HZ is influenced by demographics, healthcare access, and vaccination and etc. Higher incidence observed in older adults, women, and certain racial groups. Socio-economic factors, stress, and chronic diseases might contribute to HZ risk. Although, HZ shows no seasonal pattern, though some studies suggest higher incidence in warmer months. This retrospective study aims to evaluate HZ incidence and risk factors in western Libya using medical records at the department of infectious diseases-Tripoli central hospital (2010-2014). The results shown, HZ incidence correlated strongly with age; 52% were over 50 years old. 33.5% of patients had their first HZ episode during hospitalization. Majority of patients had no family history of HZ. Higher incidence rates in spring (28.5%) and summer (33.7%) compared to winter (18%). Herpes zoster ophthalmicus (HZO) occurred in 15.5% of cases, with some eye complications. Common underlying conditions included hypertension (22%), diabetes (19.5%), and GIT issues (15%). 26% of patients reported no other diseases besides HZ. The study provides insights into HZ epidemiology in Libya, highlighting age and health conditions and concluded that minor seasonal variations in HZ incidence were noted, with peaks in summer and spring. Males had higher co-infection rates with HIV and HCV.

Keywords: Herpes Zoster, Shingles, Libya, PHN and Seasonal Variations.

Introduction

Herpes zoster (HZ, Zoster, or shingles) is the clinical manifestation characterized as a unilateral vesicular exanthema with acute neuritis [1]. It is a debilitating illness resulting from the reactivation of the varicella zoster virus (VZV), which is acquired during primary infection (chickenpox) [2]. The virus persists lifelong as latency infection in the dorsal roots of the cranial and spinal ganglia of humans. Especially in the elderly, the virus can reactivate as herpes zoster (HZ) due to decreasing VZV-specific T-cell-immunity, making the person at high risk for development of HZ [3]. The estimated lifetime risk of HZ in the general population is approximately 30%, with the risk increasing sharply after 50 years of age [4]. However, unlike varicella, HZ occurs predominantly in the elderly stage, and its appearance has no epidemic character. Many studies have shown that HZ shows no seasonal pattern [5], whereas others have shown a higher incidence in the warmer time of the year, as a consequence of increased exposure to ultraviolet (UV) light [6]. However, the epidemiology of herpes zoster (shingles) is influenced by various factors, including demographic trends, healthcare access, and vaccination practices [7]. The diagnosis of HZ is based on the clinical signs and symptoms without any further laboratory procedures requirements, since the etiologic diagnosis of HZ is rarely necessary [8]. On the other hand, HZ is associated with a number of risk factors, the most important of which are age, gender, race and certain chronic diseases. Incidence of HZ increases with certain conditions that impair cell-mediated immunity, and can be severe, resulting in hospitalisation; in some cases, serious complications can occur. A greater incidence of herpes zoster was shown in older people, women, black race [9-12].

It has been speculated that the socio-economic status, place of residence, alcohol consumption, drug addiction and stress could contribute to the development of herpes zoster. Altogether, the high-risk groups for the incidence of herpes zoster are patients with cancers, HIV infection, autoimmune diseases, hypertension, diabetes mellitus and some other chronic diseases [10,11,13].

HZ is not generally associated with high mortality rates, but its complications can severely impact patients' health and quality of life. Effective healthcare for HZ involves a multi-faceted approach focusing on prevention through vaccination, prompt diagnosis and treatment, management of symptoms and complications, and continuous patient education and support [14]. Preventive measures such as vaccination are crucial for reducing the overall impact of herpes zoster on both individual patients and the healthcare

system. Therefore, this study was designed to evaluate the incidence and epidemiological features as well as the risk factors associated with HZ infection in the western part of Libya.

Methods

Study design

This study is a retrospective study designed to collect data from files of HZV positive patients admitted to department of infectious diseases-Tripoli central hospital. The study was carried out in compliance with the Helsinki Declaration on the ethical principles of medical research involving human subjects following approval by the department review committee of University of Tripoli and a subsequent permission from hospital. Informed consent was waived due to the retrospective nature of the study, as all the data were collected from routine medical records. Confidentiality was guaranteed by omitting names or any personal identifiers. In addition, data were kept secured via out the research process to limit accessibility to a third party

Data collection

The study used data from files of patients admitted to the hospital between 2010 and 2014. Records containing complete prescribing drugs, diagnostic and complications information were used and some of extra data were taken from medical staff when required. All demographic data including age, sex, marital state and risk factors were collected under the supervision of the medical staff.

Statistical analysis

Statistical analysis carried out using the statistical package for the social science program (SPSS.25), all results will be expressed as numbers and percentages, chi-squared tests will be used to test the significance, and P -value < 0.05 is considered as an indication of significant difference.

Results

Characteristics of participants

Demographic characteristics and risk factors of our studied population are outlined in table 1. The patients were transferred from different geographic areas of west side of Libya and admitted to the infectious diseases department, Tripoli central hospital. Of the 200 study subjects, 46.5% (93 subjects) were male and 53.5% (107 subjects) were female, with a relative ratio of 0.87. Therefore, no significant association of HZ and gender was detected, however, we observed a trend of increased probability for zoster in females than males (p -value=0.472). The age of the HZ patients was not normally distributed, ranging from 1 – 90 years with a mean of 58 ± 16.23 years, although HZ was observed among patients of all ages. No significant difference was observed between both genders among all age groups of (p -value=0.275).

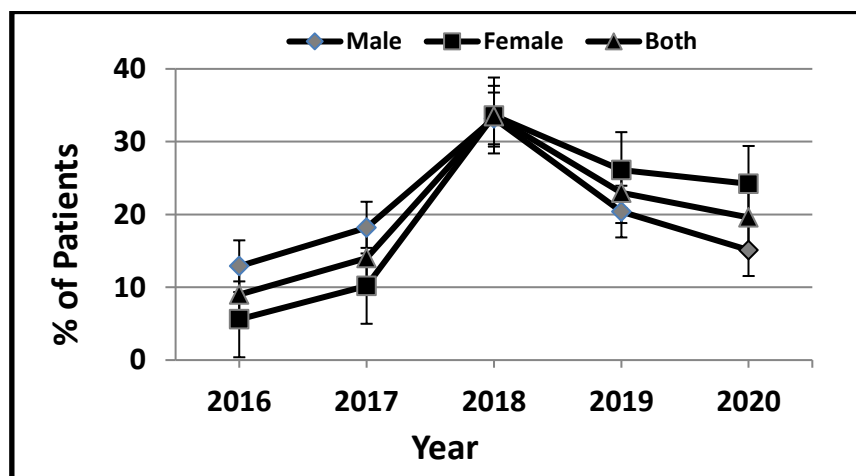
The incidence of the disease was strongly correlated with age, and clearly half of the patients were over 50 yr old (105/200, 52%). The age-adjusted incidence increased with age, ranging from 2.0 per 100 person-5 years in the childhood group (4/200, 2%) to 86.0 per 100 person-5 years (172/200, 86%) in >30 yr-old HZ patients. A striking increase in HZ incidence was seen over the age of 50 yr. Moreover, 33.5% (67/200) of patients were diagnosed with HZ during a hospital admission and this was their first episode of the diseases, therefore it is categorized as primarily attack. Remarkably, 66.5% (133/200) of admitted patients had experienced recurrent episodes of HZ infection. The majority of them had experienced more than one episode annually. The standardized diagnosis rate was slightly higher, but not significant (p -value= 0.581) among women than men. The majority of the cases were married 148/200 (74%, males 59 and females 89) as compared to 52/200 single cases (significantly different p -value = 0.002), and only 5 females were pregnant. Of 200 HZ patients, 197 (98.5%) of the cases have no history of family carrier of the disease. More than 60% of patients were admitted to the hospital after 3-5 days of symptoms and about 20% of patients admitted after 5 days of disease.

Seasonal occurrence

The annual occurrence of HZ cases was not significantly different between males and females. According to data, the highest incidence rate of HZ was recorded during 2018 (33.5%) followed by 2019, 2020, 2017 and 2016, which comprised 23%, 20%, 14%, and 9% respectively (Figure 1). The further analysis of seasonal incidence rates has shown that, which were obtained after grouping the months by seasons, spring (28.5%) and summer (33.7%) exhibited higher incidence rates than winter (18%) and autumn (20.6%). The incidence rates did increase remarkably in summer and spring, although insignificant ($p=0.405$).

Table 1. Demographic characteristics of patients

Variables	Total 200 (100%)	Males 93(46.5%)	Females 107(53.5%)	P value
Age, mean years	58±16.23	51±19.5	59±15.1	0.472
≤10 y	4 (2%)	1 (1.1%)	3 (2.8%)	0.275
11-30 y	24 (12%)	9 (9.6%)	15 (14%)	
31-50 y	67 (34%)	37 (39.7%)	30 (28%)	
>50 y	105 (52%)	46 (49.4%)	59 (55.1%)	
Frequency of viral infection				
Primarily infection	67 (33.5%)	33 (35%)	34 (32%)	0.581
Recurrent infection	133 (66.5%)	60 (65%)	73 (68%)	
Marital state				
Married	148 (74)	59 (63.4%)	89 (83.2%)	0.002
Single	52 (26)	34 (36.6%)	18 (16.8%)	
Pregnancy *				
Pregnant	-----	-----	5 (4.7%)	
Non pregnant	-----	-----	102 (95.3%)	
Family virus carriers				
Family carriers	3 (1.5)	1(1.1%)	2 (1.9%)	0.645
Family noncarriers	197 (98.5)	92(98.9%)	105 (98.1%)	
Days of symptoms before admission				
< 3 days	18 (9)	8 (8.6%)	10 (9.34%)	0.79
3-5 days	135 (68)	65 (69.9%)	70 (65.4%)	
> 5 days	47(23)	20 (21.5%)	27 (25.2%)	

**Figure 1. Distribution of Herpes Zoster patients**

In male subjects, summer showed the highest incidence rate (37.65%) followed by spring (28%) as compared to other seasons. In contrast, in female subjects, no notable variation was found among spring, autumn and summer seasons. Interestingly, winter showed the least incidence rate in female, while male showed the lowest incidence rate in autumn. The male seasonal incidence rate showed a pattern that was similar to the seasonal incidence rate observed in the female subjects (Fig.2).

Affected site

The dermatomal distribution of the initial herpes zoster cases is shown in table 2. Unilateral involvement, whether left or right, of the thoracic region was most frequent and accounted for 52% of the cases (104/200; 42 males and 62 females). Herpes zoster ophthalmicus (HZO) was reported in 15.5% of the cases, and about 3% of this group has suffered from different eye complications. Cervical, lumbar, facial, and sacral involvement were each seen in about 15%, 11%, 3.5%, and 3% of the cases, respectively. None of the initial episodes were bilateral and only 3% of the cases (6 cases) were disseminated. Generally, the zoster episodes were more frequent in right site than the left site (122 vs. 78 cases). For 85% (n = 170) of HZ patients, this was their first episode of the disease and 15% (n=30) had experienced recurrent episode of HZ. Fisher's exact

test has showed that the sex ratio (male/female) of the individuals with zoster episodes in left and right sites was not significantly different ($P=0.561$, 95%CI=0.6259-1.263).

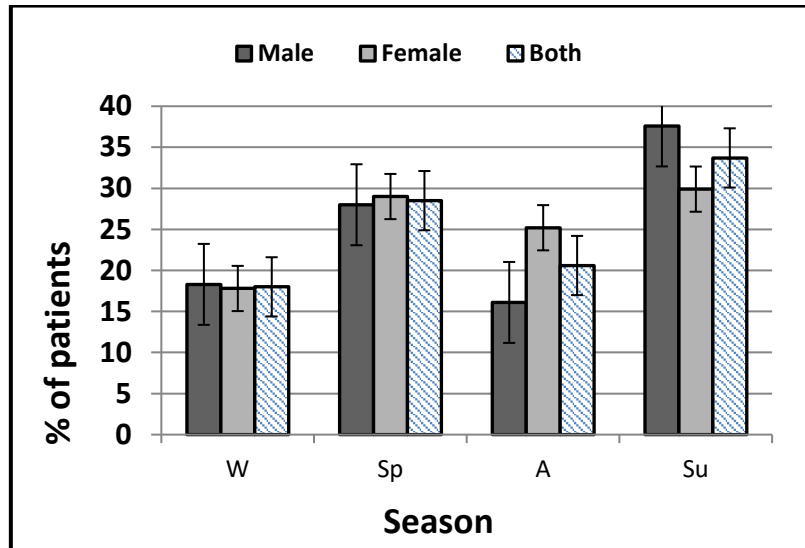


Figure 2. Percentage of HZ patients, (A) Year variation, and (B) seasonal variations

Table 2. Affected Sites of Herpes Zoster

Distribution	All cases: 200 (100%)								
	Male 93 (46.5%)			Female 107 (53.5%)			Both sexes 200 (100%)		
	Lt	Rt	Total	Lt	Rt	total	Lt	Rt	Total
Ophthalmic	7	10	17	8	6	14	15	16	31(15.5)
Facial	0	3	3	3	1	4	3	4	7(3.5)
Cervical	6	12	18	5	7	12	11	19	30(15)
Thoracic	19	23	42	23	39	62	42	62	104 (52)
Lumbur	2	10	12	3	7	10	5	17	22(11)
Sacral	0	1	1	2	3	5	2	4	6(3)
Total	34	59	93	44	63	107	78	122	200
P value	0.367			0.505			0.567		

Underlying disease

Studying the association between risk factors of interest and HSV infection has revealed that high proportion of HSV patients were suffering from some underlying diseases as shown in table 3. Of the 200 patients, 148 (74%) reported to suffer from other disease which was defined as associated risk factors with HZV. The most prevalent diagnoses were hypertension (22%), diabetes mellitus (19.5%), GIT problems (15%), alcohol and drug addiction (15%), heart diseases (10%) kidney diseases (10%), asthma and allergic reactions (8%), hypothyroidism (3%), rheumatoid arthritis and malignancy (2% for each). 52 (26%) patients reported not having any disease other than HSV.

Table 3. Underlying Health Conditions in Herpes Zoster Patients

Key risk factors of interest	Cases N (%)			Odd ratio (CI 95%)	Relative risk (RR)
	Total (n=200)	Males (n=93)	Females (n=107)		
Hypertension	44 (22%)	12 (12.9%)	32(29.9%)	0.35	0.43
Diabetes mellitus	39(19.5%)	14 (15.1%)	25(23.36%)	0.58	0.64
Asthma	8(4%)	3(3.22%)	5(4.67%)	0.69	0.68
Heart disease	10(5%)	6(6.4%)	4(3.73%)	1.78	1.73
Kidney problems	10(5%)	7(7.42%)	3(2.8%)	2.82	2.68
GIT problems	15(7.5%)	9(9.7%)	6(5.6%)	1.8	1.73
Rheumatoid arthritis	2(1%)	-----	2(1.86%)	-----	-----
Hypothyroidism	3(1.5%)	-----	3(2.8%)	-----	-----
Malignancy	2(1%)	2(2.2%)	-----	-----	-----
Alcohol & Drug addiction	15(7.5%)	14(15%)	1(0.9%)	18.78	16.11

Discussion

The present study was conducted to examine the association between shingles and different personal and seasonal factors. The retrospective analysis of clinical records from infectious diseases department, Tripoli central hospital, was applied. The places of residence of the study subjects were mostly in the western areas of Libya, and the incidence during the study period was not affected by weather conditions such as temperature, daily temperature range, humidity, or duration of daylight.

It is known that older individuals and the immunocompromised patients are at a higher risk of developing shingles (Herpes Zoster) because of the increased likelihood of the virus reactivating. Accordingly, this study affirming such finding as the incidence of shingles increased with ageing, this study has found that the highest incidence rate was observed in the individuals older 50 years old. The incidence among this group (105 cases/ 52%) was more than three times that of their younger than 30 aged individuals (28 cases / 14%). Nevertheless, study conducted in Austria have revealed that over 70 % of shingles cases occur in adults aged 50 and over [15]. In general, shingles are known to affect all communities all over the world with different rates, ranging from 1.5 to 3 persons/1,000 annually [16]. In the USA, the rate is noticeably higher where shingles affect 15-16 persons/1,000 each year, which is attributed to the fact that most have had chickenpox as a child [17]. In south western area of Asia, shingles are known to affect 0.88-4.8 persons/ 1,000 annually [18]. Comparable to this study the prevalence of shingles was with a relative ratio of 0.87 persons/ 1,000 annually. Regarding the incidence of amongst childhood this study revealing that it was ranging from 2.0 per 100 person-5 years in the childhood group, however, several studies have reported that the rate of occurrence among individuals under the age of 10 is extremely low (0.74 / 1,000 persons) as compared to individuals over the age of 60 (7.8 / 1,000 persons), even much higher among individuals 75 years and older (18.4 / 1,000 persons) [19-21].

In associations of shingles and gender, we found that only slight variation between males (93 cases/ 46.5%) and females (107 cases/53.5%). Different studies have had support the potential association between the female gender and elevated risk of shingles, where they found a significantly higher rate of incidence among female subjects being 55 years of age or older, which was attributed to differences in the immune systems between the genders. Due to the biological differences between the genders, the virus is more likely to reactivate in the female body than in the male body. The study also cited the higher exposure rate of females to children with chickenpox as one of the reasons behind the higher incidence rate [22-24].

In this study we examined the association between shingles and seasonal factors. In terms of seasonal incidence rates, which were obtained after grouping the months by seasons, summer and spring exhibited higher incidence rates than winter and autumn, with comparable results between males and females. In agreement to our results, study conducted during 2015 has concluded similar results, with little variation between males and females [25]. In addition, several studies have found that occurrence of shingles increased in the summer and fall and decreased in the winter where a higher rate of occurrence among females and individuals in the 50-70 years age group [26,27]. Although, these observations had been explained by Zak-Prelich et al. whom reported that exposure to UV rays increased the rates of shingles affecting the face among the male subjects, and Nelson [19] who reported that exposure to short day lengths affects several parameters of the immune system [28,29].

The dermatological distribution of herpes zoster in this study has revealed that no correlation was found between the affected site and time of occurrence. However, the thoracic vertebrae site has showed a greater incidence rate followed by ophthalmic and cervical regions as compared to other sites, such results were in agreement to different studies [30,31].

To address the risk factors associated with the HZ incidence, this study categorized the participants into the 10 risk factor groups: hypertension, diabetes mellitus, asthma, cardiac disorder, renal disorders, GIT disorders, rheumatoid arthritis, thyroid problems, malignancy, alcohol and drug addiction. The obtained results revealed that the highest risk of HZ was recorded among patients with cardiovascular diseases, diabetes mellitus, GIT problems and alcohol/drug addiction. In agreement to our results, a study had been published during 2009 had revealed the incidence of diabetes mellitus shown to be elevated in HZ patients [11]. Yet, other study demonstrating a clear correlation between HZ and cardiovascular [32]. Our study has been shown an association between an increased risk of HZ and several clinical conditions; include obstructive pulmonary disease, Asthma, inflammatory bowel disease, chronic kidney disease, and depression, especially among patients older than 60 years' old [33-35]. Regarding the habits of patients with HZ, the obtained results showed higher incidence of HZ in patients who consumed alcohol and drug addiction. Nevertheless, these data are interesting from an immunological aspect, because immunosuppressive effects of alcohol might affect the reactivation of latent VZV [36].

Conclusion

The study found that the incidence of herpes zoster was not significantly correlated with sex. Though, age was a significant factor, with a higher incidence observed in individuals over 50 years old. However, the study noted minor seasonal variations in HZ cases, with higher incidences recorded during the summer and

spring seasons compared to winter and autumn. Nevertheless, this study highlighted that male had a higher percentage of co-infections with HIV and HCV compared to females, indicating a potential link between these conditions and the incidence of HZ. In summary, this study offers valuable insights into the epidemiology of herpes zoster in Libya, emphasizing the importance of age, underlying health conditions, and seasonal factors in understanding the disease's incidence and management.

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المستخلص

الهربس النطاقي هو مرض يسببه فيروس الحماق النطاقي يظل الفيروس كامناً في العقد الجذرية الظهرية ويمكن أن ينشط مرة أخرى، وخاصة في كبار السن. ومع ذلك، يتأثر علم الأوبئة لـ HZ بالتركيبة السكانية، والوصول إلى الرعاية الصحية، والتطعيم وما إلى ذلك. لوحظ ارتفاع معدل الإصابة لدى كبار السن والنساء وبعض المجموعات العرقية. قد تساهم العوامل الاجتماعية والاقتصادية والإجهاد والأمراض المزمنة في خطر الإصابة بالهربس النطاقي. بشكل عام، لا يظهر الهربس النطاقي أي نمط موسمي، على الرغم من أن بعض الدراسات تشير إلى ارتفاع معدل الإصابة في الأشهر الأكثر دفئاً. تهدف هذه الدراسة الاستيعادية إلى تقييم معدل الإصابة بالهربس النطاقي وعوامل الخطر في غرب ليبيا باستخدام السجلات الطبية في قسم الأمراض المعدية - مستشفى طرابلس المركزي (2010-2014). أظهرت النتائج أن معدل الإصابة بالهربس النطاقي يرتبط ارتباطاً وثيقاً بالعمر؛ 52% كانوا فوق سن 50 عامًا. أصيب 33.5% من المرضى بأول نوبة هربس نطاقي أثناء دخولهم المستشفى. لم يكن لدى غالبية المرضى تاريخ عائلي للإصابة بالهربس النطاقي. معدلات الإصابة أعلى في الربيع (28.5%) والصيف (33.7%) مقارنة بالشتاء (18%). حدث الهربس النطاقي العيني في 15.5% من الحالات، مع بعض مضاعفات العين. وشملت الحالات الكامنة الشائعة ارتفاع ضغط الدم (22%) والسكري (19.5%) ومشاكل الجهاز الهضمي (15%). أفاد 26% من المرضى بعدم وجود أمراض أخرى إلى جانب الهربس النطاقي العيني. تقدم الدراسة رؤى حول وبائيات الهربس النطاقي العيني في ليبيا، مع تسليط الضوء على العمر والظروف الصحية وخلصت إلى ملاحظة اختلافات موسمية طفيفة في حدوث الهربس النطاقي العيني، مع ذروة في الصيف والربيع. كان لدى الذكور معدلات إصابة مشتركة أعلى بفيروس نقص المناعة البشرية وفيروس التهاب الكبد سي.