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Cytomegalovirus reactivation in critically ill or immunocompromised patients increases mortality

Abstract

Introduction: In critically ill patients or immunocompromised, cytomegalovirus (CMV) frequently reactivates. This reactivation is linked to extended hospital and ICU stays, increased need for mechanical ventilation, and higher incidences of sepsis, healthcare-associated infections (HAIs), morbidity and mortality. This study to describe CMV reactivation and outcomes in patients treated at or admitted to a university hospital.

Methods: We conducted a retrospective cohort study of patients with suspected CMV reactivation treated at a university hospital in central Brazil from November 2021 to July 2023. Data were abstracted from medical charts and entered a form prepared in EpiData Entry software version 3.1(//www.epidata.dk/) for statistical analysis.

Results: Among one hundred patients with clinical suspicion of CMV reactivation by the attending medical team, thirty-one cases (31.0%) had detectable viral load in blood samples. In patients with CMV reactivation, mortality reached 19.35%, compared to 5.80% in patients with undetectable viral load (p= 0.045). Mortality and CMV reactivation were significantly (p<0.050) higher in patients infected with the human immunodeficiency virus (HIV), those with shock or healthcare-associated infections (HAIs), and those requiring mechanical ventilation (MV). Patients with suspected CMV reactivation who were treated with ganciclovir had a significantly higher mortality (25.00%) than those who did not use ganciclovir (6.25%) (p=0.025).

Conclusions: CMV reactivation, HIV infection, shock, MV, intensive care unit admission, or HAIs were associated with increase patient mortality. However, further studies on the use of antivirals for treatment or prophylaxis of CMV reactivation in non-transplant critically ill patients, including patients with HIV infection, are necessary, as ganciclovir may be toxic.

Keywords: cytomegalovirus reactivation, mortality, critically ill patient, mechanical ventilation, HIV, ganciclovir

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Introduction

Cytomegalovirus (CMV), also known as human herpesvirus 5, is a member of the Herpesviridae family. CMV particles consist of a 120-200-nm envelope containing linear double-stranded DNA.[1] CMV can be transmitted through sexual exposure, blood or blood product transfusion, organ transplantation from HIV-positive donors, occupational exposure in susceptible workers, and close contact between individuals, such as during family gatherings.[2–5]

CMV infection is usually asymptomatic or may present as a mononucleosis syndrome in an immunocompetent host.[1,6] Conversely, in critically ill patients with sepsis, several viruses, most often CMV can be reactivated. In these patients, CMV reactivation worsens the prognosis, increasing healthcare-associated infections (HAIS) such as ventilator-associated pneumonia (VAP), bacteremia, and fungal infections.[7]

CMV reactivation can be detected by polymerase chain reaction (PCR) in 33% of critically ill, immunocompetent, CMV-seropositive patients. In these patients, CMV reactivation is associated with prolonged hospital and ICU stays, increased need for mechanical ventilation (MV), and higher rates of sepsis, morbidity, and mortality.[8–18]

Ganciclovir is an antiviral widely used to inhibit CMV replication. However, it is associated with bone marrow suppression (myelotoxicity) and can cause serious toxicity in patients with renal failure. Underdosing ganciclovir can lead to acquired drug resistance, such as the mutation of the UL97 gene, requiring the use of foscarnet, which is even more toxic.[19–21]

The present study aims to describe CMV reactivation and outcomes in outpatients and patients admitted to a university hospital in Mato Grosso, central Brazil, due to the lack of studies on CMV reactivation in non-transplant patients in this region.

Methods

Location, population, and data collection

This retrospective cohort study of patients with suspected CMV reactivation was conducted in a public university hospital located in Cuiaba, Mato Grosso, in the Central-West region of Brazil. These data were abstracted from electronic health records and medical charts of outpatients and inpatients from November 2021 to July 2023.

Patient data

Patient's data were obtained from medical records. The study included patients of both sexes, regardless of age, HIV infection, or other immunosuppressive diseases, whether treated in outpatient units or admitted to a ward or intensive care unit (ICU). Inclusion criteria were patients with the presence of IgG antibody reactive to CMV and clinical suspicion of CMV reactivation by the attending medical team. Suspected CMV reactivation was defined by the absence of retinitis, esophagitis, CMV colitis or organ transplantation, but with the presence of fever, asthenia, clinical worsening or systemic inflammatory response syndrome without specific cause in

immunocompromised patients, together with the identification of IgG antibodies to CMV and CMV viral load present in a blood sample. Exclusion criteria were the absence of reactive IgG antibodies to CMV or the absence of collection of CMV viral load.

Several data were recorded, including sex, age, comorbidities, complications, length of stay, CMV load, and outcomes such as progression to cure or death at the end of hospitalization. The research protocol was approved by the Ethics Research Committee of Júlio Muller Hospital, and was registered in the National System of the Ethical Evaluation of Human Research Projects (CAAE 76003223.5.0000.5541).

Data analysis

Data on patient age, sex, outpatient care or place of admission, underlying pathology, reason for admission, presence of healthcare-associated infections, shock, need for hemodialysis, presence of CMV and outcome were stored in the EpiData Entry v.3.1 database (http://www.epidata.dk/). Associations between clinical or epidemiological characteristics as well as CMV reactivation and outcome were analyzed using appropriate tests for categorical variables and continuous normal or parametric distributions using the EpiData Analysis v.2.2 software (http://www.epidata.dk/). A value of 5% was used as the maximum alpha error limit allowed to reject the null hypothesis.

Results

Among 130 patients with clinical suspicion of CMV reactivation by the attending medical team from November 2021 to July 2023, 30 patients were excluded because CMV viral load was not collected. One hundred patients with clinical suspicion of CMV reactivation were included in the study, 31 (31.0%) had detectable viral load in their blood samples. The mortality rate among patients with suspected CMV reactivation was 10.0%. Specifically, six patients (19.35%) of the 31 patients with detectable viral load died, compared with four patients (5.80%) of the 69 patients with undetectable viral load, a statistically significant difference (p = 0.045).

In this study, the majority of patients were male (60%). The most prevalent age group for CMV reactivation was 18 to 64 years (48%). The medical specialty with the highest number of screenings for CMV reactivation was Pediatrics (46%).

CMV reactivation rates and mortality were significantly higher in patients with HIV infection (51.85% and 22.22%, respectively) compared to those without HIV infection (23.29% and 5.48%) (p=0.002 and p=0.026). Similarly, reactivation rates and mortality were significantly higher in patients with shock (53.85 and 61.54%) than in those without shock (27.59% and 2.30%) (p= 0.028 and p= 0.000), and in patients requiring mechanical ventilation (58.33% and 75.0%) compared to those who did not (27.59% and 1.15%) (p=0.037 and p=0.000). Twenty patients (20.0%) with suspected CMV reactivation were treated with ganciclovir, and they experienced significantly higher mortality rates (25.0%) compared to those who did not receive ganciclovir (6.25%) (p=0.025). Additional data on the 100 patients with suspected CMV reactivation are outlined in Table 1.

Table 1 Descriptive statistics and outcomes of patients with suspected CMV reactivation at the university hospital of Cuiaba, Mato Grosso (MT), Brazil, from November 2021 to July 2023

Variable	Cases, n (%)	Deaths, n (%)	p-value	Cases of detectable CMV, n (%)	p-value
Total	100 (100.0)	10 (10.00)	-	31 (31.0)	-
Sex					
Female	40 (40.0)	4 (10.00)	0.625	12 (30.00)	0.5198
Male	60 (60.0)	6 (10.00)		19 (31.67)	
Sector					
Adult ICU	20 (20.0)	9 (45.00)	-	12 (60.00)	-
Internal Medicine	27 (27.0)	1 (3.70)	0	12 (44.44)	0.224
Pediatrics	46 (46.0)	0 (0.00)	0	7 (15.22)	0
Outpatient Centers	7 (7.0)	0 (0.00)	0.035	0	0.007
Age (years)*					
≤ 17	50 (50.0)	0 (0.0)	0.002	08 (16.0)	0.001
≥ 18	50 (50.0)	8 (16.0)		23 (46.0)	
HIV					
Yes	27 (27.0)	6 (22.22)	0.022	14 (51.85)	0.007
No	73 (73.0)	4 (5.48)		17 (23.29)	
Diabetes mellitus					
Yes	4 (04.0)	1 (25.00)	0.348	2 (50.00)	0.365
No	96 (96.0)	9 (9.38)		29 (30.21)	
Shock					
Yes	13 (13.0)	8 (61.64)	0	7 (53.85)	0.028
No	87 (87.0)	2 (2.30)		24 (27.59)	
MV					
Yes	12 (12.00)	9 (75.00)	0	07 (58.33)	0.037
No	87 (87.00)	1 (1.15)		24 (27.59)	
HAIs					
Yes	16 (16.00)	6 (37.50)	0	12 (75.00)	0
No	84 (84.00)	4 (4.76)		19 (22.62)	
Hemodialysis					

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Table 1 Continued...

Yes	7 (7.0)	6 (85.71)	0	3 (42.86)	0.374
No	93 (93.0)	4 (4.30)		28 (33.11)	
Acyclovir use					
Yes	14 (14.00)	03 (21.43)	0.144	7 (50.00)	0.091
No	86 (86.00)	07 (8.14)		24 (27.91)	
Ganciclovir use					
Yes	20 (20.00)	5 (25.00)	0.025	15 (75.00)	0
No	80 (80.00)	5 (6.25)		16 (20.00)	

*Younger than two years of age: 15 patients (three with detectable CMV); between two and 12 years of age: 28 patients (four with detectable CMV); between 13 and 17 years of age: seven patients (one with detectable CMV); between 18 and 64 years of age: 48 patients (21 with detectable CMV); and older than 64 years: two patients (two with detectable CMV).

Variables and outcomes of the 31 patients with CMV reactivation and the 69 patients without CMV reactivation are detailed in Table 2.

Table 2 Descriptive statistics and outcomes of patients with undetectable and detectable CMV at the university hospital of Cuiaba, Mato Grosso (MT), Brazil, in November 2021 and July 2023

Variable	Cases of undetectable CMV, n (%	Deaths, n (%)	p-value	Cases of detectable CMV, n (%)	Deaths, n (%)	p-value
Total						
Sex	69 (100.0)	4 (5.80)	-	31 (100.0)	6 (19.35)	-
Female	28 (40.58)	3 (10.71)	0.322	12 (30.77)	2 (16.67)	0.573
Male	41 (59.42)	2 (4.88)		19 (31.15)	4 (21.05)	
Age (years)*						
≤ 17	42 (60.87)	0 (0.00)	0.02	08 (25.81)	0 (0.0)	0.137
≥18	27 (39.13)	4 (14.81)		23 (74.19)	6 (26.09)	
Sector**						
Adult ICU	8 (11.59)	4 (50.50)	0	12 (60.00)	5 (41.67)	0.021
Others	61 (88.41)	0 (0.00)		19 (46.15)	1 (5.26)	
CMV viral load						
<1000 copies/dl	-	-	-	19 (61.29)	3 (15.79)	0.426
≥ 1000 copies/dl	-	-		12 (38.71)	3 (25.0)	
Ganciclovir use						
Yes	5 (7.25)	0 (0.00)	0.735	15 (48.39)	5 (33.33)	0.072
No	64 (92.75)	4 (6.25)		16 (51.61)	1 (6.25)	
Aciclovir use						
Yes	7 (10.14)	1 (14.30)	0.354	7 (22.58)	2 (28.57)	0.413
No	62 (89.86)	3 (4.84)		24 (77.42)	4 (16.67)	
HIV						
Yes	13 (18.84)	1 (7.69)	0.575	14 (45.16)	4 (28.57)	0.235
No	56 (81.16)	3 (5.36)		17 (54.84)	2 (11.76)	
Diabetes mellitus						
Yes	2 (2.90)	0 (0.00)	0.886	02 (6.45)	1 (50.00)	0.354
No	67 (97.10)	4 (5.97)		29 (93.55)	5 (17.24)	
Shock						
Yes	6 (8.70)	4 (66.67)	0	7 (22.58)	4 (57.14)	0.013
No	63 (91.30)	0 (0.00)		24 (77.42)	2 (8.33)	
MV						
Yes	5 (7.25)	4 (80.00)	0	07 (58.33)	5 (71.43)	0
No	64 (92.75)	0 (0.00)		24 (27.91)	1 (4.17)	
HAIs						
Yes	4 (5.80)	2 (50.00)	0.014	12 (38.71)	4 (33.33)	0.137
No	65 (94.20)	2 (3.08)		19 (61.29)	2 (10.53)	
Hemodialysis						
Yes	4 (5.80)	3 (75.00)	0	3 (9.68)	2 (66.67)	0.087
No	65 (94.20)	1 (1.54)		28 (90.32)	4 (14.29)	

*69 patients with undetectable CMV= younger than two years of age: 12 patients; between two and 12 years of age: 24 patients; between 13 and 17 years: six patients; between 18 and 64 years of age: 27 patients; and older than 64 years of age: zero patients.

31 patients with detectable CMV= younger than two years of age: three patients; between two and 12 years of age: four patients; between 13 and 17 years of age: one patient; between 18 and 64 years of age: 21 patients; and older than 64 years of age: two patients.

** Other sectors= Internal medicine, cases with undetectable CMV : 15 patients (no deathes); Internal medicine, cases with detectable CMV : 12 patients (one death); Pediatrics, cases with undetectable CMV : 39 patients (no deathes); Pediatrics, cases with detectable CMV : 07 patients (no deathes); Outpatient Centers, cases with undetectable CMV : 07 patients (no deathes); Outpatient Centers, cases with detectable CMV: no patients.

The length of stay ranged from 1 to 131 days, with an average of 24.45 days. The period with the highest number of CMV reactivation diagnoses was between 1 to 4 days of hospitalization (36.0%). Further details are provided in Supplementary Table 1.

HIV infection (27.0%) was the most common reason for hospitalization or outpatient care among patients with suspected CMV reactivation, followed by autoimmune diseases (19.0%) and lung diseases (10.0%). Additional data are outlined in Supplementary Table 1.

CMV reactivation rates and mortality were significantly higher in patients admitted to the adult ICU (60.00% and 45.00%) compared to those admitted or treated in others sector (19.00% and 1.00%), with p-value less than 0.005. A total of 16 patients (16.0%) had healthcare-associated infections (HAIs), accounting for 29 infections. Among these, four patients had three infections, five patients had two infections, and seven patients had only one infection during the same hospitalization.

CMV reactivation rates and mortality were significantly higher in patients with HAIs (75.00% and 37.50%, respectively) compared to those without HAIs infection (22.62% and 4.76%), whith p-value 0.000. Among patients with HAIs, there were 14 cases (48.28%) of bloodstream infection (BSI), seven cases (24.14%) of respiratory infection (including five VAPs and two nosocomial pneumonias), five cases (17.24%) of urinary tract infection (UTI), and three cases (10.34%) of unknown focus. The microorganisms most frequently causing HAIs were *Klebsiella pneumonia* (33.33%, nine cases), coagulase-negative staphylococci (CNS) (25.93%, seven cases), *Pseudomonas aeruginosa* (14.81%, four cases), *Acinetobacter baumanni* (11.11%, three cases), *Cândida spp* (11.11%, three cases) and *Stenotrophomonas maltophilia* (3.71%, one case).

Discussion

In this study, CMV reactivation was identified in 31% of patients, with higher mortality rates observed in those with CMV reactivation compared to those without. The study included both inpatients (ICU and ward) and outpatients, including patients with HIV infection. In contrast, many international studies have focused only on critically ill adult ICU patients without HIV infection. An international study reported CMV reactivation in 33% of critically ill, immunocompetent ICU patients and associated CMV reactivation with prolonged hospitalization and mortality within 30 days of ICU admission.[13] Additionally, a meta-analysis of 2,400 immunocompetent ICU patients found detectable CMV in 27% of cases.[22]

In the present study, HIV infection was associated with increased mortality and CMV reactivation in patients. A study involving children with HIV admitted to four African hospitals found that CMV viremia was common hospitalized children (54%). CMV levels higher than 1000 iu/ml were linked to a higher risk of mortality, longer hospitalization, and associated complications, regardless of HIV load.[23] Other international studies demonstrate that the presence of CMV DNA in the plasma of HIV-infected patients increases the risk of death.[24–26] CMV infection may contribute to immunological modulation, and increased susceptibility to other infections, further precipitating clinical decline in critically ill, patients.[13]

Treatment for retinitis, colitis and esophagitis due to CMV is well established in patients with immunosuppression due to HIV or other immunosuppressive diseases. The antiviral ganciclovir is known to cause myelotoxicity characterized by anemia, leukopenia, neutropenia or thrombocytopenia.[19–21,27,28] Nonetheless, antiviral treatment indication must be improved for critically ill patients with detectable CMV because mortality was higher among patients who used ganciclovir in this study. Among the 16 patients with CMV reactivation who did not use ganciclovir, one patient died (6.25%). All these patients had a CMV load lower than 3500 copies/dl. The SAPS 3 scores for these 16 patients ranged from 23 to 72 points. The patient who died had a SAPS 3 score of 72 points, indicating a 60% risk of death, with HIV infection and headache being the reasons for hospitalization, ultimately evolving to brain death. In contrast, the remaining 15 patients, who survived and did not use ganciclovir had a SAPS 3 scores of 46 or lower, corresponding to a 12.1% risk of death.

SAPS 3 may be used as an indicator for antiviral treatment in CMV reactivation, though it has some limitations, such as not accounting for patients under 40 years of age, those with rheumatological disease, corticosteroid therapy, or non-neoplastic hematological diseases. Despite these limitations, SAPS 3 is a modern prognostic scoring system designed to predict ICU mortality and may be applicable in settings with a high incidence of patients with HIV infection.[29] In this study, SAPS 3 was also used to score patients with confirmed CMV reactivation who were admitted to a ward due to ICU beds shortages. Critically ill patients are frequently placed in semi-intensive care units within general wards when ICU resources are unavailable.

Fifteen patients with CMV reactivation were treated with ganciclovir, and five of these patients died. The SAPS 3 scores for these fifteen patients ranged from 24 to 62, with the highest score indicating a 39.8% risk of death. The viral load in this subgroup ranged from 50 to 120.894 copies/dl. The reasons for hospitalization of the five patients who died were sepsis in an 81-year-old patient, HIV and Monkeypox, sepsis and choledocholithiasis, HIV and neurocryptococcosis, and HIV in a comatose patient. These five patients who died were critically ill, and therefore, neither CMV reactivation nor ganciclovir use may necessarily be directly related to mortality in this study. Data on these patients with confirmed CMV reactivation are detailed in Supplementary Table 2.

In this study, viral load did not significantly impact mortality, possibly due to the sample size. Data on patient viral loads are outlined in Supplementary Table 1. There is currently no standardized viral load threshold for initiating antiviral treatment, such as ganciclovir, in non-transplant immunocompromised or immunocompetent ICU patients. Real-time PCR, with its high sensitivity, can detect low viral loads during the latent stage of infection, but a positive test does not always confirm active viral reactivation. Thus, defining appropriate cutoff values for PCR tests is crucial.[30] Ganciclovir use in critically ill ICU patients with CMV reactivation should be closely monitored, weighing the risk-benefit ratio considering potential the side effects, including hematological complications (e.g., neutropenia, anemia, thrombocytopenia), renal dysfunction and mental disorders.[19–21] In a

retrospective cohort study, ganciclovir treatment was not associated with better long-term prognosis in non-immunocompromised patients with CMV reactivation and no organ involvement.[31]

A randomized clinical trial involving 124 adult patients admitted to the ICU with a wide range of diagnoses and without immunosuppressed or neutropenic patients evaluated three groups, one using valacyclovir, another group using valganciclovir (450 mg daily) and a third group using placebo, requiring premature discontinuation of the group using valacyclovir due to higher mortality, despite a significantly lower risk of CMV reactivation in the antiviral treatment groups.[32] Another randomized, double-blind, placebo-controlled clinical trial evaluated 156 ICU patients with 88% of patients presenting severe sepsis, evaluating the use of ganciclovir 5 mg/kg/day in one group and the use of placebo in the other group. In this clinical trial, CMV reactivation was significantly lower in the ganciclovir group, along with a greater number of days without mechanical ventilation, but with no differences in mortality, length of hospital stay, or difference in plasma IL-6 levels between days zero and 14.[13]

In this study, mortality and CMV reactivation were higher in patients admitted to adult ICU, with shock, renal dysfunction under dialysis, HAIs, or those requiring mechanical ventilation (MV). Our results align with several studies showing that CMV reactivation worsens outcomes, particularly in immunosuppressed patients or those with septic shock, leading to higher overall mortality, longer ICU and hospital stays, and increased need for MV. These complications and worsened outcomes can be explained by conditions triggered by CMV reactivation, including direct lung injury, amplified systemic inflammation and secondary immunosuppression, which elevate the risk of HAIs. Another contributing factor may be the increase in CD4 and CD8 T-cell apoptosis, compromising the patient's immune response. Additionally, the need for blood transfusion in critically ill ICU patients and the use of corticosteroids or catecholamines may further impair host immunity.[7,22]

A study conducted in Londrina, Brazil, showed CMV reactivation in 17.58% of critically ill ICU patients with sepsis. In these patients, interleukin-10 and nitric oxide levels were increased, and CMV reactivation was associated with kidney failure in sepsis, as well as an increased risk of mortality.[33]

A study conducted in Minas Gerais, Brazil, reported CMV reactivation in 59% of older women and 8% of younger women, with 82% of the older women classified as frail presenting with CMV reactivation. Immunosenescence hinders CD8 T-cells from effectively monitoring infected cells. Concurrently, CMV replication impairs cellular immunity, leading to discussions about the potential for CMV vaccination in the future, particularly for older individuals, like to the chickenpox vaccine.[34]

This study describes the relationship between CMV reactivation, mainly in patients admitted to adult ICU or with HIV infection, and progression to a worse outcome. It also describes the worsening of the outcome in patients who used ganciclovir. However, this study has limitations because it is only descriptive and has a small sample, requiring larger and randomized studies, including HIV-infected patients, to better indicate antivirals for CMV prophylaxis in these patients, with the aid of a specific CMV viral load value and the use of severity scores, such as SAPS 3, for example.

Conclusion

This study on CMV reactivation in non-transplant immunocompromised patients is the first of its kind in the central region of Brazil. Further research is needed to better understand the use of antiviral in the treatment or prophylaxis of CMV reactivation in non-transplant, critically ill patients, including patients admitted to adult ICUs or HIV infection.

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Conflict of interest

There was no type of conflict of interest during the development of the study.

References

1. Cohen JI, Corey GR. Cytomegalovirus infection in the normal host. *Medicine (Baltimore)*. 1985;64(2):100–114.
2. Gandhi MK, Khanna R. Human cytomegalovirus: clinical aspects, immune regulation, and emerging treatments. *Lancet Infect Dis*. 2004;4(12):725–738.
3. Jordan MC, Rousseau WE, Noble GR, et al. Association of cervical cytomegaloviruses with venereal disease. *N Engl J Med*. 1973;288(18):932–934.
4. Pass RF, Little EA, Stagno S, et al. Young children as a probable source of maternal and congenital cytomegalovirus infection. *N Engl J Med*. 1987;316(22):1366–1370.
5. Adler SP. Molecular epidemiology of cytomegalovirus: viral transmission among children attending a day care center, their parents, and caretakers. *J Pediatr*. 1988;112(3):366–672.
6. Horwitz CA, Henle W, Henle G, et al. Clinical and laboratory evaluation of cytomegalovirus-induced mononucleosis in previously healthy individuals. Report of 82 cases. *Medicine (Baltimore)*. 1986;65(2):124–134.
7. Imlay H, Limaye AP. Current Understanding of Cytomegalovirus Reactivation in Critical Illness. *J Infec Dis*. 2020;221(Suppl 1):S94–S102.
8. Cook CH, Yenchar JK, Kraner TO, et al. Occult herpes family viruses may increase mortality in critically ill surgical patients. *Am J Surg*. 1998;176(4):357–360.
9. Heininger A, Jahn G, Engel C, et al. Human cytomegalovirus infections in nonimmunosuppressed critically ill patients. *Crit Care Med*. 2001;29(3):541–547.
10. Jaber S, Chanques G, Borry J, et al. Cytomegalovirus infection in critically ill patients: associated factors and consequences. *Chest*. 2005;127(1):233–241.
11. Kutza AS, Muhl E, Hackstein H, et al. High incidence of active cytomegalovirus infection among septic patients. *Clin Infect Dis*. 1998;26(5):1076–1082.
12. Von Müller L, Klemm A, Weiss M, et al. Active cytomegalovirus infection in patients with septic shock. *Emerg Infect Dis*. 2006;12(10):1517–1522.
13. Limaye AP, Kirby KA, Rubenfeld GD, et al. Cytomegalovirus reactivation in critically ill immunocompetent patients. *JAMA*. 2008;300(4):413–422.
14. Kalil AC, Florescu DF. Prevalence and mortality associated with cytomegalovirus infection in nonimmunosuppressed patients in the intensive care unit. *Crit Care Med*. 2009;37(8):2350–2358.
15. Ong DSY, Klouwenberg PMCK, Verduyn Lunel FM, et al. Cytomegalovirus seroprevalence as a risk factor for poor outcome in acute respiratory distress syndrome*. *Crit Care Med*. 2015;43(2):394–400.
16. Frantzeskaki FG, Karampi ES, Kottaridi C, et al. Cytomegalovirus reactivation in a general, nonimmunosuppressed intensive care unit population: incidence, risk factors, associations with organ dysfunction, and inflammatory biomarkers. *J Crit Care*. 2015;30(2):276–281.

17. Ong DSY, Spitoni C, Klein Klouwenberg PMC, et al. Cytomegalovirus reactivation and mortality in patients with acute respiratory distress syndrome. *Intensive Care Med*. 2016;42(3):333–341.
18. Ong DSY, Bonten MJM, Spitoni C, et al. Epidemiology of Multiple Herpes Viremia in Previously Immunocompetent Patients With Septic Shock. *Clin Infect Dis*. 2017;64(9):1204–1210.
19. Takahata M, Hashino S, Nishio M, et al. Occurrence of adverse events caused by valganciclovir as pre-emptive therapy for cytomegalovirus infection after allogeneic stem cell transplantation is reduced by low-dose administration. *Transpl Infect Dis*. 2015;17(6):810–815.
20. Biron KK. Antiviral drugs for cytomegalovirus diseases. *Antiviral Res*. 2006;71(2-3):154–163.
21. Gilbert C, Boivin G. Human cytomegalovirus resistance to antiviral drugs. *Antimicrob Agents Chemother*. 2005;49(3):873–883.
22. Li X, Huang Y, Xu Z, et al. Cytomegalovirus infection and outcome in immunocompetent patients in the intensive care unit: a systematic review and meta-analisis. *BMC Infect Dis*. 2018;18(1):289–299.
23. Wamalwa D, Njuguna I, Maleche-Obimbo E, et al. Cytomegalovirus Viremia and Clinical Outcomes in Kenyan Children Diagnosed With Human Immunodeficiency Virus (HIV) in Hospital. *Clin Infect Dis*. 2022;74(7):1237–1246.
24. Spector SA, Wong R, Hsia K, et al. Plasma cytomegalovirus (CMV) DNA load predicts CMV disease and survival in AIDS patients. *J Clin Invest*. 1998;101(2):497–502.
25. Brantsæter AB, Johannessen A, Holberg-Petersen M, et al. Cytomegalovirus viremia in dried blood spots is associated with an increased risk of death in HIV-infected patients: a cohort study from rural Tanzania. *Int J Infect Dis*. 2012;16(12):e879–e885.
26. Skipper C, Schleiss MR, Bangdiwala AS, et al. Cytomegalovirus viremia associated with increased mortality in cryptococcal meningitis in sub-Saharan Africa. *Clin Infect Dis*. 2020;71(3):525–531.
27. Munro M, Yadavalli T, Fonteh C, Arfeen S, Lobo-Chan AM. Cytomegalovirus Retinitis in HIV and Non-HIV Individuals. *Microorganisms*. 2020;8(1):55–75.
28. Yeh PJ, Wu RC, Chiu CT, et al. Cytomegalovirus Diseases of the Gastrointestinal Tract. *Viruses*. 2022;14(2):352–365.
29. Merve EV, Kapp J, Pazi S, et al. The SAPS 3 score as a predictor of hospital mortality in a South African tertiary intensive care unit: A prospective cohort study. *Plos One*. 2020;15(5):e0233317.
30. Razonable RR, Hayden RT. Clinical Utility of Viral Load in Management of Cytomegalovirus Infection after Solid Organ Transplantation. *Clin Microbiol Rev*. 2013;26(4):703–727.
31. Park GE, Ki HK, Ko JH. Impact of antiviral treatmente on long-term prognosis in non-immunocompromised patients with CMV reactivation. *BMC Infect Dis*. 2021;21(1):414–419.
32. Cowley NJ, Owen A, Shiels SC, et al. Safety and efficacy of antiviral therapy for prevention of cytomegalovirus reactivation in immunocompetent critically ill patients: a randomized clinical trial. *JAMA Intern Med*. 2017; 177:774–873.
33. Silva TF, Concato VM, Tomiotto-Pellissier F, et al. Reactivation of Cytomegalovirus Increases Nitric Oxide and IL-10 Levels in Sepsis and is Associated with Changes in Renal Parameters and Worse Clinical Outcome. *Sci Rep*. 2019;9(1):9016.
34. Thomasini RL, Pereira DS, Pereira FSM, et al. Aged-associated cytomegalovirus and Epstein-Barr virus reactivation and cytomegalovirus relationship with the frailty syndrome in older women. *PLoS One*. 2017;12(7):e0180841.

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