

# Impacts of the HIV and COVID-19 syndemy: Integrative review

**Impactos da sindemia HIV e COVID-19: Revisão integrativa**

**Impactos del síndrome de VIH y COVID-19: Revisión integrativa**

## RESUMO

Objetivou-se identificar na literatura científica os impactos na saúde da população acometida pela coinfeção HIV/COVID-19. Desenvolve-se uma revisão integrativa, durante os meses de junho e julho de 2022 em três bases de dados: LILACS, MEDLINE/Pubmed e SciELO, com os descritores HIV e COVID-19. Foram encontrados 342 artigos, mas 20 compuseram a amostra. Os resultados foram agrupados em quatro categorias a saber: Impactos Clínicos, Hematológicos, Psicológicos e Sociais. Conclui-se que a população coinfectada apresentou impactos negativos na sua condição de saúde, sendo necessário um olhar mais direcionado para o público em questão, buscando melhorar a assistência prestada.

**DESCRIPTORES:** HIV; COVID-19; Coinfeção.

## ABSTRACT

The objective was to identify in the scientific literature the impacts on the health of the population affected by HIV/COVID-19 coinfection. An integrative review was developed during the months of June and July 2022 in three databases: LILACS, MEDLINE/Pubmed and SciELO, with the descriptors HIV and COVID-19. A total of 342 articles were found, but 20 made up the sample. The results were grouped into four categories, namely: Clinical, Hematological, Psychological and Social Impacts. It is concluded that the co-infected population had negative impacts on their health condition, requiring a more focused look at the public in question, seeking to improve the care provided.

**DESCRIPTORS:** HIV; COVID-19; Coinfection.

## RESUMEN

El objetivo fue identificar en la literatura científica los impactos en la salud de la población afectada por la coinfección VIH/COVID-19. Se desarrolló una revisión integradora durante los meses de junio y julio de 2022 en tres bases de datos: LILACS, MEDLINE/Pubmed y SciELO, con los descriptores VIH y COVID-19. Se encontraron un total de 342 artículos, pero 20 conformaron la muestra. Los resultados se agruparon en cuatro categorías, a saber: impactos clínicos, hematológicos, psicológicos y sociales. Se concluye que la población coinfectada tuvo impactos negativos en su condición de salud, requiriendo una mirada más focalizada en el público en cuestión, buscando mejorar la atención prestada.

**DESCRIPTORES:** VIH; COVID-19; Coinfección.

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ORCID: 0000-0002-8864-5369**INTRODUCTION**

The pandemic caused by SARS-CoV-2, responsible for causing a severe acute respiratory syndrome, also called COVID-19, is considered a public health emergency that affects the population since the end of 2019. Infection with the Human Immunodeficiency Virus (HIV) is causing a syndemy with an important impact on public health.<sup>(1)</sup>

As the COVID-19 pandemic affected the world, there was the confinement of people and consequent social isolation, leading to the closure of health facilities. In the case of HIV, it had negative impacts, as it influenced the reduction of access to health services, such as consultations and distribution of medicines, increasing the risk of mortality for this population.<sup>(1-2)</sup>

From January 2012 to November 2021, 14,071 new HIV cases and 10,215 AIDS cases were diagnosed in the state of Ceará. Since 2015, there has been a decline in the AIDS detection rate, which went from 13.0/100,000 inhabitants (2015) to 5.9/100,000 inhabitants (2021), configuring a decrease of 54.62%.<sup>(3)</sup> A matter of debate includes the frequency and severity of COVID-19 in these immunocompromised patients, with continued treatment and access to antiretrovirals (ART) being important, whereas maintenance of suppressed viral load and a normal CD4 T lymphocyte count are likely to decrease the risk of severe cases of COVID-19.<sup>(1)</sup>

Both infections cause damage to the health of the affected victims, generating challenges and uncertainties in the monitoring and management of the care provided. The simultaneous impact of these infections can predispose victims to more severe clinical symptoms and a worse prognosis<sup>(4)</sup>, as the population living with HIV (PLHIV) may be more vulnerable and prone to more serious complications from COVID-19 when compared to the general population.<sup>(2)</sup>

Given the above, it is necessary and important to assess the impact of the syndemy on the health of these people, identifying the severity of the results. Thus, the research seeks to identify the impact of these infections on the health of these victims, in order to propose measures to improve the health care provided based on the findings, with a targeted and individualized look at this most vulnerable public. In addition, it may serve as a subsidy to encourage and create government services and programs to monitor these patients, always seeking to improve their quality of life.

Thus, the objective was to identify in the scientific literature the impacts on the health of the population affected by HIV/COVID-19 coinfection.

**METHOD**

This is an integrative review, which is structured through the collection and

comparison of data available in the literature to probe the knowledge on the proposed theme and was developed in the following steps: Identification of the theme; Literature search; Data collect; Data analysis, Interpretation of results and Presentation of the review.<sup>(5)</sup>

We sought to answer the following guiding question, formulated based on the PICO strategy<sup>(6)</sup>: “What are the impacts on the health of the population affected by HIV/COVID-19 coinfection?”

The electronic search of the studies was carried out in June and July 2022, in three databases: Latin American and Caribbean Literature in Health Sciences (LILACS), the Medical Literature Analysis and Retrieval System Online portal (MEDLINE/Pubmed) and the Scientific Electronic Library Online (SciELO). The descriptors “COVID-19” and “HIV” were used.

From the crossing carried out, 342 articles were found, of which 252 were excluded for not answering the research question, thus, 90 publications were pre-selected, of which 20 made up the final sample of the review. Seven duplicate publications and 63 articles that did not address HIV/COVID-19 coinfection were excluded, as they dealt with an association with TB; vaccine impacts; neoplasms; food security; reduction of testing; hepatitis C; post-exposure prophylaxis to HIV; zika; transfusion medicine; hemophilia; syphilis; sexuality and prevention in men who have sex with men.

The inclusion criteria consisted of complete articles, available electronically, without excluding languages, without time frame, which present discussions about the impacts of HIV/COVID-19 coinfection on the affected population. Repeated publications and literature reviews were excluded.

Data analysis was performed through translation and reading of the articles in full. The information was transcribed and organized from a validated instrument that investigated the methodological development, impacts and outcomes of HIV/COVID-19 coinfection, conclusion and levels of evidence.<sup>(7)</sup>

The levels of evidence were determined as follows: Level I – Evidence from a systematic review or meta-analysis of multiple randomized controlled clinical trials or from clinical guidelines, based on systema-

tic reviews of randomized controlled clinical trials; Level II - Evidence from individual controlled and randomized studies; Level III - Evidence from experimental studies without randomization; Level IV - Evidence from cohort or case-control; Level V - Evidence from a systematic review of descriptive and qualitative studies; Level VI - Evidence from a descriptive or qualitative study; Level VII - Evidence obtained from the opinions of authorities or reports from expert committees.<sup>(8)</sup>

After analysis, the 22 articles were grouped into four categories divided into 1- Clinical, 2- Hematological, 3 - Psychological and 4 - Social impacts.

**RESULTS**

As for the characterization of the studies, the year of variation ranged from

2020 to 2022, twelve of which were carried out on the American continent, four on the Asian continent, three on the European continent and one on the African continent. As for the levels of evidence, level VI prevailed (Chart 1).

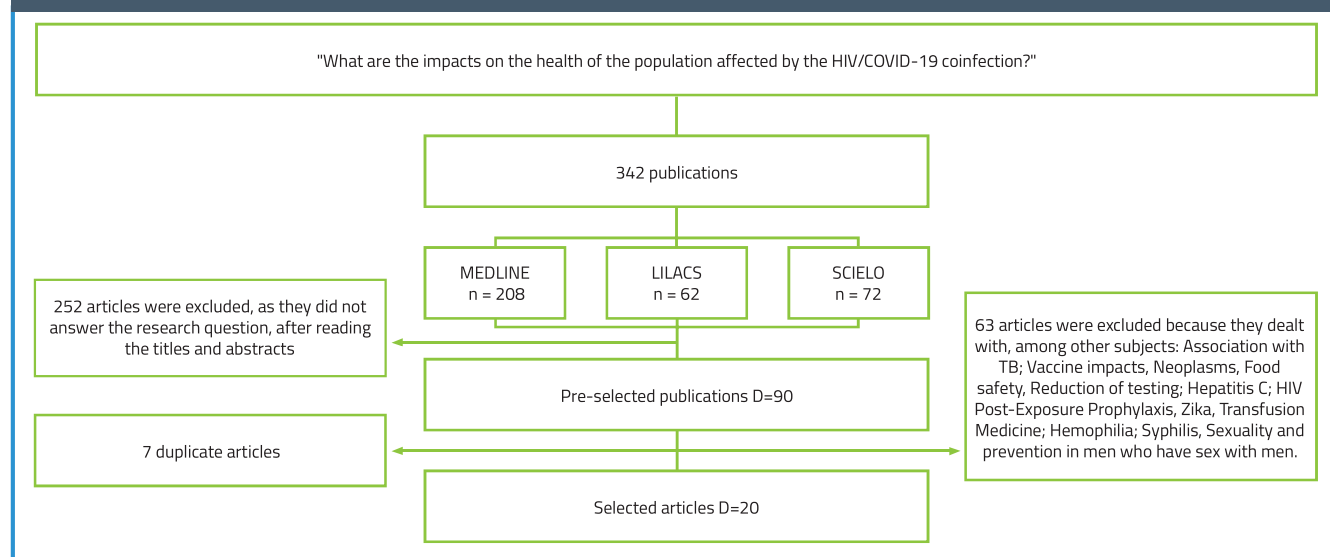
The results were divided into four categories, namely: 1- Clinical Impacts, 2- Hematological Impacts, 3- Psychological Impacts and 4 - Social Impacts.

**DISCUSSION**

The results were divided into categories covering clinical, hematological, psychological and social impacts, which will be described in the following paragraphs. Clinical and hematological impacts were the ones with the most outcomes.

PLWHA and COVID-19 were more likely to have fever, headache, myalgia and

Figure 1 shows the identification, selection and inclusion of scientific productions.



Source: Authors, 2022

Table 1- Results found according to Author, year, country of study, methodological design, main findings, level of evidence and category. Fortaleza, Ceará, 2022.

AUTHOR/ YEAR	COUNTRY OF CONDUCT OF THE STUDY	METHODOLOGICAL DESIGN	RESULTS	LEVEL OF EVIDENCE	CATEGORY
Matsuda et al., 2022	Brazil	Ecological Study	Higher mortality. Interruption in exams	VI	1



Cunha et al., 2022	Brazil	Cross-sectional study	No follow-up appointments. Inadequate adherence to ART	VI	4
Bhaskaran et al., 2021	England	Cohort	Higher mortality	IV	1
Longueira et al., 2021	Argentina	Cross-sectional study	The most reported symptoms were headache, anosmia, fever, odynophagia and dysgeusia.	VI	1
Geretti et al., 2021	England, Scotland, Wales	Cohort	More symptoms of fever, headache, myalgia, tachycardia, cough and chest pain. Lower white blood cell and platelet count, higher C-reactive protein (CRP) count. Higher mortality	IV	1, 2
Calza et al., 2021	Italy	Case series	Higher prevalence of comorbidities	VI	1
Yang et al., 2021	China	Case-control	Longer time with symptoms. Lower levels of IgG	IV	1, 2
Dandachi et al., 2021	USA	Clinical trial	More symptoms of fever, fatigue, dyspnea, Changes in mental status. Longer hospitalization time. Higher mortality	I	1, 3, 1, 1
Huang et al., 2021	China	Cohort	Níveis mais baixos de anticorpos IgG e IgM	IV	2
Hu et al., 2021	Wuhan - China	Cross-sectional study	Severe form of the disease. Higher viral load	VI	1
Ho et al., 2021	New York	Cross-sectional study	Severe form of the disease. Lymphopenia. Drop in CD4 rates. Higher mortality. Increase in inflammatory markers	VI	1, 2
Cooley et al., 2021	USA	Cross-sectional study	More depressive and anxiety symptoms, Greater use of tobacco and marijuana	VI	3, 4
Silva et al., 2021	Brazil	Case study	Severe form of the disease	VI	1
Pereira; Gir; Santos, 2021	Brazil	Cross-sectional study	Social isolation, Difficulties in accessing health services, Change in behavior and emotions in the home environment, Change in eating habits	VI	3, 4
Menghua et al., 2020	China	Case report	Prolonged duration of viral spread, Lymphopenia	VI	1, 2
Parker et al., 2020	South Africa	Case report	Increased fever time, Cough, Myalgia, Diarrhea, and Dyspnea Acute respiratory distress and Hyposaturation, Via advanced area Transfer to ICU, Lymphopenia, Thrombocytopenia, Low CD4 count, CRP level changed, Hepatic transaminitis	VI	1, 2
Carballo; Erazo, 2020	Honduras	Case series	Respiratory symptoms, fever, cough and dyspnea Severe hypoxia Ventilatory support, Higher mortality	VI	1
Larzabal et al., 2020	Argentina	Case report	More symptoms of dyspnea and sputum. bilateral lung opacities	VI	1
Bessa et al., 2020	Brazil	Case report	Dyspnea and asthenia. hemiparesis	VI	1
Carballo; Erazo; Chevez, 2020	Honduras	Case report	Intermittent fever, pharyngeal hyperemia, dry cough, dyspnea and hyposaturation Leukocytosis. bilateral interstitial infiltrates. Septic shock. severe immunosuppression. Low adherence to ART. increased fever time. Hepatomegaly	VI	1, 2, 4

Source: Authors, 2022

tachycardia, cough, chest pain.<sup>(9-11)</sup> There was also a longer duration of symptoms, including fever, in which co-infected patients had higher body temperatures and longer duration of symptoms, statistically proven.<sup>(12-13)</sup> This also entailed prolonged duration of viral shedding.<sup>(11,14)</sup>

Of the hematological markers, this co-infected population had lower total white blood cell and platelet counts, higher C-reactive protein (CRP) counts<sup>(9,13)</sup> and Lymphopenia.<sup>(12,14-15)</sup> In a review developed, it was identified that lymphopenia can be explained with a defective immune response to SARS-CoV-2, this can be explained by the expression of the ACE2 receptor by lymphocytes. In this way, there would be a direct infection of the SARS-CoV-2 to the lymphocytes, leading them to lysis.<sup>(16)</sup> In a recent meta-analysis, it was observed that 35% to 75% of patients developed lymphopenia and that this was a frequent characteristic identified among patients who died.<sup>(17)</sup> Thus, monitoring this parameter is an important marker due to the risk of complicating the patient's clinical condition.

Other important findings were increased viral load<sup>(18)</sup>, drop in CD4+ rates<sup>(12)</sup> and severe inflammatory responses with increased inflammatory markers, including C-reactive protein, fibrinogen, D-dimer, interleukin 6, interleukin 8, and tumor necrosis factor  $\alpha$ .<sup>(15)</sup> It is observed that after the onset of the first symptoms, there is an increase in the clinical manifestations of the disease with the development of inflammatory mediators and cytokines, which also leads to lymphopenia.<sup>(16)</sup> PLWHA who died had higher levels of inflammatory markers and more severe lymphopenia than those who recovered, i.e. inflammation was closely linked to disease severity in COVID-19.<sup>(15)</sup> IGg and IGm levels were also significant, as they were lower in patients with higher viral load.<sup>(12,19)</sup> Monitoring these parameters can help identify patients who may need better follow-up.

These factors directly impact the health of this exposed population, even increasing the risk of mortality<sup>(9,10,15)</sup> due to the longer

hospitalization time<sup>(10)</sup>, of acquiring the most severe forms and worst outcomes of the disease<sup>(10,18,20)</sup>, as it has a weaker immune system. The highest risk of mortality in this population has been identified in several studies<sup>(9,21-23)</sup>, especially when they had another comorbidity.<sup>(21)</sup>

**In the case of HIV, it had negative impacts, as it influenced the reduction of access to health services, such as consultations and distribution of medicines, increasing the risk of mortality for this population.**

In the category of psychological impacts, there was the highest prevalence of depressive and anxiety symptoms, in addition to symptoms of loneliness.<sup>(24)</sup> Psychiatric disorders such as anxiety, depression and post-traumatic stress are common in PLWHA, most of the time due to the stigma experienced daily by these people. In addition, the pandemic itself caused these symptoms, worsening existing mental di-

sorders, due to concerns related to the imminent future, the uncertainty, in addition to the social isolation experienced, all of which contributed to an increase in mental disorders. Thus, balanced mental health is necessary, providing psychosocial care and ensuring access to health services.<sup>(25)</sup>

Associated with these symptoms is the use of substances such as tobacco and marijuana, and their use is related to greater symptoms of depression.<sup>(24)</sup> Substance use can lead to health complications for PLWHA, including worsening adherence to ART, causing negative impacts, increasing the risk of complications, increase in viral load, decrease in CD4+ T lymphocyte levels, increased risk of morbidity and mortality and acquisition of opportunistic diseases.<sup>(26)</sup>

## CONCLUSION

Several impacts on the health of people co-infected with HIV/COVID-19 can be identified, negatively interfering in their recovery process and coping with the disease. Among these impacts, the clinical and hematological ones were highlighted, such as higher mortality, prevalence of the most severe form of the disease, more intense and lasting flu-like symptoms.

In view of what has been exposed and the impacts identified, this population may be more exposed and vulnerable, requiring a more targeted look from governments to improve access to health services, given that some organs had a temporary interruption in their care, which worsened access to ART and increased the risk of complications and aggravations of co-infection.

As a limitation of the study, there was the absence of publications with level I and II evidence, perhaps because the search was carried out in only three databases. For future studies, more research in other databases is recommended so that studies with clinical trials that compare populations with and without HIV can be identified in order to have comparative results with scientific value.

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