

HERPES ZOSTER AFTER COVID VACCINATION
HERPES ZOSTER APÓS A VACINAÇÃO DO COVID
HERPES ZOSTER DESPUÉS DE LA VACUNACIÓN CONTRA EL COVID

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ABSTRACT: Vaccination is an important intervention in preventing the spread of coronavirus (SARS-CoV-2). Messenger RNA vaccines were the first to be commercialized, although cutaneous adverse events have been reported in clinical trials for both vaccines, they have not been well characterized. Given the above, the study aims to report cases of herpes zoster after coronavirus vaccination. This is an integrative literature review carried out using the Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS) and Medical Literature Analysis and Retrieval System Online (MEDLINE) databases. of the following Health Sciences Descriptors (DeCS): “herpes zoster”, “vaccination” and “coronavirus”. Combined with each other by the Boolean operator AND. As inclusion criteria: articles available in full, in Portuguese, Spanish and English, that addressed the theme, in the last ten years (2012-2022). As exclusion criteria: articles that did not contemplate the theme and repeated studies in the databases. Four variables emerged to be studied. Herpesvirus co-infection was present in 45% of positive SARS-CoV-2 cases in moderate to critical clinical status, with EBV and HHV-6 being the most prevalent co-infection, especially in cases of immunosuppression, which may contribute to the worsening of the condition clinical.

Keywords: Herpes Zoster. Vaccination. Coronavirus.

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RESUMO: A vacinação é uma intervenção importante na prevenção da disseminação do coronavírus (SARS-CoV-2). As vacinas de RNA mensageiro foram as primeiras a serem comercializadas, embora eventos adversos cutâneos tenham sido relatados em ensaios clínicos para ambas as vacinas, eles não foram bem caracterizados. Diante do exposto o estudo objetiva relatar casos de herpes zoster pós vacinação do coronavírus. Trata-se de uma revisão integrativa da literatura realizada através das bases de dados Scientific Electronic Library Online (SciELO), Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e Medical Literature Analysis and Retrieval System Online (MEDLINE), através dos seguintes Descritores em Ciências da Saúde (DeCS): “herpes zoster”, “vacinação” e “coronavírus”. Combinados entre si pelo operador booleano AND. Como critérios de inclusão: artigos disponíveis na íntegra, nos idiomas português, espanhol e inglês, que abordassem a temática, nos últimos dez anos (2012-2022). Como critérios de exclusão: artigos que não contemplavam o tema e estudos repetidos nas bases de dados (Ercole et al., 2014). Emergiram 4 variáveis a serem estudadas. A coinfeção por Herpesvírus mostrou-se presente em 45% dos casos SARS-CoV-2 positivo em estado clínico moderado a crítico, sendo a coinfeção mais prevalente pelo EBV e HHV-6, principalmente nos casos de imunossupressão, podendo contribuir com agravamento do quadro clínico.

Palavras-chave: Herpes Zoster. Vacinação. Coronavírus.

RESUMEN: La vacunación es una intervención importante para prevenir la propagación del coronavirus (SARS-CoV-2). Las vacunas de ARN mensajero fueron las primeras en comercializarse, aunque se han reportado eventos adversos cutáneos en ensayos clínicos para ambas vacunas, no han sido bien caracterizados. Dado lo anterior, el estudio tiene como objetivo reportar casos de herpes zoster después de la vacunación contra el coronavirus. Esta es una revisión integradora de literatura realizada utilizando las bases de datos Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS) y Medical Literature Analysis and Retrieval System Online (MEDLINE) de los siguientes Descriptores de Ciencias de la Salud (DeCS).): “herpes zoster”, “vacunación” y “coronavirus”. Combinados entre sí por el operador booleano AND. Como criterio de inclusión: artículos disponibles en su totalidad, en portugués, español e inglés, que abordaron el tema, en los últimos diez años (2012-2022). Como criterios de exclusión: artículos que no contemplaran el tema y estudios repetidos en las bases de datos. Surgieron cuatro variables a estudiar. La coinfección por herpesvirus estuvo presente en el 45% de los casos SARS-CoV-2 positivos en estado clínico moderado a crítico, siendo EBV y HHV-6 la coinfección más prevalente, especialmente en casos de inmunosupresión, lo que puede contribuir al empeoramiento. de la condición clínica.

Palabras clave: Infección de herpes. Vacunación. Coronavírus.

I. INTRODUÇÃO

In the province of Wuhan, China, in December 2019, an make bigger in instances of pneumonia of unknown purpose was once described. Bronchoalveolar lavage samples had been accrued from sufferers who had a frequent history, these samples have been examined

the use of molecular biology techniques and recognized a new virus on January 7, 2020. This new virus belongs to the Coronaviridae family, of pathogens accountable for inflicting respiratory diseases, the new Coronavirus (SARS-CoV-2, first named 2019-nCoV) was once characterised as the etiologic agent of the Coronavirus ailment 2019 (COVID-19) mentioned in China (da Silva Bomfim et al., 2020).

Coronaviruses are enveloped viruses with genetic fabric composed of RNA strand of fine polarity. frequent cold. However, zoonotic coronaviruses, such as SARS-CoV-2, can evolve into greater aggressive lines and infect humans, main to deadly diseases. Coronaviruses are transmitted interpersonally, by way of infection by way of viral particles eradicated via coughing and/or sneezing and can also additionally contaminate frequently used surfaces (Lima et al., 2021).

The analysis of a new coronavirus comes with numerous challenges, however molecular strategies such as the polymerase chain response (PCR) have been viewed the gold general for detection of viral RNA. The analysis is made from respiratory tract swab samples, however research have already recognized the presence of viral RNA in stool and blood samples. Patients identified with COVID-19 have a excessive viral load, even in asymptomatic persons or with moderate symptoms, opposite to what is located in extreme acute respiratory syndrome due to coronavirus (SARS-CoV) and respiratory syndrome by Middle East coronavirus (MERS), making molecular diagnostic strategies extraordinarily applicable for the present day context. Currently, the advice of the World Health Organization (WHO) is to function laboratory prognosis in all suspected cases (Hott, 2022).

Infection with the Coronavirus motives an imbalance in the respiratory and gastrointestinal tracts, mainly as cited before in instances of SARS and MERS. However, in relation to Covid-19, in a few cases, signs associated to the gastrointestinal tract (such as diarrhea) have been observed, which we have reviews to date respiratory signs and symptoms such as pneumonia and a cytokine “storm”. should lead to latent Herpesvirus reactivation (Tartari et al., 2020).

Co-infection can also show up due to resistance to antibacterial drugs, inhibition of the host's immune response, and terrible prognosis of the disease. Epstein Barr virus (EBV), different Coronaviruses and some respiratory viruses which includes influenza A virus and rhinovirus/enterovirus may also be the most frequent copathogens. microorganisms such

as viruses, micro organism and fungi. Among the essential viral copathogens, influenza A and B viruses, rhinovirus / enterovirus, parainfluenza virus, metapneumovirus, respiratory syncytial, human immunodeficiency virus (HIV), dengue virus (DENV), hepatitis B virus (HBV), cytomegalovirus (CMV) (Ferreira et al., 2020).

Patients hospitalized in serious situation with wonderful COVID-19 ought to current co-infection with Herpesvirus, via viral reactivation, which can also expand morbidity and/or mortality. The dedication of co-infection by means of Herpesvirus with excessive sensitivity and specificity via molecular diagnosis, may additionally assist in the scientific administration of high quality COVID-19 patients. Thus, our scientific speculation is that sufferers hospitalized in a reasonable to indispensable scientific situation who have a advantageous RT-qPCR COVID-19 may additionally current co-infection with Herpesvirus, which motives accelerated morbidity and/or mortality. This work may additionally make contributions to the identification of sufferers at risk, directing these sufferers to follow the most fabulous cure and hence lowering the size of medical institution remain and the morbidity rate (Tartari et al., 2020). Given the above, the study aims to report cases of herpes zoster after coronavirus vaccination.

2. METODOLOGIA

This is an integrative literature review carried out using the Scientific Electronic Library Online (SciELO), Latin American and Caribbean Literature in Health Sciences (LILACS) and Medical Literature Analysis and Retrieval System Online (MEDLINE) databases. of the following Health Sciences Descriptors (DeCS): “herpes zoster”, “herpes zoster”, “vaccination” and “coronavirus”. Combined with each other by the Boolean operator AND. As inclusion criteria: articles available in full, in Portuguese, Spanish and English, that addressed the theme, in the last ten years (2012-2022). As exclusion criteria: articles that did not contemplate the theme and repeated studies in the databases (Ercole et al., 2014).

3. RESULTADOS E DISCUSSÃO

The following variables emerged, namely: The structure of the coronavirus, Viral multiplication and epidemiology, Vaccine for the coronavirus and coinfections, Herpesviridae family

3.1 The structure of the coronavirus

Coronaviruses can infect a large vary of hosts. Coronavirus contamination can be viewed in mice, rats, chickens, turkeys, pigs, dogs, cats, rabbits, horses, cattle, and humans, and can purpose a range of serious illnesses, along with gastroenteritis and respiratory tract illnesses. In the mid-1960s, three human coronaviruses HCoV-229E and HCoV-OC43 had been recognized and studied and can purpose the frequent cold (Belasco & Fonseca, 2020).

In the years 2002 and 2003 there was once an incidence of SARS - CoV (Severe Acute Respiratory Syndrome - coronavirus) and in 2012 of MERS - CoV (Middle East Respiratory Syndrome - coronavirus) each epidemics confirmed the manageable for transmission of CoVs rising from animals to human and from man or woman to person. Altogether there are seven human coronaviruses (HCoVs) with the plausible to infect humans, such as they are: HCoV229E, HCoV - OC43, HCoV - NL63, HKU1, SARS - CoV, MERS - CoV and SARS - CoV - 2 (Lima, 2020).

The new Coronavirus was identified as the etiological agent of cases of pneumonia of unknown etiology that occurred in December 2019, in the province of Wuhan, in the city of Hubei, China. Initially, a new Betacoronavirus was classified as first named 19-nCoV. However, after viral identification and the identification of the target organs, the International Taxonomy Committee (ICTV) - classified it in a new nomenclature, becoming: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease was named: COVID-19 (from the English Coronavirus disease 2019). In China in the years of 2002 and 2003 cases of SARS-CoV were identified and, another epidemic a few years later, MERS-CoV was observed in countries in the Middle East (Belasco & Fonseca, 2020; da Silva Bomfim et al., 2020).

The SARS-CoV-2 virus belongs to the Coronaviridae family, to the Sabercovirus subgenus and Betacoronavirus genus Betacoronaviruses originate from the same common ancestor, which infect bats. SARS-CoV-2 has an 88% similarity with the genome of two other betacoronaviruses that are derived from bats (bat-SL-CoVZC45 and bat-SL-CoVZXC21), being phylogenetically more similar to these species than to viruses SARS-CoV (79% similarity) and MERS-CoV (50% similarity) (Lima, 2020).

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The coronavirus is a single-stranded RNA virus with advantageous polarity, with a spherical form that resembles the look of a “crown”. The viral shape is composed of envelope (E), membrane (M), spike protein (S), nucleocapsid (N) and genomic RNA. Spike S protein and nucleocapsid N protein supply steadiness to the viral particle. In addition, the N protein is worried with virion assembly, it is a structural protein that performs a vital function in the transcription and meeting of the virus (Romanov, 2020).

3.2 Viral multiplication and epidemiology

The viral multiplication cycle of SARS-CoV-2 is nonetheless now not properly understood. However, in accordance to the work via QIN et al., 2020, there is a hyperlink between the S protein and the angiotensin-converting enzyme two (ACE₂) receptors of the host's respiratory cells. According to the work, the telephone floor proteases cleave the S protein subunit, which mediates the fusion of the virus with the mobilephone membrane. This generates a sequence of conformational changes, ensuing in the fusion of the virus with the host mobile phone and subsequently the launch of the virus's genetic material. After releasing the genetic material, the virus makes use of the cell equipment to make copies of the viral RNA, which will later be launched to infect other cells (Rothan & Byrareddy, 2020).

At the quit of January 2020, in accordance to the World Health Organization (WHO), 2,798 established instances of COVID-19 had been reported, with 98.7% of the

instances existing in China. Due to the massive variety of stated cases, on January 30, 2020, the WHO declared that the outbreak of the new coronavirus used to be a Health Emergency Public Health of International Importance (ESPII) in order to cease the unfold of the virus. On March 11, 2020, the WHO introduced COVID-19 as a pandemic, as the geographic distribution of the sickness covers the whole world (Sun et al., 2020).

At the opening of the pandemic, the make bigger in the wide variety of instances used to be big in China, with its speedy unfold to different nations such as Japan, Thailand, Singapore, the United States of America and Germany. According to the WHO record , till April 22, 2020, the whole range of instances of COVID-19 was once 2,471,136 proven instances worldwide, with 169,134 deaths. Comparing to SARS and MERS, SARS-CoV-2 unfold barely faster, due to elevated globalization and the center of attention of the epidemic, surpassing the quantity of instances and deaths from the disease (Rothan & Byrareddy, 2020).

In Brazil, in January 2020, COVID-19 was once being viewed an "imminent danger" epidemic, however after the notification of ten applicable cases, it was once viewed a suspected case requiring instant attention. Between January 18 and February 21, 2020, fifty one suspected instances have been reported, with moderate symptoms, and amongst these, forty nine had a records of tour to China. Thus, the Ministry of Health declared COVID-19 a Public Health Emergency of National Importance. Brazil used to be the first united states of america in Latin America with a tested case of COVID-19 on February 26, 2020. With a demonstrated analysis of the first case, there was once the enlarge in instances of COVID-19, considering then the range of instances every day will increase exponentially. At the opening of March 2021, Brazil had 13,599,994 proven cases, 358,425 deaths, incidence/100 thousand inhabitants of 6471.7 and mortality/100 thousand inhabitants is 170.6 (Sun et al., 2020; da Silva Bomfim et al., 2020).

3.3 Vaccine for the coronavirus and coinfections

In the improvement of vaccines for COVID-19, quite a few techniques are being adopted, such as the use of inactive or stay attenuated viruses, virus-like particles (VLPs), viral vectors and protein-based, DNA-based and mRNA-based vaccines . Most of the candidate vaccines have been focused on the protein of the viral spicula that may additionally be the principal inducer of neutralizing antibodies. It is believed that vaccines

based totally on protein S can also set off antibodies that block binding to the viral receptor, and elimination of the virus genome (Algaadi, 2022).

Typically vaccine improvement can take 10-15 years, however with the fast sequencing of the SARS-CoV-2 gene, improvement of an tremendous vaccine quickly moved forward. As of June 2020 , there had been 124 vaccine candidates for COVID-19 prophylaxis in development. However a wide variety decreased range of candidate vaccines will enter section 1, mixed section half of or segment two of grownup human scientific trials, we can look at some vaccines below improvement and their approach used in (Pona et al., 2020).

Some research are searching at vaccines already used can be repurposed. In the United States of America, an oral polio vaccine has been investigated as a viable candidate. In nations such as the Netherlands, Australia and South Africa, multicenter randomized medical trials are being carried out involving the administration of the BCG vaccine. In Egypt, a measles vaccine trial used to be registered for the prophylaxis of COVID-19. Infection with the SARS-CoV-2 coronavirus can growth to greater extreme prerequisites with problems such as acute respiratory misery syndrome (ARDS), cardiac lesions and secondary infections (bacterial, fungal, different viruses). As co-infections with different pathogens (of viral, bacterial and fungal origin) are located in 50% of extreme instances of COVID-19 (Algaadi, 2022).

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The differential diagnosis of co-infection with other viral pathogens is essential for patients with COVID-19 infection, as it helps to prevent the aggravation and progression of the disease or even the patient's death. To reduce the morbidity and/or mortality rate of COVID-19, it is essential to pay attention to possible coinfections, ensuring a comprehensive and safe treatment for patients (Pona et al., 2020).

3.4 Herpesviridae family

Human Herpesviruses (HHV) belong to the Herpesviridae family, are ubiquitous viruses, once the primary infection occurs, this virus remains latent in the body of the affected individual throughout life. Generally, in healthy individuals, these viruses often cause benign infections, but in immunosuppressed individuals, the infection can cause clinical manifestations of varying severity (Crimi et al., 2019).

The Herpesviridae family can be divided into 3 subfamilies (Alphaherpesvirus, Betaherpesvirus and Gammaherpesvirus). All viruses in this family are double-stranded

DNA viruses. The subfamilies are distinguished by their pathogenesis and viral and structural characteristics. The Alphaherpesvirus subfamily is composed of Herpes Simplex Type 1, Herpes Simplex Type 2 and Varicella Zoster virus. In the subfamily Betaherpesvirus we have the cytomegalovirus, Herpesvirus 6 and Herpesvirus 7, as for the Gammaherpesvirus we have Epstein-Bar and Herpesvirus associated with Kaposi's Sarcoma (HHV-8). The HHV viral cycle is composed of 5 stages, which are the entry of the virus into the host cell, expression of viral genes, replication of the viral genome, assembly of the progeny and exit from the host cell (Crimi et al., 2019).

The laboratory diagnosis for Herpesviruses can be performed through viral isolation by cell culture, the PCR technique and serology. high sensitivity and specificity in detecting the viral genome. This method can differentiate viral species and strains. Serological tests can demonstrate recent infection or even previous immunization, these can be performed by Western blotting (WB), ELISA and indirect immunofluorescence reaction (RIF) techniques , but they have a lot of cross-reactivity (Koch et al., 2020).

Herpes simplex virus type 1 (HSV-1) was one of the first Herpesviruses described in the literature, classified in the Alphaherpesvirus subfamily, genus Simplex virus. Primary HSV-1 infection usually occurs in childhood or adolescence, with manifestations in the oral/facial region. This virus establishes latency at the site of the trigeminal ganglia. Viral transmission is through contact with respiratory droplets, saliva and mucocutaneous secretions of an infected person. Virus reactivation latent occurs through various stimuli such as stress and immunosuppression (Giacobbe et al., 2022).

The primary infection in 90% of the cases may not present clinical manifestations, an asymptomatic infection occurring, being detectable through the presence of antibodies. , balanitis, keratoconjunctivitis and cutaneous herpes. And complications such as herpetic meningoencephalitis or varicelliform eruption may occur depending on the state of immunosuppression. HSV-1 infections can be treated with topical, oral or intravenous acyclovir or other antivirals such as valacyclovir, famciclovir, foscarnet IV: and cidoclovir due to narrow therapeutic window (Koch et al., 2020).

The laboratory diagnosis for HSV-1 can be performed through swab for cytological study, serology techniques and PCR. The swab for cytological study is done by the Tzanck method, a cytological technique that uses of the base of the vesicle on the skin and HE staining, in order to search for multinucleated giant cells with inclusion bodies (virions).

atypical cases and immunocompromised patients. Serology demonstrates previous exposure to the virus and is indicated when there are complaints of recurrent genital or lip discomfort, but without the presence of lesions (Giacobbe et al., 2022).

The Varicella Zoster Virus (VZV, also called Herpesvirus 3) had its DNA genome described . This virus infects humans through air and contact with the skin lesions of an infected individual, the viral target site are T lymphocytes, epithelial cells and ganglia. The primary infection causes chickenpox (chicken pox), later the VZV becomes latent in ganglionic neurons. Factors such as immunosuppression status , advancing age can contribute to the reactivation of VZV causing herpes zoster, with complications such as: chronic pain (neural post-herpetic disease-PHN), severe neurological, ocular, multiple visceral and gastrointestinal disorders (Katsikas Triantfyllidis et al., 2021).

There is an attenuated vaccine for VZV formulated in Japan in 1974, for the immunization of children under 12 years of age. The vaccine is authorized for use in some countries around the world, including Australia, Brazil, Canada, China, Germany, Greece, Israel, Italy, Japan, Uruguay, Qatar, South Korea, Spain and Taiwan (Kennedy & Gershon, 2018).

Initially, treatment is performed with the administration of antivirals and analgesics, within the first 72 hours after diagnosis, with the aim of reducing the duration and intensity of pain . It was observed that treatment with Aciclovir, Valaciclovir and Fanciclovir can accelerate the healing process of cutaneous and mucosal lesions. , including analgesics, narcotics, tricyclic antidepressants, anticonvulsants, percutaneous electrical nerve stimulation, nerve blocks and topical anesthetics (Katsikas Triantfyllidis et al., 2021).

Diagnosis of the varicella zoster virus can initially be made based on observation of the clinical picture, but if the VZV infection/reactivation does not present any rash, viral confirmation is required. Virological identification requires PCR viral load detection technique and positive antiVZV IGM serology (Kennedy & Gershon, 2018).

The Epstein-Barr virus (EBV or HHV-4) is a linear DNA virus, with 172 kilobases, which encodes approximately 100 viral proteins, its genome is located inside an envelope. EBV is an oncogenic virus, it can cause nasopharyngeal carcinoma, Burkitt's lymphoma, Hodgkin's lymphoma and diffuse B-cell lymphoma. EBV transmission occurs mainly by saliva, however there may be transmission through blood products and transplanted organs (Houen & Trier, 2021).

This virus is extremely common, presenting antibodies to almost 90% of the adult population. In developed countries, the primary infection usually occurs in adolescence or even adulthood, causing infectious mononucleosis, which is a lymphoproliferative disease. However, in developing countries, the primary infection usually occurs in the first five years the number of cases in childhood is greater than the number of cases in adolescence and adulthood, and especially in regions without basic sanitation and with high population density. Brazil it is considered a country of intermediate endemicity (Gold et al., 2021).

In immunosuppressed patients, it causes opportunistic infection, and a diagnosis is made for monitoring. Clinical manifestations of EBV infection include anemia, thrombocytopenia, lymphadenopathy, rash, pneumonia, hemophagocytic syndrome and lymphoma. Treatment for EBV in cases of immunosuppression requires the administration of drugs such as Acyclovir, Ganciclovir and Foscarnet, oral corticosteroids such as Prednisone. The use of corticosteroids should be administered with caution. In case of tonsillar involvement, Ampicillin or Penicillin should be avoided due to the high prevalence of rashes (Houen & Trier, 2021).

The laboratory diagnosis for EBV can be made through serology, RTqPCR, biopsy using in situ hybridization technique. Molecular biology techniques such as chain reaction (PCR) or quantitative PCR (qPCR) are performed in the diagnosis and prognosis of EBV infections in blood and/or serum samples. While the immunofluorescence technique and immunoenzymatic assays (ELISA) can detect specific antibodies induced by EBV (Gold et al., 2021).

Human cytomegalovirus (HCMV) is a member of the Herpesviridae family, with a double-stranded DNA of approximately 236 kbp, with a worldwide seroprevalence of between 55 and 100%. After the primary infection, the Herpesvirus genome persists in the body throughout life, in certain cells entering a latency period. This period can be interrupted by reactivation of the infection due to several factors. The reactivation of the virus allows its dissemination with active replication and an increase in the viral load, since there is a release of extracellular virions (Griffiths & Reeves, 2021).

About 90% of the world's population has infections caused by some virus of the Herpesviridae family immunocompetent individuals, the infection caused by HCMV is mostly asymptomatic. In immunosuppressed patients, Herpesvirus reactivates and can cause severe disease, which leads to increased morbidity and mortality of these individuals.

HCMV infection may have clinical/laboratory manifestations such as: cytopenia, nephritis, pneumonia, retinitis, colitis and esophageal ulcers (Herbein, 2018).

Antiviral compounds such as Ganciclovir (GCV), Foscarnet (FOS) and Cidofovir (CDF) are the first choice for the treatment of CMV infection/reactivation, but these have many side effects. New anti-CMV drugs have been investigated in randomized clinical trials of phase II and III, and these may be promising: Maribavir, Letermovir and Brincidofovir, both of which do not have myelosuppressive properties or renal toxic effects. (The laboratory diagnosis of HCMV is obtained by different techniques, such as PCR, pp65 antigenemia (early phosphoprotein 65 monitoring) (Griffiths & Reeves, 2021).

Herpesvirus 6 reactivations cause cutaneous manifestations (pityriasis rosea) and Kawasaki disease mainly in children. Risk factors for Herpesvirus 6 reactivation may include: advanced age, immunosuppressive conditions, environmental factors such as stress. In cases of stem cell transplantation, solid organ transplantation or immunosuppression due to other causes, viral reactivation is common, but asymptomatic in most cases, in others it can cause encephalitis or severe illness in other organs (Eliassen et al., 2018).

Herpesvirus 6 infections have generally mild clinical manifestations and do not require therapy. But anti-CMV viral drugs such as ganciclovir, aciclovir, foscarnet and cidofovir seem to have efficient inhibition of viral replication (Hill, 2019).

The laboratory diagnosis of HHV-6 can be made through culture, serology and polymerase chain reaction (PCR). In adults, 95% have positive serology for HHV-6. Viral culture of HHV-6 can be performed in the acute phase isolated from PBMC of patients with rashes. HHV-6 DNA can be detected in saliva, throat swabs and nasal mucosa of children and adults. PCR detecting HHV-6 DNA has been used in the diagnosis of solid organ transplant recipients (Aimola et al., 2020).

CONSIDERAÇÕES FINAIS

Herpesvirus co-infection was present in 45% of positive SARS-CoV-2 cases in moderate to critical clinical status, with EBV and HHV-6 being the most prevalent co-infection, especially in cases of immunosuppression, which may contribute to the worsening of the condition clinical. In general, patients co-infected with Herpesvirus had high serum ferritin concentrations, on admission and after seven days, suggesting that co-

infection with Herpesvirus may contribute to a greater inflammatory picture. Longitudinal analysis of patients co-infected by Herpesvirus showed alterations in urea and hemoglobin concentrations and in the presence of lymphopenia. In this way, the presence of Herpesviruses could favor anemia, renal dysfunction and inefficient cellular responses in patients hospitalized with COVID-19. Patients co-infected with Herpesvirus and aged over 60 years had a higher number of deaths, probably due to associated comorbidities and immunosuppression status.

REFERÊNCIAS

Ercole, F. F., Melo, L. S. D., & Alcoforado, C. L. G. C. (2014). Revisão integrativa versus revisão sistemática. *Revista Mineira de Enfermagem*, 18(1), 9-12.

da Silva Bomfim, V. V. B., dos Santos Aleluia, E., dos Santos Dias, M. A., de Matos Leal, V., Gomes, J. P., do Carmo, K. S., ... & dos Santos, M. M. (2020). Pandemia do SARS COVID-19: estudo bibliométrico. *Revista Eletrônica Acervo Saúde*, 12(10), e4141-e4141.

Ferreira, A. D. F., Romão, T. T., Macedo, Y. S., Pupe, C., Nascimento, O. J., & Fellow of the American Academy of Neurology (FAAN). (2020). COVID-19 and herpes zoster co-infection presenting with trigeminal neuropathy. *European journal of neurology*, 27(9), 1748-1750.

Tartari, F., Spadotto, A., Zengarini, C., Zanoni, R., Guglielmo, A., Adorno, A., ... & Pileri, A. (2020). Herpes zoster in COVID-19-positive patients. *International Journal of Dermatology*.

Lima, E. J. D. F., Almeida, A. M., & Kfoury, R. D. Á. (2021). Vacinas para COVID-19-o estado da arte. *Revista Brasileira de Saúde Materno Infantil*, 21, 13-19.

Hott, M. C. M. (2022). Covid-19: Vacina boa é a aplicada de forma adequada. *Journal of Health & Biological Sciences*, 10(1), 1-3.

Romanov, K. B. (2020). Coronavirus disease COVID-2019. *Safety and Risk of Pharmacotherapy (E-Journal)/Безопасность и риск фармакотерапии*, 03-Aug.

Belasco, A. G. S., & Fonseca, C. D. D. (2020). Coronavírus 2020. *Revista brasileira de enfermagem*, 73.

Lima, C. M. A. D. O. (2020). Informações sobre o novo coronavírus (COVID-19). *Radiologia Brasileira*, 53, V-VI.

Algaadi, S. A. (2022). Herpes zoster and COVID-19 infection: a coincidence or a causal relationship?. *Infection*, 50(2), 289-293.

Pona, A., Jiwani, R. A., Afriyie, F., Labbe, J., Cook, P. P., & Mao, Y. (2020). Herpes zoster as a potential complication of coronavirus disease 2019. *Dermatologic therapy*.

Kennedy, P. G., & Gershon, A. A. (2018). Clinical features of varicella-zoster virus infection. *Viruses*, 10(11), 609.

Katsikas Triantafyllidis, K., Giannos, P., Mian, I. T., Kyrtsolis, G., & Kechagias, K. S. (2021). Varicella zoster virus reactivation following COVID-19 vaccination: a systematic review of case reports. *Vaccines*, 9(9), 1013.

Gold, J. E., Okyay, R. A., Licht, W. E., & Hurley, D. J. (2021). Investigation of long COVID prevalence and its relationship to Epstein-Barr virus reactivation. *Pathogens*, 10(6), 763.

Houen, G., & Trier, N. H. (2021). Epstein-Barr virus and systemic autoimmune diseases. *Frontiers in immunology*, 11, 587380.

Griffiths, P., & Reeves, M. (2021). Pathogenesis of human cytomegalovirus in the immunocompromised host. *Nature Reviews Microbiology*, 19(12), 759-773.

Herbein, G. (2018). The human cytomegalovirus, from oncomodulation to oncogenesis. *Viruses*, 10(8), 408.

Eliassen, E., Lum, E., Pritchett, J., Ongradi, J., Krueger, G., Crawford, J. R., ... & Hudnall, S. D. (2018). Human herpesvirus 6 and malignancy: a review. *Frontiers in oncology*, 8, 512.

Aimola, G., Beythien, G., Aswad, A., & Kaufer, B. B. (2020). Current understanding of human herpesvirus 6 (HHV-6) chromosomal integration. *Antiviral Research*, 176, 104720.

Hill, J. A. (2019). Human herpesvirus 6 in transplant recipients: an update on diagnostic and treatment strategies. *Current opinion in infectious diseases*, 32(6), 584.