

Complications of herpes zoster hospitalizations in a reference hospital in Fortaleza-Ceará, 2009-2018

Complicações de internações por herpes zoster em um hospital de referência em Fortaleza-Ceará, 2009-2018

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Abstract

Objective: the aim of this study was to relate sociodemographic, epidemiological and clinical conditions to the occurrence of severe cases of HZ in reference hospital of Fortaleza. **Methods:** this is a cross-sectional analytical study, based on medical records of patients admitted from 2009 to 2018. Pearson's χ^2 test or Fisher's exact test were used when appropriate. **Results:** we analyzed 196 medical records. The presence of complications occurred in 69.9%, the most affected region was the cranial (68.9%), and 1.5% died. The presence of vesicles (PR=1.37; 95%CI: 1.03-1.82; p=0.01) and the choice of antibiotic associated antiviral therapy (PR=0.58; 95%CI: 0.46-0.73; p=0.00) were significantly associated with the severity. **Conclusions:** the disease may be more severe at ages over 50. The presence of lesions in vesicles was associated with a higher prevalence of complications and the use of antibiotics and antivirals as a protective factor.

Keywords: Herpes zoster; Varicella Zoster Virus Infection; Epidemiology; Risk factors.

Resumo

Objetivo: relacionar condições sociodemográficas, epidemiológicas e clínicas à ocorrência de casos graves de HZ em hospital de referência de Fortaleza. **Métodos:** trata-se de um estudo analítico transversal, baseado em prontuários de pacientes internados de 2009 a 2018. Foram utilizados o teste χ^2 de Pearson ou o teste exato de Fisher, quando apropriado. **Resultados:** foram analisados 196 prontuários. A presença de complicações ocorreu em 69,9%, a região mais acometida foi a craniana (68,9%), e 1,5% foi a óbito. A presença de vesículas (RP=1,37; IC95%: 1,03-1,82; p=0,01) e a escolha da terapia antiviral associada a antibióticos (RP=0,58; IC95%: 0,46-0,73; p=0,00) foram significativamente associadas com a gravidade. **Conclusões:** a doença pode ser mais grave a partir dos 50 anos. A presença de lesões em vesículas foi associada à maior prevalência de complicações e o uso de antibióticos e antivirais como fator de proteção.

Palavras-chave: Herpes Zoster; Infecção pelo Vírus da Varicela-Zoster; Epidemiologia, Fatores de risco.

INTRODUCTION

Herpes Zoster (HZ) is an infectious disease caused by the reactivation of primary infection by the VZV. Some symptoms, such as pain, itching, or tingling, appear before the appearance of a skin lesion at the reactivation site. In almost all cases, HZ causes a painful rash that completely disappears in 2 to 4 weeks¹.

During primary infection, VZV infects sensory nerve cells through retrograde axonal transport, going to the dorsal root ganglia near the spinal column or due to viremia of infected T cells, establishing latency for an indefinite period².

Otherwise, if the immune system declines, the VZV is reactivated and, through anterograde transport, proceeds to the sensory cutaneous nerves causing a painful unilateral eruption along the dermatome, mainly in the thoracic, cranial, cervical, or

lumbar regions³.

There are two types of vaccine, one that has the live attenuated virus, with 70% protection effectiveness and another non-living subunit recombinant vaccine, that has 90% effectiveness, and can be administered to immunocompromised individuals^{4,5}. In Brazil, there is a live attenuated virus vaccine that prevents HZ, however, it is only available in the private health network and at a relatively high cost, approximately US\$ 125.00, limiting access to almost all the population that depends on the public health system⁶.

HZ incidence coefficients in North America, Europe, and Asia range from 3 to 5 cases per 1,000 person-years. These values tend to increase as the age grows and, in individuals over 70 years old, the incidence ranges more than double and became

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from 10 to 12 cases per 1,000 person-years⁷. Approximately 1% to 4% of HZ cases are hospitalized due to complications and about 30% of those have a weakened or suppressed immune system. On the other hand, HZ mortality is generally low with values below 0.1/per 100,000 inhabitants in the general population, however, it can increase to 1.2 to 7.2 per 100,000 inhabitants in individuals over 85 years old⁸.

Complications associated with HZ can be: cutaneous, such as bacterial skin infections; ophthalmological problems, such as decreased visual acuity, keratitis, uveitis, and progressive retinal necrosis; neurological disorders such as post-herpetic neuralgia (PHN), facial paralysis, meningitis, meningoencephalitis, meningoradiculitis, and even cerebellitis; pulmonary complications such as pneumonia may still appear; liver diseases such as hepatitis; cardiac disorders such as myocarditis, pericarditis or even cause myocardial infarction^{9,10}.

Besides all these complications, HZ is not a compulsory notification disease in Brazil, and few studies show the characteristics of hospitalized cases of HZ and the factors associated with its main complications. Thus, this study aimed to describe clinical and epidemiological characteristics and explore the association between these factors and complications in hospitalized HZ disease at an infectious diseases reference hospital.

METHODS

Study design

This is a cross-sectional analytical study based on medical records of patients from Fortaleza city who were hospitalized by HZ between the years 2009 to 2018 at an infectious diseases reference hospital, located in the city of Fortaleza in the state of Ceará, Brazil, and that has not been transferred to other units.

The local of study is a public hospital of the Health Department of the Ceará State, recognized as the reference in the treatment of infectious diseases and a teaching hospital, accredited by the Ministries of Health and Education with a medical residency in infectious diseases, as well as a multi-professional residency.

Case definition: A severe case of HZ was defined as a patient who had any kind of complication associated with the condition, namely: cutaneous, cardiac, liver, neurological, respiratory complications, genitourinary alterations, or any other alteration observed⁹.

Independent variables: The independent variables were divided into sociodemographic; epidemiological and clinical aspects corresponding to evolution, laboratory data, and treatment.

HIV-positive individuals were classified as immunodeficiency. In chronic disease, we highlight diabetes, cancer, asthma, kidney diseases, neuropsychiatric diseases, and cardiovascular diseases. The variable "Go to the doctor" was considered every

time the individual looked for medical attention until admission. For the clinical aspects and evolution, we looked for variables such as period of hospitalization, time living with HZ, characteristics of the HZ lesions, location of the HZ lesions, type of HZ lesions, development of a complication, the type of complication, as well as the number of complications. Other variables also were used in this study: the presence of fever, need for intensive care, hematological changes, the evolution of the case (discharge or death), and the type of therapy used. The variable time living with HZ was the time in days from the HZ diagnosis until the hospitalization by HZ.

The relevant changes in the hemogram exam were observed and anemia was classified as a reduction in blood hemoglobin rate lower than expected. Thrombocytopenia was classified as a reduction in the number of platelets compared to reference values. They were included in "other changes" such as thrombocytosis (higher than expected platelet count), neutropenia (reduced neutrophil count in the blood), leukocytosis (increased number of leukocytes), and any other relevant changes found.

Statistical analysis

The collected data were stored in the Epi Info™ version 7.2 program (CDC, Center for control of diseases and Prevention) for later statistical analysis.

Stata version 15.1 (StataCorp, College Station, Texas, USA) was used for statistical analysis. Initially, we calculated the relative frequencies of each qualitative variable and the central trend measures for quantitative variables. Then, a bivariate analysis was carried out with the presence of clinical complications as the outcome variable. Each group of characteristics: sociodemographic, epidemiological, and clinical, were related to the development of complications, to identify any associated factors for the presence of clinical complication.

The results were presented in tables and figures. An error of 5% was assumed and Pearson's Chi-square test or Fisher's exact test were used when appropriate. The prevalence ratio was calculated as well as its 95% confidence interval.

We also performed a spatial distribution of the neighborhood of residence of all those cases. We created thematic maps in ArcMap version 9.2 software (Environmental Systems Research Institute -ESRI, Redlands, CA, USA).

The study was submitted to and approved by the SJH ethics and research committee in Fortaleza-CE, under number 3.106.633.

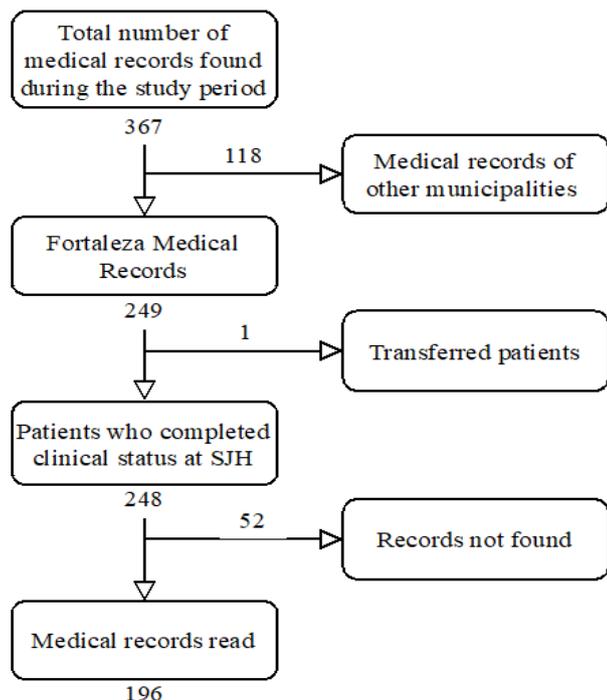
RESULTS

A total of 367 medical records were found during the study, but only 248 hospitalization records were distributed between 2009 and 2018. Of these, it was possible to collect data in 196 (79.0%) of the records, the other ones were not found in the Sector of

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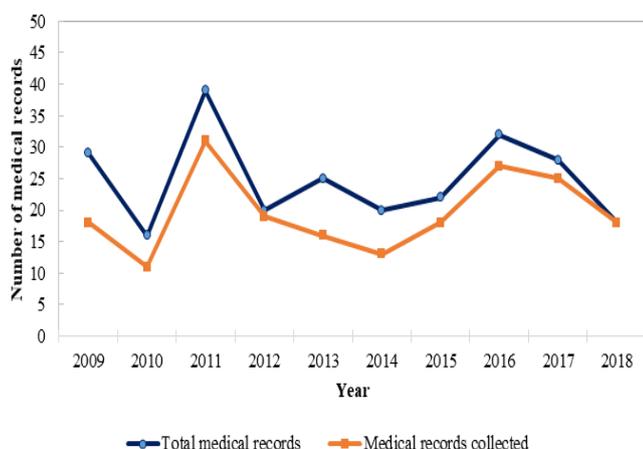
Medical and Statistics Archive of the hospital (Figure 1).

Figure 1. Sample selection process of the medical records during the research.



The year 2011 had the highest number of hospitalizations with 15.7%. From 2012 to 2015, the number of cases remained between 20 to 25 per year, and only in 2016 increased to 31 (12,5%) and decreased in the following years (Figure 2).

Figure 2. Distribution of the number of medical records per HZ hospitalized in the SJH in Fortaleza-CE, 2009- 2018.



HZ hospitalized patients were most frequently male (52.0%), had an active occupation in the labor market (27.5%), and were in elementary school (39.0%). The median age of these patients was 43 years, with an interquartile range of 22 to 65 years. The largest number of hospitalizations occurred in the age group above 50 years (42.3%).

The pilgrimage for medical care was also described so that

53.1% of the affected individuals looked for medical care more than once for the complete resolution of their condition. The median time from disease progression to medical demand was 5 days, with an interquartile range from 4 to 7 days. The period of hospitalization had a median of 7 days and an interquartile range of 5 to 8.5 days. The presence of factors that could worsen the condition was 58.0%. Of these, 34.0% had some type of chronic disease, another 21.0% had HIV infection. About 1.0% of the pregnant women were affected by the reactivation of the VZV. Of the HZ hospitalizations, about 70.0% had some type of complication associated with the condition. A total of 16.0% of patients had more than one type of complication. The most common complications were cutaneous (50.0%) and neurological (16.8%). The cutaneous complications observed were bacterial infections (55.1%), cellulitis (33.7%), atypical lesions (6.1%), and edema (5.1%). As for neurological, neuralgia occurred in 75.8%, headache (15.1%), and other neurological manifestations (9.1%).

Hematological changes were observed in 57 people (38.0%), and in 30 of them (20.0%) there was a decrease in platelet count. The situation was extreme for 3.0% of patients, leading to the need for intensive care. Of the studied hospitalizations, 1.5% died (Table 1).

Table 1. Characteristics of hospitalizations for HZ in the SJH in Fortaleza-CE, 2009- 2018.

Variables	n	%
Sociodemographic		
Sex		
Male	102	52,04
Female	94	47,96
Age group (in years)		
1-10	18	9,18
11-20	28	14,29
21-30	22	11,22
31-40	26	13,27
41-50	19	9,69
>50	83	42,35
Schooling		
Illiterate	11	5,64
Elementary School	76	38,97
High school	36	18,46
University education	5	2,56
Ignored	67	34,36
Occupation		
Active	54	27,55
Retired	47	23,98
Unemployed	14	7,14
From Home	12	6,12

Variables	n	%
Student	38	1,39
Ignored	31	15,82
<i>Epidemiological</i>		
Visits to the doctor		
1	92	46,94
2	92	46,94
3		4,59
4	3	1,53
Risk factors		
No	83	42,35
Yes	113	57,65
Types of risk factors		
Immunodeficiency	42	21,43
Chronic disease	67	34,18
Pregnant	2	1,02
Transplanted	1	0,51
<i>Clinics and evolution</i>		
Characteristics of injuries		
Disseminated	22	11,22
Place	174	88,78
Types of injuries		
Stains	2	1,04
Papules	24	11,44
Vesicles	149	77,20
Pustules	18	9,33
Crust	20	10,36
Reactivation region		
Cervical	3	1,72
Cranial	120	68,97
Dorsal	4	2,30
Thoracic	23	13,22
Other *	24	13,79
Fever		
No	94	48,21
Yes	101	51,79
Complication		
No	59	30,10
Yes	137	69,90
Number of complications		
1	105	53,57
2	25	12,76
3	5	2,55
4	1	0,51

Variables	n	%
Types of complications		
Cutaneous	98	50,00
Respiratory	9	4,59
Neurological	33	16,84
Cardiac	1	0,51
Hepatic	3	1,53
Genitourinary changes	4	2,05
Other**	27	13,78
Types of hematological changes		
Anemia	30	20,00
Thrombocytopenia	30	20,000
Thrombocytosis	1	0,67
Other***	4	2,67
Intensive Care Unit (ICU)		
No	190	96,94
Yes	6	3,06
Outcome		
Cure	193	98,47
Death	3	1,53

* Flank, lumbar, upper limbs, lower limbs, inguinal region, thighs, buttocks;

** Conjunctivitis, decreased visual acuity, blurred vision, otalgia, otitis, disseminated HZ;

*** Eosinophilia, leukocytosis, monocytosis.

A total of 137 patients (70.0%) presented some type of complication associated with the HZ infection. There was no statistical difference between the prevalence of complications between the sexes (PR=0.93; 95%CI: 0.78-1.12; p=0.474), and likewise, the variables occupation and education, with p-values of 0.12 and 0.90, respectively.

The age group was significantly associated with the risk of having complications with advancing age, in particular, ages above 50 years old (PR=1.87; 95%CI: 1.10-3.16; p=0.00).

However, patients classified as retired had a 35% higher prevalence of complications than the active ones (95%CI: 1.07-1.68; p=0.12). There was no difference in the prevalence of complications in HIV-positive people, as well as in those with chronic disease or even in individuals who received an organ transplant.

In clinical characteristics, the presence of vesicles (PR:1.37; 95%CI: 1.03-1.82; p=0.01) and the choice of therapy with the use of antivirals associated with antibiotics conferred superior protection (PR:0.58; 95%CI: 0.46-.73; p=0.00).

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Table 2. Association between the presence of complications and independent variables of hospitalized cases of HZ in the SJH in Fortaleza-CE, 2009- 2018.

Variables	Total	Complications	%	PR	C195%	p-value
Sociodemographic						
Sex						
Male	102	69	67,65	3	-	
Female	94	68	72,34	0,93	0,78 – 1,12	0,474
Age group (in years)						
1-10	18	8	44,44	1	-	
11-20	28	21	75,00	1,68	0,96 – 2,95	
21-30	22	14	63,64	1,43	0,78 – 2,62	
31-40	26	12	46,15	1,03	0,53 – 2,01	
41-50	19	13	68,42	1,53	0,84 – 2,80	
>50	83	69	83,13	1,87	1,10 – 3,16	0,001
Occupation						
Active	54	35	64,81	1	-	
Retired	47	41	87,23	1,35	1,07 – 1,68	
Unemployed	14	11	78,57	1,21	0,86 – 1,69	
From Home	12	8	66,67	1,02	0,65 – 1,60	
Student	38	27	71,05	1,09	0,82 – 1,45	0,121
Schooling						
Illiterate	11	7	63,64	1	-	
Elementary school	76	55	72,37	1,13	0,71 – 1,81	
High school	36	25	69,44	1,09	0,66 – 1,79	
University education	5	4	80,00	1,25	0,67 – 1,35	0,907
Epidemiological						
Immunodeficiency						
No	154	109	70,78	1	-	
Yes	42	28	66,67	0,94	0,74 – 1,19	0,607
Chronic disease						
No	129	89	68,99	1	-	
Yes	67	48	71,64	1,03	0,86 – 1,26	0,701
Transplanted						
No	195	136	69,74	1	-	
Yes	1	1	100,0	1,43	1,30 – 1,57	1,000
Clinics and evolution						
Vesicles						
No	44	24	54,55	1	-	
Yes	149	111	74,50	1,37	1,03 – 1,82	0,011
Therapeutics used						
Antiviral	107	91	85,05	1	-	
Antibiotic	5	4	80,00	0,94	0,60 – 1,46	
Antiviral + antibiotic	84	42	50,00	0,58	0,46 – 0,73	0,000

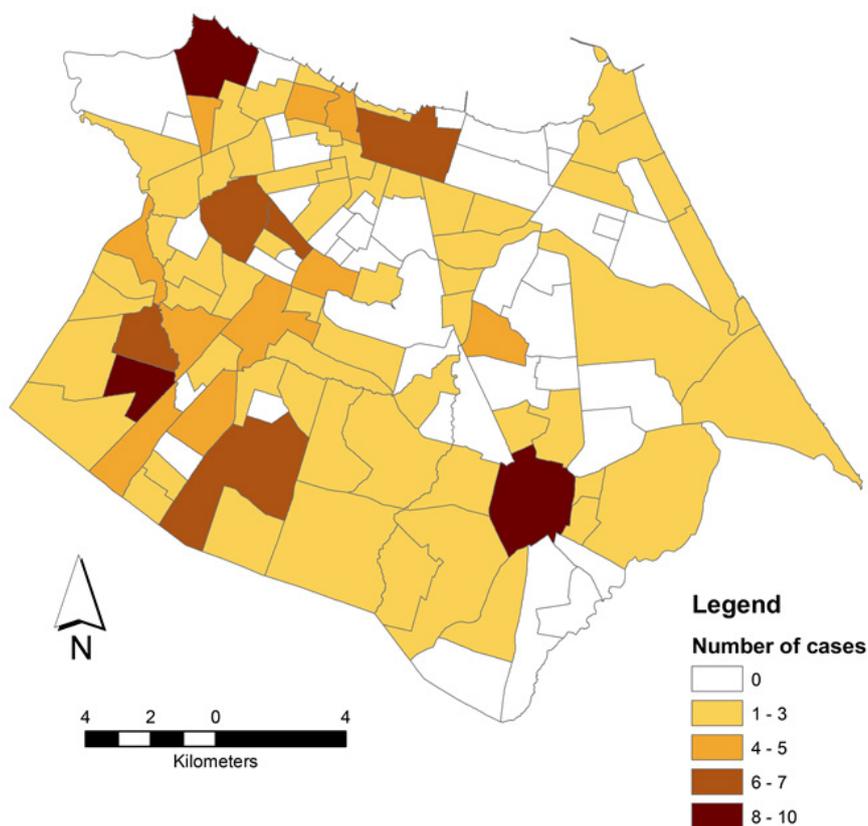
Variables	Total	Complications	%	PR	C195%	p-value
Haematological changes						
No	93	66	70,97	1	-	
Yes	57	39	68,42	0,96	0,77 – 1,20	0,741

Legend: PR - prevalence ratio; CI - Confidence interval; p-value - level of significance.

The spatial distribution of the neighborhood of residence of patients who were hospitalized for HZ encompasses about 63.8% (n =76) of the neighborhoods of Fortaleza-CE. Some neighborhoods in the city located in the southwest (23.9%),

west (19.9%), and southeast (19.4%) regions stood out with high hospital admissions. Thirty-two neighborhoods (27.0%) had only one hospitalization at the referral hospital over the study period (Figure 3).

Figure 3. Spatial distribution of the number of hospitalized patients for HZ in the SJH in Fortaleza-CE, 2009- 2018.



DISCUSSION

This is the first study to investigate the factors associated with severity in the occurrence of hospitalizations for HZ in Fortaleza that is known. The complications of HZ are poorly studied and, consequently, epidemiological information is scarce. In our study, there was an association between the presence of complications and clinical factors, such as the presence of vesicles, and being over 50 years of age. In addition, there was an oscillation in the number of hospitalizations per HZ over the study period.

As a limitation of the study, we can highlight the lack of some medical records in the sector in some years. Some information needed to fill in the variables was either missing or incomplete, thus leading to a high number of ignored data. Another limitation is that this study was carried out in only one hospital

in the capital. Thus, the present study represents a sample of HZ cases in Fortaleza.

The incidence of HZ tends to increase as the population ages increase¹¹, this association may be due to the occurrence of immunosenescence, which is characterized by the natural decline of T-cell function as the age increases and consequent fall in response to VZV¹², or manifests itself in people with weakened immune systems, usually due to health problems and the use of immunosuppressive drugs¹³. The risk of having PHN, which is a type of HZ complication, was also associated with age over 50, immunosuppression conditions, and comorbidities¹⁴.

In the literature, we did not find similar results that associated the presence of vesicles and the severity picture, however,

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most cases of HZ happen with a cutaneous manifestation or the appearance of local infections and, in extreme cases, skin necrosis is possible¹⁵. The same happened with therapy, but studies report that if started correctly and in time, it can decrease the severity of symptoms and avoid possible complications^{16,17}.

The southwest region of the city of Fortaleza is the most populous in the city, as well as the one with the lowest HDI, which justifies the largest number of visits, given that a large part of this population lives in conditions of extreme poverty, without access to basic health services. When it comes to presenting the signs and symptoms of HZ they already need specialized care. In some cases, for the diagnosis and treatment of HZ, the patient comes to seek medical attention more than once. Some studies report that individuals come to see the specialist more than 5 times¹⁸.

Our study observed that the majority of those involved in the research had some factor that could worsen the condition, this finding corroborates with another study that reports that patients with underlying diseases are 1.8 to 8.4 times at risk of developing HZ¹⁹. The presence of chronic diseases such as rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, chronic obstructive pulmonary disease, asthma, chronic kidney disease, type 1 diabetes, depression, and even family history was associated with an increased risk of having HZ²⁰.

The cranial region showed the highest frequency of reactivation by the virus in our study. Infection rates in this region in other studies ranged from 11.5% to 14%¹⁵. Reactivations of the virus in the cranial nerve, specifically the trigeminal nerve, can cause ophthalmic HZ and consequent ocular manifestations such as periorbital skin lesions, conjunctivitis, retinal necrosis, uveitis, and keratitis²¹.

In some studies, the disseminated form of HZ has not been so reported²², in our study just over 10% of the population had virus reactivation in more than one dermatome. In Argentina, this number was much higher, where of 80 patients admitted to the hospital with suspected disseminated HZ, 51.2% were confirmed²³.

The presence of complications occurred in almost 70% of the patients involved in this study, with just over 15% of these having more than one complication. This number was even higher compared to other studies²⁴. This can be explained by the greater number of hospitalizations with patients over 50 years old and with some risk factors that can decrease cell-mediated immune responses to VZV, and it is this decline that seems to explain the increased incidence and severity of HZ and its complications in the elderly²⁵.

Cutaneous complications in the study in question were the most recurrent, about half of those involved in the research had this

type of complication. Secondary bacterial infection is usually caused by staphylococcal or streptococcal infections, and if not diagnosed in time can lead to septicemia²⁶.

The risk of PHN is associated with advanced age, severe acute pain, severe skin lesions, and patients with severe immunosuppression²⁷. The rates of patients who develop PHN after HZ range from 8.6% to 49.3%¹⁸.

Complications observed in our study, such as: respiratory (pneumonia and respiratory failure), as well as hepatic (hepatitis) and complications in the genitourinary system (urinary tract infection - UTI or renal failure), are rarely reported in studies, but associated complications are possible to HZ in adults or children⁹.

The presence of cardiac complications was observed in only one patient with changes in heart rate. Other studies have observed a 1.2 to 1.7-fold increase in the risk of myocardial infarction one week or months after the diagnosis of HZ²⁸.

The types of hematological changes were the same as those observed in another study conducted in Argentina, but the highest frequency occurred in thrombocytopenia, followed by leukopenia, these types of hematological changes are frequent in patients affected by viral infections²³.

The literature provides information on the importance of diagnosis and treatment with the use of antiviral drugs within 72 hours, after the appearance of the rash to reduce complications²⁵. The therapy used corroborates other studies that have observed the use of antiviral in conjunction with other symptomatic drugs in Brazil and worldwide²⁹. The frequency of deaths from HZ was low, even lower than other similar studies that observed a percentage of 14.6% over five years²³. In Europe, mortality rates ranged from 0 to 19.5/ per 100,000 inhabitants⁸.

HZ was more frequent in the adult population and with some comorbidity associated with the condition. This makes this population the most vulnerable to reactivation of the virus and is conducive to the need for hospitalization. We can also conclude that the disease should not be underestimated due to the risk of possible complications associated with the condition. The risk factors associated with severity were the presence of vesicles and the therapy used incorrectly.

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REFERENCES

1. Bader MS. Herpes zoster: diagnostic, therapeutic, and preventive approaches. *Postgrad Med* [Internet]. 2013 Sep [cited 2020 Feb 2];125(5):78-91. Available from: <https://www.tandfonline.com/doi/abs/10.3810/pgm.2013.09.2703>. doi: 10.3810/pgm.2013.09.2703.
2. Zerboni L, Sen N, Oliver SL, Arvin AM. Molecular mechanisms of varicella zoster virus pathogenesis. *Nat Rev Microbiol* [Internet]. 2014 Feb [cited 2020 Feb 6 10]; 12(3): 197-210. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24509782>
3. Depledge DP, Sadaoka T, Ouwendijk WJD. Molecular Aspects of Varicella-Zoster Virus Latency. *Viruses* [Internet]. 2018 Jun [cited 2020 Feb 2]; 10(7): 349. Available from: <https://pubmed.ncbi.nlm.nih.gov/29958408/>. doi: 10.3390/v10070349.
4. Sly JR, Harris AL. Recombinant Zoster Vaccine (Shingrix) to Prevent Herpes Zoster. *Nurs Womens Health* [Internet]. 2018 Oct [cited 2020 Feb 2]; 22(5):417-422. Available from: <https://pubmed.ncbi.nlm.nih.gov/30145235/>. doi: 10.1016/j.nwh.2018.07.004.
5. Centers for Disease Control and Prevention. Shingles (Herpes Zoster) Vaccination [Internet]. EUA: CDC; 2018 [cited 2020 Feb 2]. Available from: <https://www.cdc.gov/vaccines/vpd/shingles/index.html>
6. Yawn BP, Saddier P, Wollan PC, St. Sauver JL, Kurland MJ, Sy LS. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. *Mayo Clin Proc* [Internet]. 2007 Nov [cited 2020 Feb 2]; 82(11):1341-1349. Available from: <https://pubmed.ncbi.nlm.nih.gov/17976353/>. doi: 10.4065/82.11.1341.
7. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: Towards a global perspective. *BMJ Open* [Internet]. 2014 Jun [cited 2020 Feb 2]; 4(6): e004833. Available from: <https://pubmed.ncbi.nlm.nih.gov/24916088/>. doi: 10.1136/bmjopen-2014-004833.
8. Bricout H, Haugh M, Olatunde O, Prieto RG. Herpes zoster-associated mortality in Europe: a systematic review. *BMC Public Health* [Internet]. 2015 May [cited 2020 Feb 2];15(466): 466. Available from: <https://bmcpubhealth.biomedcentral.com/articles/10.1186/s12889-015-1753-y>. doi: 10.1186/s12889-015-1753-y.
9. Volpi A. Severe Complications of Herpes Zoster. *Herpes* [Internet]. 2007 Sep [cited 2020 Feb 2];14(Suppl 2): 35A-39A. Available from: <https://pubmed.ncbi.nlm.nih.gov/17939894/>.
10. Nagel MA, Gilden D. Varicella Zoster Complications. *NIH Public Access* [Internet]. 2013 Aug [cited 2020 Feb 2];15(4): 439-453. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3752706/>. doi: 10.1007/s11940-013-0246-5.
11. Pinchinat S, Cebrián-Cuenca AM, Bricout H, Johnson RW. Similar herpes zoster incidence across Europe: results from a systematic literature review. *BMC Infect Dis* [Internet]. 2013 Apr [cited 2020 Feb 2];13(170):170. Available from: <https://pubmed.ncbi.nlm.nih.gov/23574765/>. doi: 10.1186/1471-2334-13-170.
12. Pawelec G, Larbi A, Derhovanessian E. Senescence of the human immune system. *J Comp Pathol* [Internet]. 2010 Jan [cited 2020 Feb 2];142 (Suppl 1):S39-44. Available from: <https://pubmed.ncbi.nlm.nih.gov/19897208/>. doi: 10.1016/j.jcpa.2009.09.005.
13. Forbes HJ, Bhaskaran K, Thomas SL, Smeeth L, Clayton T, Langan SM. Quantification of risk factors for herpes zoster : population based case-control study. *BMJ* [Internet]. 2014 May [cited 2020 Feb 2]; 348(g2911): 13. Available from: <https://www.bmj.com/content/348/bmj.g2911>
14. Forbes HJ, Bhaskaran K, Thomas SL, et al. Quantification of risk factors for postherpetic neuralgia in herpes zoster patients. *Neurology* [Internet]. 2016 Jul [cited 2020 Feb 2];87(1): 94-102. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4932239/>. doi: 10.1212/WNL.0000000000002808.
15. Chandrakala C, Tharini GK. A Clinical Study on 100 Cases of Herpes Zoster in a Tertiary Care Hospital. *Int J Sci Study*. 2017[cited 2020 Feb 6]; 5(9): 138-143.
16. Sahoo F, Hill JA, Xie H, Leisenring W, Yi J, Goyal S, et al. Herpes Zoster in Autologous Hematopoietic Cell Transplant Recipients in the Era of Acyclovir or Valacyclovir Prophylaxis and Novel Treatment and Maintenance Therapies. *Biol Blood Marrow Transplant* [Internet]. 2017 Mar [cited 2020 Feb 6]; 23(3): 505-511. Available from: <https://pubmed.ncbi.nlm.nih.gov/28039754/>. doi: 10.1016/j.bbmt.2016.12.620. Epub 2016 Dec 28.
17. Oxman MN. Immunization to reduce the frequency and severity of herpes zoster and its complications. *Neurology* [Internet]. 1995 Dec [cited 2020 Feb 6]; 45(12 Suppl 8): S41-6. Available from: <https://pubmed.ncbi.nlm.nih.gov/8545018/>
18. Toniolo-Neto J, Psaradellis E, Karellis A, Rampakakis E, Rockett T, Sampalis JS, et al. Measuring herpes zoster disease burden in São Paulo, Brazil: a clinico-epidemiological single-center study. *Clinics* [Internet]. 2018[cited 2020 Feb 2]; 73:1-8. Available from: <https://pubmed.ncbi.nlm.nih.gov/30043824/>. doi: <https://doi.org/10.6061/clinics/2018/e243>
19. Hata A, Kuniyoshi M, Ohkusa Y. Risk of Herpes zoster in patients with underlying diseases: a retrospective hospital-based cohort study. *Infection* [Internet]. 2011 Dec [cited 2020 Feb 2]; 39(6): 537-544. Available from: <https://pubmed.ncbi.nlm.nih.gov/21800108/>. doi: 10.1007/s15010-011-0162-0.
20. Kawai K, Yawn BP. Risk Factors for Herpes Zoster: A Systematic Review and Meta-analysis. *Mayo Clin Proc* [Internet]. 2017 Dec [cited 2020 Feb 2]; 92(12): 1806-1821. Available from: <https://pubmed.ncbi.nlm.nih.gov/29202939/>. doi: 10.1016/j.mayocp.2017.10.009.
21. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* [Internet]. 2020 Mar [cited 2020 Feb 10]; 395(10229): 1054-1062. Available from: <https://pubmed.ncbi.nlm.nih.gov/32171076/>. doi: 10.1016/S0140-6736(20)30566-3.
22. Rozenek M, Romani A, Aronson S, Ramilo MC, Abellán V, Pérez MA, et al. Herpes zoster en adultos mayores en un hospital privado de la ciudad de Buenos Aires, junio 2013 - mayo 2014. *Med (B. Aires)* [Internet]. 2017[cited 2020 Feb 10]; 77(1): 24-30. Available from: <https://pubmed.ncbi.nlm.nih.gov/28140307/>
23. Bollea-Garlatti ML, Bollea-Garlatti LA, Vacas AS, Torre AC, Kowalczuk AM, Ferreuro RL, et al. Características clínicas y evolutivas de una población con herpes zoster diseminado: un estudio de cohorte retrospectiva. *Actas Dermosifiliogr* [Internet]. 2017[cited 2020 Feb 6];108(2):145-152. Available from: <https://www.actasdermo.org/es-linkresolver-caracteristicas-clinicas-evolutivas-una-poblacion-S0001731016303623>
24. Chan DYW, Edmunds WJ, Chan HL, et al. The changing epidemiology of varicella and herpes zoster in Hong Kong before universal varicella vaccination in 2014. *Epidemiol Infect* [Internet]. 2018 Apr [cited 2020 Feb 6];146(6): 723-734. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6533643/>. doi: 10.1017/S0950268818000444.
25. Oxman MN. Clinical manifestations of herpes zoster. In: Arvin AM, editor. *Varicella-Zoster Virus*. New York: Cambridge University Press [Internet]; 2010[cited 2020 Feb 6]:246-275. doi:10.1017/cbo9780511601194.015
26. John AR, Canaday DH. Herpes Zoster in the Older Adult. *Infect Dis Clin North Am* [Internet]. 2017 Dec [cited 2020 Feb 2]; 31(4): 811-826. doi:10.1016/j.idc.2017.07.016
27. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci* [Internet]. 2020 May [cited 2020 Feb 2]; 63(5): 706-711. doi:10.1007/s11427-020-1661-4.

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28. Minassian C, Thomas SL, Smeeth L, Douglas I, Brauer R, Langan SM. Acute Cardiovascular Events after Herpes Zoster: A Self-Controlled Case Series Analysis in Vaccinated and Unvaccinated Older Residents of the United States. *PLoS Med* [Internet]. 2015 Dec [cited 2020 Feb 10]; 12(12): e1001919. doi:10.1371/journal.pmed.1001919.
29. Antonioli L, Rodrigues C, Borges R, Goldani LZ. Epidemiology and clinical characteristics of herpes zoster in a tertiary care hospital in Brazil. *Braz J Infect Dis* [Internet]. 2019 Mar-Apr [cited 2020 Feb 6]; 23(2): 143-145. doi:10.1016/j.bjid.2019.03.001

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