Characteristic and Outcomes of PLWH Hospitalized with COVID-19 Coinfection: A Literature Review Study

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Abstract

Information on the characteristics and outcomes of HIV patients hospitalized due to COVID-19 coinfection was limited. This was a literature review that was conducted by searching, compiling, and analyzing various studies focusing on the characteristics and outcomes of HIV patients hospitalized with COVID-19. The findings of this study indicated that people living with HIV (PLWH) had a higher risk of hospitalization and poor outcomes. Hospitalized HIV patients with COVID-19 were more prevalent among males, the elderly, those with comorbidities, and those with low CD4 counts. Common signs and symptoms included fever, cough, dyspnea, and fatigue or myalgia. Patient outcomes could be unfavorable, especially if the patient was immunocompromised.

Keywords: Characteristic; COVID-19; Hospitalized; HIV; Outcome

1. Introduction

Coronavirus Disease 2019 (COVID-19) was first detected in China in December 2019. The cause of COVID-19 is Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). This virus, also known as 2019 nCoV, belongs to the coronavirus family and is the seventh known to infect humans. It is believed to be a zoonotic virus originating from a seafood market in Wuhan, China. The ongoing global COVID-19 pandemic has resulted in high morbidity and mortality rates (Zhu et al., 2020).

Everyone has the potential to be infected with SARS-CoV-2 and experience severe symptoms. Weak immune conditions increase the risk of severe symptoms, leading to hospitalization, intensive care, ventilator support, and even death due to COVID-19. HIV is identified as a condition that can lead to worse clinical outcomes for COVID-19 patients (Díez et al., 2021). People Living With HIV (PLWH) are twice as likely to be hospitalized due to COVID-19 co-infection compared to non-infected individuals (Puyat et al., 2023). HIV causes immunosuppression, resulting in a higher risk of severe COVID-19 compared to those not infected (Mirzaei et al., 2020). HIV impairs the immune system by targeting CD4, and a correlation is observed between low CD4 counts, lymphopenia, and the severity of the disease in individuals with HIV and COVID-19 co-infection (Danwang et al., 2022). Low CD4 counts are associated with poor outcomes in HIV patients with COVID-19 co-infection (Dandachi et al., 2020).

The relationship between HIV and COVID-19 is still not fully understood. Factors such as male gender, age 45-75, BMI, diabetes, and chronic cardiac diseases or hypertension can elevate the severity of COVID-19 in individuals with HIV (Bertagnolio et al., 2022; Shapiro et al., 2022).

2. Material and Methods

This is a literature review that is conduct by searching, compiling, and analyzing various studies focusing on the characteristics and outcomes of HIV patients hospitalized with COVID-19. The sources were cited from PubMed and Google Scholar. The Search term used for searching were about “HIV”, “COVID-19”, “Characteristic”, and “Hospitalized”. Studies were included in the review after a series of duplicate removal, title and abstract screening, and full-text screening.

3. Result and Discussion

3.1. HIV and COVID-19 Coinfection

The clinical interaction between HIV and COVID-19 remains unclear. Research conducted has yielded conflicting results, with some studies indicating that the outcomes of COVID-19 in individuals living with HIV (PLWH) are similar or even better than those without HIV infection. However, other studies state that low CD4 lymphocyte counts and untreated HIV lead to worse outcomes. In summary, individuals with well-controlled HIV are not at an increased risk of experiencing worse COVID-19 outcomes. Current guidelines suggest that PLWH may have a higher risk of adverse outcomes compared to those without HIV infection (Kamis et al., 2021).

The increased risk of severe COVID-19 is based on the assumption that PLWH are more likely to be in an immunosuppressed state. HIV infection is associated with abnormal humoral and T-cell immune responses, rendering PLWH susceptible to various opportunistic infections (Mirzaei et al., 2020). Studies conducted by Kamis et al. (2021) and Barbera et al. (2021) found that older age, low CD4 counts, and comorbidities are significantly associated with hospitalized HIV patients with COVID-19 coinfection..

3.2. Sign and Symptoms

PLWH who are hospitalized due to COVID-19 may experience various symptoms. According to research conducted by (Ceballos et al., 2021), the most common symptoms in PLWH with COVID-19 include fever (88%), cough (69.4%), dyspnea (66.7%), hypotension (50%), fatigue or myalgia (41.7%), and diarrhea (36.1%). Additionally, PLWH may also experience persistent symptoms such as chest pain, headache, and abdominal pain, which are associated with inflammatory markers and HIV (Geretti et al., 2020).

3.3. Sociodemographics

References A study conducted by (Ceballos et al., 2021) indicates that (93.5%) of hospitalized PLWH due to COVID-19 are male, with an average age of 44 years. Furthermore, research conducted by (Geretti et al., 2020) also found a similar pattern, with (65.1%) of patients being male and a median age of 56 years. A study by (Ming Jie Lee et al., 2021) also discovered that (61.8%) of patients were male, with a median age of 57 years. These findings suggest that the majority of PLWH hospitalized with COVID-19 are male, but there is also a significant proportion of female patients.

3.4. Comorbidity

In general population, the most influential factors contributing to severe illness and mortality in PLHIV appear to be age and the presence of concurrent health conditions. Common comorbidities observed in PLHIV hospitalized with COVID-19 include hypertension, cardiovascular disease, diabetes, and respiratory disease (Ceballos et al., 2021; Geretti et al., 2020; Ming Jie Lee et al., 2021). A multicenter case-series study revealed that 84.1% of PLHIV hospitalized with COVID-19 had pre-existing comorbidities, with fever, cough, and dyspnea being the most frequent (Cabello et al., 2021). Additionally, a meta-analysis indicated that PLHIV with coexisting diabetes, hypertension, cardiovascular disease, and respiratory disease are more prone to severe COVID-19 outcomes (Wang and Jonas, 2021). Moreover, global data compiled by the World Health Organization (WHO) suggested that PLHIV often encounter adverse social determinants of health and have a high prevalence of comorbidities linked to worse COVID-19 outcomes, such as cardiovascular disease, which may elevate their risk of severe COVID-19 independently of their HIV disease or immune status (WHO., 2023).

3.5. CD4

The CD4 count of PLHIV who are hospitalized with COVID-19 is a crucial variable to consider when predicting COVID-19 outcomes. A study from the University of Missouri revealed that PLHIV with a CD4 count of 200 cells/mm³ faced an increased risk of intensive care unit (ICU) admission, mechanical ventilation, or death (Mounika et al., 2023). Additionally, research conducted by (Shapiro et al., 2022) found an independent association between a CD4 count <350 cells/mm³, a lower nadir CD4 (<200 cells/mm³), and a lower CD4/CD8 ratio with the rate of hospitalization. Another study reported that markers of disease severity in PLHIV hospitalized with COVID-19 were stratified by CD4 count and HIV-1 viral load, with a CD4 count below 200 cells/µL being associated with greater disease severity (Boswell et al., 2023). (Ming Jie Lee et al., 2021) also found that the median CD4 count of patients was 352 cells/mm³.

3.6. Outcomes

HIV patients hospitalized due to COVID-19 exhibit different outcomes depending on the patient's immune status. PLHIV with advanced HIV disease, lower CD4 T-cell counts, or non-suppressed viral loads appear to be at an increased risk of poor outcomes and death due to COVID-19 (WHO., 2023). In 2020, the in-hospital mortality rate was higher in PLHIV compared to the control group (27.9% vs. 17.7%). However, in 2021, there was no significant difference in mortality between the two groups (25.0% vs. 25.1%) (Sales et al., 2023). A cohort study conducted by (Tesoriero et al., 2021) found that PLHIV were more likely to be admitted to the hospital and die in the hospital compared to non-PLHIV. Another study reported increased rates of intensive care unit admission, mechanical ventilation, and mortality in HIV-positive patients, although these differences were not statistically significant. However, in a study conducted by (Díez et al., 2021), it was found that well-controlled patients did not experience adverse outcomes.

4. Conclusion

People Living with HIV (PLWH) have a higher risk of hospitalization and poorer outcomes. Hospitalized HIV patients with COVID-19 are more prevalent among males, elderly, those with comorbidities, and those with low CD4 counts. Common signs and symptoms include fever, cough, dyspnea, fatigue, or myalgia. Patient outcomes may be unfavorable if the patient is immunocompromised.

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References

Barbera, L.K. et al. (2021). Risk factors for hospitalization in people with HIV and COVID-19. Topics in Antiviral Medicine, [online] pp.206–207. Available at: https://pesquisa.bvsalud.org/global-literature-on-novel-coronavirus-2019 ncov/resource/pt/covidwho-1249931

Bertagnolio, S., Thwin, S.S., Silva, R., Nagarajan, S., Jassat, W., Fowler, R., Haniffa, R., Reveiz, L., Ford, N., Doherty, M. and Diaz, J. (2022). Clinical features of, and risk factors for, severe or fatal COVID-19 among people living with HIV admitted to hospital: analysis of data from the WHO Global Clinical Platform of COVID-19. The Lancet HIV, [online] 9(7), pp.e486–e495. doi:https://doi.org/10.1016/S2352-3018(22)00097-2

Boswell, M.T., Maimela, T., Hameiri-Bowen, D., Riley, G., Malan, A., Steyn, N., Nolutshungu, N., de Villiers, T.R., de Beer, Z., Mathabathe, J., Tshabalala, K., Abdullah, F., Ramlall, R., Heystek, M., Basu, D., Rheeder, P., Ueckermann, V. and van Hougenhouck-Tulleken, W. (2023). COVID-19 severity and in-hospital mortality in an area with high HIV prevalence. Southern African Journal of HIV Medicine, [online] 24(1), p.1412.doi:https://doi.org/10.4102/sajhivmed.v24i1.1412.

Cabello, A., Zamarro, B., Nistal, S., Victor, V., Hernández, J., Prieto-Pérez, L., Carrillo, I., Álvarez, B., Fernández-Roblas, R., Hernández-Segurado, M., Becares, J., Benito, J.M., Rallón, N., Téllez, R., Castaño, Á.L., Herrero, A. and Górgolas, M. (2021). COVID-19 in people living with HIV: A multicenter case-series study. International Journal of Infectious Diseases, 102, pp.310–315. doi:https://doi.org/10.1016/j.ijid.2020.10.060.

Ceballos, M.E., Ross, P., Lasso, M., Dominguez, I., Puente, M., Valenzuela, P., Enberg, M., Serri, M., Muñoz, R., Pinos, Y., Silva, M., Noguera, M., Dominguez, A. and Zamora, F. (2021). Clinical characteristics and outcomes of people living with HIV hospitalized with COVID-19: a nationwide experience. International Journal of STD & AIDS, 32(5), pp.435–443. doi:https://doi.org/10.1177/0956462420973106.

Danwang, C., Noubiap, J.J., Robert, A. and Yombi, J.C. (2022). Outcomes of patients with HIV and COVID-19 co-infection: a systematic review and meta analysis. AIDS Research and Therapy, 19(1). doi:10.1186/s12981-021- 00427-y.

Díez, C., Del Romero-Raposo, J., Mican, R., López, J.C., Blanco, J.R., Calzado, S., Samperiz, G., Portilla, J., García-Fraile, L.J., Gutiérrez, F., Gómez-Sirvent, J.L., Suárez-García, I., Amador, C., Novella, M., Arribas, J.R., Moreno, S., González-García, J., Jarrín, I., Berenguer, J. and Moreno, S. (2021). COVID-19 in hospitalized HIV-positive and HIV-negative patients: A matched study. HIV Medicine, 22(9), pp.867–876. doi:https://doi.org/10.1111/hiv.13145.

Geretti, A.M., Stockdale, A.J., Kelly, S.H., Cevik, M., Collins, S., Waters, L., Villa, G., Docherty, A., Harrison, E.M., Turtle, L., Openshaw, P.J.M., Baillie, J.K., Sabin, C.A. and Semple, M.G. (2020). Outcomes of Coronavirus Disease 2019 (COVID-19) Related Hospitalization Among People With Human Immunodeficiency Virus (HIV) in the ISARIC World Health Organization (WHO) Clinical Characterization Protocol (UK): A Prospective Observational Study. Clinical Infectious Diseases, 73(7), pp.e2095–e2106. doi:https://doi.org/10.1093/cid/ciaa1605.

Kamis, K.F., et al. (2021). Risk Factors for Hospitalization in People With HIV and COVID-19. Journal of Acquired Immune Deficiency Syndromes (1999), [online] 88(3), p.e22. doi:10.1097/QAI.0000000000002780.

Ming Jie Lee, Snell, L.B., Douthwaite, S., Fidler, S., Fitzgerald, N., Goodwin, L., Hamzah, L., Ranjababu Kulasegaram, Lawrence, S., Lwanga, J., Marchant, R., Orkin, C., Palfreeman, A., Padmini Parthasarathi, Manish Pareek, Ring, K., Sharaf, H., Shekarchi-Khanghahi, E., Simons, R. and Jhia Jiat Teh (2021). Clinical outcomes of patients with and without HIV hospitalized with COVID-19 in England during the early stages of the pandemic: a matched retrospective multi-centre analysis (RECEDE-C19 study). Hiv Medicine, 23(2), pp.121–133. doi:https://doi.org/10.1111/hiv.13174.

Mirzaei, H., McFarland, W., Karamouzian, M. and Sharifi, H. (2020). COVID-19 Among People Living with HIV: A Systematic Review. AIDS and Behavior. doi:10.1007/s10461-020-02983-2.

Mounika, V.L., Kumar, V.U., Dhingra, S., Ravichandiran, V., Pandey, K., Parihar, V.K. and Murti, K. (2023). CD4 + Count: a Variable to Be Considered to Prioritize COVID-19 Vaccination in PLHIV. Current Pharmacology Reports. doi:https://doi.org/10.1007/s40495-023-00312-4.

Puyat, J.H., Fowokan, A., Wilton, J., Janjua, N.Z., Wong, J., Grennan, T., Chambers, C., Kroch, A., Costiniuk, C.T., Cooper, C.L., Lauscher, D., Strong, M., Burchell, A.N., Anis, A.H. and Samji, H. (2023). Risk of COVID-19 hospitalization in people living with HIV and HIV-negative individuals and the role of COVID-19 vaccination: A retrospective cohort study. International Journal of Infectious Diseases, [online] 135, pp.49–56. doi:https://doi.org/10.1016/j.ijid.2023.06.026.

Sales, T.L.S., Souza-Silva, M.V.R., Delfino-Pereira, P., Neves, J.V.B., Sacioto, M.F., Assis, V.C.M. de, Duani, H., Oliveira, N.R. de, Sampaio, N. da C.S., Ramos, L.E.F., Schwarzbold, A.V., Jorge, A. de O., Scotton, A.L.B.A., Castro, B.M. de, Silva, C.T.C.A. da, Ramos, C.M., Anschau, F., Botoni, F.A., Grizende, G.M.S. and Nascimento, G.F. (2023). COVID-19 outcomes in people living with HIV: Peering through the waves. Clinics, [online] 78, p.100223. doi:https://doi.org/10.1016/j.clinsp.2023.100223.

Shapiro, A.E., et al. (2022). Factors associated with severity of COVID-19 disease in a multicenter cohort of people with HIV in the

United States, March- December 2020. JAIDS Journal of Acquired Immune Deficiency Syndromes, [online] p.10.1097/QAI.0000000000002989.

Tesoriero, J.M., Swain, C.-A.E., Pierce, J.L., Zamboni, L., Wu, M., Holtgrave, D.R., Gonzalez, C.J., Udo, T., Morne, J.E., Hart-Malloy, R., Rajulu, D.T., Leung, S.-Y.J. and Rosenberg, E.S. (2021). COVID-19 Outcomes Among Persons Living With or Without Diagnosed HIV Infection in New York State. JAMA Network Open, 4(2), p.e2037069. doi:https://doi.org/10.1001/jamanetworkopen.2020.37069.

Wang, H. and Jonas, K.J. (2021). The likelihood of severe COVID-19 outcomes among PLHIV with various comorbidities: a comparative frequentist and Bayesian meta-analysis approach. [online] 24(11). doi:https://doi.org/10.1002/jia2.25841.

WHO. (2023). Coronavirus disease (COVID-19) and people living with HIV. [online] Available at: https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-(covid-19)-covid-19-and-people-living-with-hiv [Accessed 21 Aug. 2022].

Zhu, N., et al. (2020). A Novel Coronavirus from Patients with Pneumonia in China, 2019. New England Journal of Medicine, 382(8). doi:10.1056/nejmoa200101.