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From Virus to Vessel: Viral Infections and Pulmonary Hypertension — A Systematic Review and Mechanistic Synthesis

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Abstract

Pulmonary hypertension (PH) has been increasingly reported in association with several viral infections, including human immunodeficiency virus (HIV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), herpesviruses, respiratory syncytial virus (RSV), cytomegalovirus (CMV), and hepatitis C virus (HCV). However, the mechanisms linking viral infection to pulmonary vascular disease remain incompletely understood. This study was conducted as a systematic review with mechanistic synthesis in accordance with PRISMA 2020 guidelines. A structured search of PubMed, PubMed Central (PMC), the Cochrane Library, and MDPI was performed for studies published between January 2011 and February 2024. Evidence from observational human studies, animal models, case reports, and mechanistic and narrative reviews was synthesized qualitatively. Study quality was assessed using design-specific appraisal tools. Across diverse viral pathogens, pulmonary hypertension is frequently reported as a recurrent vascular phenotype characterized by immune dysregulation, endothelial injury, thrombo-inflammation, and pulmonary vascular remodeling. However, human evidence is predominantly observational and frequently based on echocardiographic assessment, limiting causal inference. Integrating clinical and experimental findings, this review proposes a stepwise pathophysiological framework linking viral infection to pulmonary hypertension. While the strongest clinical evidence exists for HIV-associated pulmonary hypertension, evidence for other viral infections remains more limited or indirect. These findings suggest a biologically plausible association between viral infection and pulmonary vascular disease while highlighting the need for prospective studies incorporating invasive hemodynamic assessment and longitudinal follow-up. Key methodological limitations include single-reviewer screening and the predominance of observational human studies relying on echocardiographic assessment and heterogeneous diagnostic approaches.

Keywords: Pulmonary hypertension, viral infections, COVID-19, HIV, endothelial dysfunction, immune dysregulation, pulmonary vascular remodeling

Introduction

Pulmonary hypertension (PH) is a hemodynamic and clinical condition characterized by elevated pulmonary arterial pressure arising from diverse etiologies and pathophysiologic mechanisms. Within this spectrum, pulmonary arterial hypertension (PAH) is a form of pre-capillary pulmonary hypertension defined by a mean pulmonary artery pressure (mPAP) >20 mmHg at rest, pulmonary arterial wedge pressure ≤15 mmHg, and pulmonary vascular resistance >2 Wood units, confirmed by right heart catheterization within an appropriate clinical context. Although hemodynamic thresholds are essential for diagnosis, final classification requires integration of clinical presentation with findings from comprehensive investigations [1]. This condition represents a serious global health concern, with prevalence estimates suggesting involvement of approximately 1% of the global population, rising to nearly 10% among individuals older than 65 years, particularly in aging societies [2].

Elevation in mPAP arises from diverse etiologies and pathogenic mechanisms. Consequently, pulmonary hypertension has been classified by the World Health Organization (WHO) into five distinct clinical groups based on underlying cause and pathophysiology outlined in **Table 1** [3,4].

Table 1. Pulmonary Hypertension Classifications.

PH Group	Category	Subtypes / Conditions
Group 1	**Pulmonary Arterial Hypertension (PAH)**	Idiopathic PAH
		Heritable PAH
		Drug- and toxin-induced PAH
		PAH associated with connective tissue diseases
		PAH associated with portal hypertension
		PAH associated with congenital heart diseases
		PAH associated with HIV infection
		PAH associated with schistosomiasis
		PAH with long-term response to calcium channel blockers

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		PAH with overt features of venous/capillary involvement (PVOD/PCH phenotype)
		Persistent pulmonary hypertension of the newborn
Group 2	**Pulmonary Hypertension due to Left Heart Disease**	PH due to heart failure with preserved LVEF
		PH due to heart failure with reduced LVEF
		Valvular heart disease
		Congenital or acquired cardiovascular conditions leading to post-capillary PH
Group 3	**Pulmonary Hypertension due to Lung Diseases and/or Hypoxia**	Obstructive lung disease
		Restrictive lung disease
		Lung diseases with mixed restrictive/obstructive pattern
		Hypoxia without lung disease
		Developmental lung disorders
Group 4	**Pulmonary Hypertension due to Pulmonary Artery Obstructions**	Chronic thromboembolic pulmonary hypertension (CTEPH)
		Other pulmonary artery obstructions
Group 5	**Pulmonary Hypertension with Unclear and/or Multifactorial Mechanisms**	Hematological disorders
		Systemic and metabolic disorders
		Other conditions
		Complex congenital heart diseases

Among these, Group 1 PAH is characterized by progressive pulmonary vascular remodeling and may develop additional pathological features superimposed on primary disease process, further worsening disease severity and progression [5–8].

Pulmonary arterial hypertension affects individuals of all ages and both sexes and is associated with increased pulmonary vascular resistance, ultimately leading to right ventricular failure and premature death. The natural history of untreated PAH is poor, with a reported median survival of approximately 2.8 years from diagnosis and a three-year survival rate of 48%. Despite advances in targeted therapies, long-term outcomes remain suboptimal, with only 58–75% of patients surviving beyond three years [9].

The biological mechanisms linking viral infections to the development of pulmonary vascular disease remain incompletely understood; however, several hypotheses have been proposed. Viral infections may promote pulmonary vascular disease through converging mechanisms including immune dysregulation, endothelial injury, chronic inflammation, and thrombo-inflammatory processes. Experimental data further support roles for viral proteins and sustained immune activation in pulmonary vascular remodeling.

Additional contributing factors, particularly in chronic viral infections, may include behavioral and treatment-related issues such as poor medication adherence [10]. Furthermore, individuals with pre-existing lung injury or altered pulmonary vascular structure or function appear to be more susceptible to viral infections, potentially amplifying disease progression [11].

Human immunodeficiency virus (HIV) infection represents one of the most well-established viral associations with pulmonary hypertension, including HIV-associated PAH. Although the precise mechanisms remain incompletely defined, three HIV-derived proteins—Nef, Tat, and gp120—have been implicated in pulmonary vascular changes characteristic of PAH [12].

Experimental studies have demonstrated the development of complex pulmonary vascular lesions in rhesus monkeys infected with simian immunodeficiency virus containing the *nef* gene, supporting a direct pathogenic role for viral factors [10]. Clinically, HIV-associated PAH occurs in approximately 1 in 200 infected individuals, representing a 100 to 500-fold increase compared with the general population [9].

More recently, coronavirus disease 2019 (COVID-19) has emerged as a potential contributor to pulmonary hypertension. COVID-19–induced hypoxemia and systemic inflammation may provoke pulmonary vasoconstriction and vascular dysfunction, thereby increasing the risk of pulmonary hypertension [9]. SARS-CoV-2 infection has been shown to cause widespread endothelial inflammation, resulting in reduced production of vasodilatory mediators such as nitric oxide and prostacyclin. This endothelial dysfunction, combined with a COVID-19–associated hypercoagulable state, promotes microvascular and macrovascular embolization as well as in situ thrombosis within the pulmonary circulation [13].

Although vaccination has played a critical role in controlling the COVID-19 pandemic, increasing evidence suggests that long-term cardiovascular and pulmonary sequelae persist beyond two years after the initial outbreak [13-14]. Group 1 PAH remains a heterogeneous condition, often idiopathic, with numerous recognized secondary causes. Viral infections exhibit diverse systemic manifestations and have been increasingly linked to the development of pulmonary hypertension in both clinical and experimental settings.

Accordingly, this review therefore focuses on viral infections associated with the development of pulmonary hypertension, with particular emphasis on underlying mechanisms and clinical implications. The viral pathogens included in this review were selected based on either documented clinical associations with pulmonary hypertension or biologically plausible mechanisms of pulmonary vascular injury supported by human, animal, or translational evidence.

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Materials and Methods

Topic: Pulmonary hypertension
Research Question: What is the clinical and mechanistic evidence linking viral infections to the development of pulmonary hypertension?
PH definition: Pulmonary hypertension was defined according to ESC/ERS guidelines as a mean pulmonary artery pressure ≥20 mmHg at rest measured by right heart catheterization [1]. Studies relying on echocardiographic estimates (esPAP/PASP >35 mmHg) or evidence of right ventricular pressure overload consistent with pulmonary hypertension were also included, reflecting the limited availability of invasive hemodynamic data, particularly in acute, chronic, and post-infectious clinical settings.

Study Design and Selection

This study was conducted as a systematic review with mechanistic synthesis to evaluate the association between viral infections and pulmonary hypertension and to integrate underlying biological mechanisms. The review followed PRISMA 2020 guidelines [15]; however, given the inclusion of heterogeneous evidence (observational studies, animal models, case reports, and mechanistic literature), a quantitative meta-analysis was not performed. Instead, findings were synthesized using a structured, qualitative, and interpretative approach.

Study screening, selection, data extraction, and quality appraisal were conducted by a single reviewer using predefined criteria and standardized frameworks; the study was not registered in the International Prospective Register of Systematic Reviews (PROSPERO) prior to study initiation. While internal consistency checks were performed, this approach may increase the risk of selection and reporting bias and is acknowledged as a limitation.

A PRISMA 2020 flow diagram summarizing the study selection process is presented in **Figure 1 and Table 2.** Following removal of duplicates, records were screened by title and abstract based on predefined eligibility criteria. All studies that proceeded to full-text assessment met predefined inclusion criteria following prior screening; therefore, no additional exclusions occurred at the full-text stage. This reflects strict application of eligibility criteria during the screening phase rather than absence of exclusion criteria. Targeted searches for non-viral conditions (e.g., tuberculosis, infective endocarditis) were conducted exclusively to identify and exclude studies during screening and were not considered eligible exposures for inclusion.

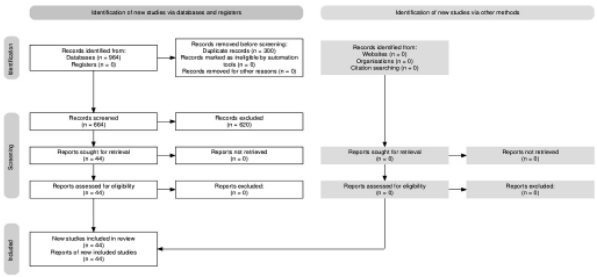

Figure 1. PRISMA flow diagram

Table 2. Study screening and Inclusion process.

IDENTIFICATION	
Records identified through databases	n = 964
Duplicates removed	n = 300
SCREENING	
Records screened	n = 664
Records excluded	n = 620
ELIGIBILITY	
Reports assessed for eligibility	n = 44
Reports excluded, with reasons	n = 0
INCLUDED	
Studies included in qualitative synthesis	n = 44

Eligibility criteria:

Inclusion criteria:

1. Studies published in the English language
2. Studies focusing on acute or chronic viral infections with established or hypothesized pulmonary vascular involvement were included, including HIV, SARS-CoV-2, herpesviruses (EBV, CMV), respiratory syncytial virus (RSV), and hepatitis C virus (HCV), and their association with pulmonary hypertension. Animal models were intentionally included to explore potential mechanistic pathways. Human and animal evidence was synthesized separately.
3. Studies including participants of all sexes and age groups.
4. Studies addressing pulmonary hypertension as an outcome or clinical phenotype.

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5. Studies published from January 2011 onward, with the final search conducted in February 2024.
6. Only peer-reviewed publications were eligible for inclusion.
7. Eligible evidence sources included observational studies, case reports and case series, animal studies, and review articles that provided mechanistic or contextual relevance. Narrative and mechanistic review articles were included as part of the eligible evidence base to support contextual interpretation and mechanistic integration. However, they were not considered primary sources for clinical outcome conclusions.

Exclusion criteria:

1. Grey literature and conference abstracts were excluded to prioritize peer-reviewed evidence and ensure methodological consistency. Conference abstracts were not screened.

This exclusion may increase the risk of publication bias and is acknowledged as a limitation.

2. Studies in which pulmonary hypertension was attributed primarily to non-viral infectious etiologies, including bacterial (e.g., tuberculosis, infective endocarditis), fungal, or parasitic infections, were excluded following initial screening.

Databases:

The literature search was conducted using PubMed, PubMed Central (PMC), the Cochrane Library, and MDPI (supplementary publisher search portal). No clinical trial registries or other study registers were searched; therefore, records identified from registers were 0 in the PRISMA flow diagram.

Search Strategy and Information Sources

A comprehensive literature search was conducted in PubMed, PubMed Central (PMC), the Cochrane Library, and MDPI from January 2011 to February 2024. The search strategy combined controlled vocabulary (Medical Subject Headings [MeSH]) and free-text keywords related to pulmonary hypertension and viral infections. Boolean operators (AND/OR) were applied to refine the search strategy. Search filters were applied to limit results to articles published in the English language between January 2011 and February 2024. No filters based on study design, population characteristics, or publication status were applied. Manual backward citation screening of reference lists from included articles and relevant reviews was also performed to identify additional eligible studies.

PubMed served as the primary bibliographic database. PubMed Central (PMC) was used primarily to facilitate access to full-text articles and to identify potentially relevant publications not readily retrievable through standard PubMed indexing at the time of the search. MDPI was included as a publisher-specific source to capture relevant open-access publications. Major bibliographic databases such as Embase, Scopus, and Web of Science were not included due to access limitations; therefore, incomplete database coverage and the potential for selection or publication bias are acknowledged as limitations.

The full reproducible search strategy, including exact search strings, MeSH terms, Boolean logic, and database-specific queries, is summarized in **Table 3.** Study selection followed predefined eligibility criteria, and eligibility decisions were cross-checked against pre-defined criteria for internal consistency. Given the systematic–mechanistic nature of the synthesis, formal inter-rater reliability statistics were not calculated.

Study Selection and Characteristics

A total of 964 records were identified using the predefined search strategy. After removal of duplicates, records were screened by title and abstract for relevance, followed by full-text assessment of potentially eligible studies. Search terms related to selected non-viral infectious conditions (e.g., tuberculosis and infective endocarditis) were included during the initial broad screening phase solely to identify and exclude studies in which pulmonary hypertension was primarily attributable to non-viral infectious etiologies**,** thereby minimizing misclassification and strengthening the specificity of viral-associated pulmonary hypertension included in the final synthesis. Following application of the eligibility criteria and quality appraisal, 44 studies were retained for data extraction and qualitative synthesis.

Of the 44 included studies, 12 were observational studies, 5 were animal studies, 9 were case reports or case series, and 9 were narrative or mechanistic review articles. These studies collectively formed the evidence base of the review and were integrated using a structured qualitative and mechanistic synthesis approach. Narrative and mechanistic review articles were included within the 44 studies to support contextual interpretation and mechanistic integration. However, primary clinical conclusions were based predominantly on observational and hemodynamic evidence. The included studies collectively evaluated viral pathogens including human immunodeficiency virus (HIV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), herpesviruses (Epstein–Barr virus and cytomegalovirus), respiratory syncytial virus (RSV), and hepatitis C virus (HCV)**.** These studies provided complementary clinical, experimental, and mechanistic perspectives on viral-associated pulmonary vascular disease.

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Table 2. Search Strategy.

Search terms / query	Database	Records identified (n)
Viral Infections AND pulmonary hypertension	PubMed	244
(("Hypertension, Pulmonary/complications"[Mesh] OR "Hypertension, Pulmonary/diagnosis"[Mesh] OR "Hypertension, Pulmonary/mortality"[Mesh] OR "Hypertension, Pulmonary/pathology"[Mesh] OR "Hypertension, Pulmonary/physiopathology"[Mesh] OR "Hypertension, Pulmonary/prevention and control"[Mesh] OR "Hypertension, Pulmonary/surgery"[Mesh] OR "Hypertension, Pulmonary/therapy"[Mesh])) AND ("Virus Diseases/classification"[Mesh] OR "Virus Diseases/complications"[Mesh] OR "Virus Diseases/diagnosis"[Mesh] OR "Virus Diseases/microbiology"[Mesh] OR "Virus Diseases/mortality"[Mesh] OR "Virus Diseases/pathology"[Mesh] OR "Virus Diseases/physiopathology"[Mesh] OR "Virus Diseases/surgery"[Mesh] OR "Virus Diseases/therapy"[Mesh])	PubMed(MesH)	69
(Pulmonary Hypertension [MeSH Major Topic]) AND (Viral Infections [MeSH Major Topic])	PubMed(advanced)	118
Pulmonary hypertension AND viral infections	Cochrane Library	68
Pulmonary hypertension AND viral infections	MDPI	20
Hepatitis AND Pulmonary Hypertension	PubMed	99
TB AND Pulmonary hypertension (screening exclusion search)	PubMed	110
Infective endocarditis AND Pulmonary hypertension (screening exclusion search)	PubMed	95
Cytomegalovirus AND Pulmonary hypertension	PubMed	16
Epstein-Barr virus AND Pulmonary hypertension	PubMed	11
RSV AND Pulmonary hypertension	PubMed	17
Influenza AND Pulmonary hypertension	PubMed	82
Herpes AND Pulmonary hypertension	PubMed	15

Study Quality Assessment and Risk of Bias

Quality assessment of the included studies was performed using standardized, design-specific appraisal tools. Animal studies were evaluated using the ARRIVE 2.0 core reporting guidelines and the SYRCLE risk-of-bias tool to assess reporting quality and internal validity. Observational studies were appraised using the Newcastle–Ottawa Scale (NOS). Case reports and case series were assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists, while narrative and mechanistic reviews were evaluated using the SANRA tool. Quality assessment was conducted by a single reviewer using standardized tools, with results cross-checked for internal consistency.

Overall, animal studies demonstrated moderate reporting quality, with consistent reporting of objectives, experimental procedures, and outcome measures, but frequent limitations related to randomization, allocation concealment, and blinding. Observational studies were predominantly of moderate to high methodological quality based on NOS scores, while case reports and case series generally demonstrated high reporting quality. Narrative reviews achieved moderate to high SANRA scores and were used exclusively for contextual and hypothesis-generating purposes rather than as sources of primary evidence. Overall, the certainty of evidence was considered low to moderate for observational human studies and moderate for mechanistic conclusions supported by convergent animal data.

Identified methodological limitations were considered when interpreting clinical associations and mechanistic conclusions, and findings were synthesized qualitatively rather than quantitatively. Meta-analysis was not performed due to substantial heterogeneity in study design, viral pathogens, outcome measures, diagnostic criteria for pulmonary hypertension, and reliance on echocardiographic versus invasive hemodynamic assessment.

Results

Most human studies relied on echocardiographic definitions of pulmonary hypertension, with variable diagnostic criteria and limited invasive hemodynamic confirmation; these limitations should be considered when interpreting the findings.

Quality appraisal

Quality appraisal results are summarized in **Tables 4–8**. Reporting quality of animal studies assessed using the ARRIVE 2.0 core items is presented in **Table 4,** while risk-of-bias assessment using the SYRCLE domain tool is shown in **Table 5.** Methodological quality of observational studies assessed using the Newcastle–Ottawa Scale is detailed in **Table 6.** Critical appraisal of case reports and case series using the Joanna Briggs Institute (JBI) checklists is presented in **Table 7,** while quality assessment of narrative and mechanistic reviews using the SANRA tool is summarized in **Table 8.**

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Quality Appraisal Tables

Table 3. ARRIVE 2.0 core items for included animal studies.

ARRIVE 2.0 Core Item	Kimura 2018 (RSV–Mouse)	Vu 2021 (RSV–Mouse, ST2)	Tarantelli 2018 (SIV–NHP)	Schweitzer 2019 (HIV–NHP)	Rabacal 2019 (HIV–NHP, Statin)
Study objectives & hypotheses	Yes	Yes	Yes	Yes	Yes
Animal species, strain, sex, age	Yes	Yes	Yes	Yes	Yes
Experimental groups & controls	Yes	Yes	Yes	Yes	Yes
Sample size reported	Yes	Yes	Yes	Yes	Yes
Sample size justification (power calculation)	Unclear	Unclear	Unclear	Unclear	Unclear
Randomization	Unclear	Unclear	Unclear	Unclear	Unclear
Allocation concealment	Unclear	Unclear	Unclear	Unclear	Unclear
Blinding of outcome assessment	Unclear	Unclear	Unclear	Unclear	Unclear
Experimental procedures described	Yes	Yes	Yes	Yes	Yes
Outcome measures clearly defined	Yes	Yes	Yes	Yes	Yes
Statistical methods described	Yes	Yes	Yes	Yes	Yes
Inclusion/exclusion criteria	Unclear	Unclear	Unclear	Unclear	Unclear
Animal welfare & monitoring	Unclear	Unclear	Yes	Yes	Yes
Ethical approval stated	Yes	Yes	Yes	Yes	Yes
Adverse events reported	Unclear	Unclear	Unclear	Unclear	Unclear
Study limitations discussed	Unclear	Unclear	Unclear	Unclear	Unclear
Generalisability / translational relevance	Yes	Yes	Yes	Yes	Yes
Data accessibility statement	Unclear	Unclear	Unclear	Unclear	Unclear

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Table 4. SYRCLE risk-of-bias domain assessment for animal studies.

SYRCLE Domain	Sequence generation (random allocation)	Baseline characteristics similar	Allocation concealment	Random housing	Blinding of caregivers/investigators	Random outcome assessment	Blinding of outcome assessors	Incomplete outcome data addressed	Selective outcome reporting
Kimura 2018	Unclear	Low	High	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Vu 2021	Unclear	Low	High	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Tarantelli 2018	High	Low	High	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Schweitzer 2019	High	Low	High	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Rabacal 2019	High	Low	High	Unclear	Unclear	Unclear	Unclear	Low	Unclear
Other sources of bias	Unclear								
	Unclear								
	Unclear								
	Unclear								
	Unclear								

Table 5. Methodological quality of observational studies assessed using the Newcastle–Ottawa Scale.

Author, Year	Calabrese, 2013	Singh, 2018	Zola, 2020	Duncan, 2021	Rajaratnam, 2021	Norderfeldt, 2021	Mahdi, 2023	Erdem, 2023
Study design	Observational	Cross-sectional	Cross-sectional	Retrospective cohort	Cross-sectional	Cohort (ICU)	Retrospective observational	Cross-sectional
Selection (★0–4)	★★★	★★★	★★★	★★★★	★★★	★★★★	★★★	★★★
Comparability (★0–2)	★	★	★★	★★	★	★★	★	★
Outcome/Exposure (★0–3)	★★	★★	★★	★★★	★★	★★	★★	★★
Total (★0–9)	★★★★★★	★★★★★★	★★★★★★★	★★★★★★★★★	★★★★★★	★★★★★★★★	★★★★★★	★★★★★★
Quality	Moderate	Moderate	High	High	Moderate	High	Moderate	Moderate

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Norderfeldt, 2022	Pagnesi, 2020	Tudoran, 2021	Tomaszewski, 2020
Prospective cohort	Retrospective cohort	Prospective cohort	Cross-sectional
****	****	****	***
**	**	**	**
***	***	**	**
**********	**********	*********	*******
High	High	High	High

Table 6. Critical appraisal of case reports and case series using Joanna Briggs Institute checklists.

Rossi, 2022	***Walter-Nicolet, 2011***	***Akagi, 2020***	***Cruz-Utrilla, 2020***	***Cueto-Robledo, 2022***	***Zhao, 2023***	***Tsuchiya, 2017***	***Ba, 2019***	***Hashimoto, 2011***	***Author, Year***
Case series	*Case series*	*Case report*	*Case report*	*Case series*	*Case report*	*Case report*	*Case report*	*Case report*	***Study type***
Yes	*Yes*	*Yes*	*Unclear*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	***Patient details***
Unclear	*Yes*	*Yes*	*Unclear*	*Unclear*	*Yes*	*Yes*	*Yes*	*Yes*	***Timeline***
Yes	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	***Diagnostics***
Unclear	*Yes*	*Yes*	*Unclear*	*Unclear*	*Yes*	*Yes*	*Yes*	*Yes*	***Intervention***
Yes	*Yes*	*Yes*	*Unclear*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	***Outcomes***
Unclear	*Unclear*	*Yes*	*No*	*Unclear*	*Yes*	*Yes*	*Yes*	*Unclear*	***Adverse events***
Yes	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	*Yes*	***Lesson***
Moderate	*High*	*High*	*Low–Moderate*	*Moderate*	*High*	*High*	*High*	*High*	***Overall quality***

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Table 7. Quality assessment of narrative and mechanistic reviews using the SANRA tool.

Suzuki, 2021	Xiang, 2022	Tian, 2023	Cueto-Robledo, 2023	Nabeh, 2021	Wang, 2023	Palakeel, 2022	Atabati, 2020	Flores, 2013	Author, Year
Hypothesis-based review	Narrative	Narrative	Narrative	Narrative	Narrative	Narrative	Narrative	Narrative	**Review type**
2	2	2	2	2	2	2	2	2	**Importance**
2	2	2	2	2	2	2	2	2	**Aims**
0	1	1	1	1	1	1	1	1	**Search**
2	2	2	2	2	2	2	2	2	**References**
2	2	2	2	2	2	2	2	2	**Reasoning**
2	2	2	2	2	2	2	2	2	**Data**
10	11	11	11	11	11	11	11	11	**Total**
Moderate-High	High	High	High	High	High	High	High	High	**Quality**

Data Extraction Summary Tables

Data extraction was performed by a single reviewer using a predefined and standardized framework and cross-checked for internal consistency prior to synthesis. Extracted variables included study design, population characteristics, viral pathogen, pulmonary hypertension definition, hemodynamic or echocardiographic parameters (including mean pulmonary artery pressure, right ventricular systolic pressure, and pulmonary vascular resistance where available), proposed mechanistic pathways (e.g., endothelial dysfunction, inflammation, immune activation, hypoxia, and vascular remodeling), and clinical outcomes. Extracted data were reviewed for consistency and are summarized in **Tables 9–11. Table 9** presents data from observational studies, **Table 10** summarizes findings from animal models, and **Table 11** details case reports and case series. Human and animal evidence was synthesized separately to minimize clinical–preclinical heterogeneity.

Table 8. Observational and non-randomized clinical studies evaluating viral infections and pulmonary hypertension.

Singh S, et al.[22]	Calabrese F, et al.[24]	**Author**
2018	2013	**Year**
Determine cardiovascular complications in HIV patients and association with CD4 count.	Assess whether herpesvirus infection in idiopathic pulmonary fibrosis (IPF) is linked to pulmonary hypertension (PH) and vascular remodeling; supported by a gamma-herpesvirus (MHV-68) mouse model.	**Purpose of study**
Observational clinical study of 100 HIV patients (≥18 not stated). Excluded: chronic renal failure, diabetes, hypothyroidism, steroid use, prior MI, congenital heart disease. Groups divided by CD4 count. Cardiac assessment + echocardiography. n = 100	Human: 55 IPF vs 41 controls lung tissue analyzed for viral genomes (only herpesviruses detected). Viral status correlated with mPAP, arterial remodeling, and clinical/morphological variables using uni/multivariable analyses (transplant + post-transplant). Animal: parallel analyses in MHV-68 infected mice. n = 55 IPF; n = 41 Controls	**Study design / sample size (n)**
Cardiac abnormalities were identified in 24% of patients. Left ventricular diastolic dysfunction occurred in 22%, pulmonary hypertension in 12%, dilated cardiomyopathy in 12%, and pericardial effusion in 7%. Cardiac abnormalities were more frequent among patients with lower CD4 counts.	Viral positivity was significantly higher in IPF than controls (p = 0.0003). Virus-positive cases had higher mPAP (p = 0.01), poorer 6-minute walk distance (p = 0.002), and higher primary graft dysfunction after transplant (p = 0.02). Greater arterial intimal thickening (p = 0.002; p = 0.004) and increased TGF-β expression (p = 0.002) were observed. Associations remained significant after multivariable adjustment.	**Results**
Cardiovascular abnormalities, including pulmonary hypertension, are common in HIV infection and are associated with greater immunosuppression	Herpesvirus infection is associated with pulmonary vascular remodeling and increased pulmonary pressures in IPF, suggesting a possible viral contribution to PH pathogenesis.	**Conclusion**

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Norderfeldt J, et al.[13]	Rajaratnam A, et al.[12]	Duncan M S, et al.[10]	Zola C E, et al.[23]
2022	2021	2021	2020
Evaluate 24-month mortality after ICU TTE diagnosis of acute PH (aPH) vs non-aPH in severe COVID-19.	Characterize PH in HIV patients using RHC and identify immunovirologic predictors (CD4, viral load); evaluate RV metrics and phenotype.	Determine if HIV increases risk of incident PH vs uninfected; assess effect of CD4 and viral load on PH risk over time.	Test if HIV/HCV coinfection is associated with echocardiographic PH (via PASP) and whether viral/immune markers relate to higher PASP in PLWH.
Retrospective ICU cohort follow-up. Initial ICU cohort: 67 ICU-treated COVID-19 patients. Follow-up included 1-month survivors: 14 aPH and 36 non-aPH. Outcomes tracked 1–24 months via EHR. n = 67	Retrospective observational review of PLWH ≥18 undergoing RHC (2000–2016). Total 62 PLWH suspected of PH underwent RHC. Groups: PH (mPAP ≥25) vs No PH (mPAP ≤25). Classified PH into PAH and PVH. n = 62	Longitudinal observational cohort (VACS). Included 13,028 with baseline PASP <35 mmHg (median PASP 28). 32% HIV, 68% uninfected. Demographics: 97% male (12,657/13,028), median age 58, 48% African American, 40% white. Stratified HIV by CD4 and viral load; multivariable + time-varying models; sensitivity analyses adjusting for HF/COPD as time-varying. n = 13,028	Cross-sectional analysis (EHR-based) from VACS cohort. Total included 6032: 2795 uninfected, 1402 HIV, 846 HCV, 989 HIV/HCV. Mean age 57; 97% male. Compared PASP and modeled predictors (incl. comorbidities). n = 6032
24-month mortality was significantly higher in those with acute PH than those without (61.5% vs 12.8%).	PH was identified in 32/62 patients (52%), including 15 PAH and 17 PVH. Patients with PH had lower CD4 counts (374±252 vs 594±367, p = 0.02) and detectable viral load (OR 12.0, CI 1–122, p = 0.04). RV function was worse in PH patients (RVFAC 36±15% vs 47±11%, p = 0.03).	Incident PH occurred more frequently in HIV-positive individuals than uninfected individuals (28.6 vs 23.4 per 1000 person-years, p = 0.0004). Adjusted HR for PH was 1.18 (95% CI 1.05–1.34, p = 0.0062). Risk was higher with CD4 <200 (HR 1.94, p < 0.0001), CD4 200–499 (HR 1.29, p = 0.0048), and viral load ≥500 copies/mL (HR 1.88, p < 0.0001).	HIV/HCV coinfection was associated with higher PASP compared with uninfected individuals (p = 0.048), whereas HIV alone (p = 0.99) and HCV alone (p = 0.43) were not significant. In PLWH models, HCV coinfection was associated with increased PASP (β 1.47, 95% CI 0.26–2.67, p = 0.0170), while higher CD4 counts were associated with lower PASP (β −0.68, 95% CI −1.10 to −0.27, p = 0.0011).
Acute PH in severe COVID-19 is associated with markedly increased long-term mortality.	HIV-associated PH is associated with immunosuppression and detectable viral replication.	HIV infection increases the risk of developing PH, particularly in patients with uncontrolled viral load and severe immunosuppression.	HIV/HCV coinfection modestly increases pulmonary pressures, with immune status (CD4 count) playing an important role.

Tomaszewski M, et al.[25]	Erdem K, et al.[19]	Mahdi N, et al.[14]	Norderfeldt J, et al.[18]
2020	2022	2023	2021
Explore associations among clinical severity, immune alterations (incl. PD-1), and EBV infection in idiopathic PAH (IPAH).	Determine whether post-COVID patients (even without prior PH risk factors) demonstrate elevated pulmonary artery pressures and RV enlargement; relate findings to severity and CT lung involvement.	In COVID-19 patients with pulmonary embolism (PE), evaluate persistent PH features on echo and outcomes; compare by comorbidity status; highlight CTEPH screening logic.	Determine occurrence of TTE-defined acute PH (aPH) in ICU COVID-19 and its association with short-term outcomes.
Observational case–control (cross-sectional).25 IPAH (various WHO classes) vs 20 controls (60% female in both). EBV load measured in blood DNA; extensive pathogen panel negative (HCV, HBV, HIV, HSV-1/2, CMV, HPV, parvovirus B19, influenza, etc.). • Immunophenotyping PBMCs; cytokines assessed. n = 25 IPAH;20 controls	Observational cohort of 91 eligible adults. Two analyses: (1) by treatment setting (ICU vs ward vs outpatient); (2) by CT severity (none vs non-severe vs severe pulmonary involvement). Evaluated in outpatient setting for cardiac symptoms.	Retrospective cohort at UK District General Hospital (Apr 2020–Oct 2021). Included 80 COVID-19 + PE patients: 49 with comorbidities, 31 without (excluding pre-existing PH). Echo features suggestive of PH at PE diagnosis and at 3 months post-treatment. n = 80	Retrospective ICU study over ~1 month (10 Apr–19 May 2020) in tertiary hospital. Enrolled 76, excluded 9, final 67. aPH defined by sPAP >35 mmHg. Outcomes assessed at 21 days post-TTE; additional 30-day ICU mortality.
EBV infection was detected in 11/25 IPAH patients (44%) but none of the controls. EBV load correlated with WHO functional class (r = 0.54, p = 0.005) and PD-1+ CD4 T cells (r = 0.56, p = 0.0035).	Post-COVID patients had higher pulmonary artery pressures and enlarged right-heart dimensions. Abnormalities correlated with severity of initial infection and degree of CT lung involvement. Elevated sPAP and RV enlargement may persist 2–3 months after recovery in individuals without prior PH risk factors.	Total deaths: 14 (13 with comorbidities; 1 without). Reported: risk of persistent PH and subsequent mortality following PE in COVID-19 higher in comorbidity group (RR 4.17 and 1.32, p < 0.001). "Upon initial echocardiography, features consistent with echocardiographic PH present in 52 patients (24 with comorbidities and 24 without)" *(as reported)*. Persistent echocardiographic PH at 3 months: 40 total (38 with comorbidities, 2 without). Chi-square association persistent	Acute PH occurred in 26/67 ICU COVID-19 patients (39%). Biomarkers were higher in the aPH group (NT-proBNP p = 0.0007; troponin T p = 0.0002). Mortality was higher at 21 days (46% vs 7%, p < 0.001) and 30 days (42% vs 7%, p < 0.002).
EBV infection and immune dysregulation may contribute to IPAH severity.	Pulmonary vascular abnormalities may persist after COVID-19 infection.	COVID-19 patients with PE, particularly those with comorbidities, are at increased risk of persistent PH and mortality.	Acute PH is common in severe COVID-19 and is associated with myocardial injury and increased short-term mortality.

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Pagnesi M, et al.[17]	Tudoran C, et al.[20]
2020	2021
Determine prevalence/characteristics and prognostic significance of PH and RVD in hospitalized non-ICU COVID-19	Track progression of PH and borderline PH after acute COVID-19 at 3 and 6 months; compare across pandemic waves; identify predictors of follow-up esPAP.
Single-centre observational cross-sectional. 211 underwent TTE; 11 excluded, final 200 (median age 62, IQR 52–74; 65.5% men). PH: esPAP >35. RVD: TAPSE <17 mm or S′ <9.5 cm/s. Primary endpoint: in-hospital death or ICU admission.	Observational longitudinal cohort. 116 post-COVID patients age 30–55 (median 48, IQR 43–52.75); 57 men (49.1%), 59 women (50.9%). Selected from 383 symptomatic post-COVID referrals; all diagnosed with post-acute COVID syndrome. • Grouped by wave: A 37, B 40, C 39. TTE: PH group esPAP >35; borderline group 30–34.81; RV function metrics (TAPSE, FAC, RV-GLS). CT and labs (incl. CRP). n = 116 (PH/BPH)
PH was present in 24/200 patients (12.0%) and RVD in 29/200 (14.5%). PH patients were older, more cardiac comorbidities, more severe infection (imaging, labs, oxygenation). RVD patients: more cardiac comorbidities but not more severe infection. Endpoint occurred more with PH: 41.7% vs 8.5%, p < 0.001. RVD was not associated with worse outcomes: 17.2% vs 11.7%, p = 0.404	PH: 51; borderline: 65. PH group older (median 52), predominantly male (54.9%), higher BMI, more severe CT injury (76.5% moderate) than borderline group (median 46, milder CT, fewer symptoms). PH esPAP range 36–55, median 44.69; 49 with RVD. Borderline esPAP 30–34.81; 35 with pathological RVF parameters. Correlations between esPAP (initial/follow-up) and CT severity, CRP, RVF parameters: p < 0.001. 3–6 months: gradual improvement; at 6 months only 8 with slightly elevated esPAP (<40) and 17 with borderline values.
PH is associated with greater disease severity and adverse outcomes in hospitalized COVID-19 patients.	Post-COVID PH may occur after infection but often improves over time.

Table 10. Animal models investigating viral-associated pulmonary hypertension

Tarantelli R A, et al.[29]	Vu L D, et al.[27]	Kimura D, et al.[26]	**Author**
2018	2021	2018	**Date**
Longitudinal Evaluation of Pulmonary Arterial Hypertension in a Rhesus Macaque (*Macaca mulatta*) Model of HIV Infection	Deficiency in ST2 signaling ameliorates RSV-associated pulmonary hypertension	New mouse model of pulmonary hypertension induced by respiratory syncytial virus bronchiolitis	**Purpose of Study**
The study population comprised 21 Chinese rhesus macaques (12 male, 9 female; *Macaca mulatta*).	This study aimed to investigate the pathophysiological mechanism of RSV-associated PH. A translational mouse model of RSV-associated PH was used, in which wild-type (WT) and suppression of tumorigenicity 2 (ST2) knockout neonatal mice were infected with RSV at 5 days old and reinfected 4 weeks later.	A mouse model of PH secondary to RSV infection, 5-day-old neonatal mice were infected with RSV and reinfected at 4 weeks.	**Study Design**
All SIV-infected macaques exhibited the expected chronic-phase decline in peripheral CD4+ T cells (mean 464.3 cells/μL) and sustained plasma viral loads (mean 2.02 × 10^6 RNA copies/mL). RV collagen deposition was significantly higher in animals with PAH than in those without PAH (8.21% vs. 4.92% collagen/170 mm^2, P = 0.01).	ST2-deficient mice demonstrated reduced RVSP, attenuated pulmonary vascular remodeling, and improved endothelial function, suggesting a potential therapeutic role for targeting ST2 signaling in RSV-associated PH.	Pulmonary hypertension-like changes were demonstrated by elevated RVSP, echocardiographic findings, histologic vascular remodeling, and morphometric analysis. The model reproduces human disease features, including Th2-biased immune responses, eosinophilia, mucus production, and airway hypersensitivity, providing a clinically relevant tool to explore molecular mechanisms and potential interventions for RSV-induced PH	**Results/Conclusion**

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Rabacal W, et al.[30]	Schweitzer F, et al.[28]
2019	2019
Statin treatment prevents the development of pulmonary arterial hypertension in a nonhuman primate model of HIV-associated PAH	Monocyte and Alveolar Macrophage Skewing Is Associated with the Development of Pulmonary Arterial Hypertension in a Primate Model of HIV Infection
28 adult Chinese rhesus macaques (*Macaca mulatta*) aged 6–10 years old were obtained.	A prospective study of simian immunodeficiency virus-associated pulmonary arterial hypertension (SIV-PAH) was conducted in 21 rhesus macaques.
Atorvastatin administration, whether prophylactic or therapeutic, effectively suppressed inflammation and fibrosis associated with SIV infection. Prophylactic treatment completely prevented SIV-PAH, while therapeutic administration during early chronic infection substantially attenuated disease progression. These findings suggest that atorvastatin may mitigate pulmonary vascular remodeling by dampening proinflammatory and profibrotic immune responses and enhancing cytokine profiles associated with PAH resistance, supporting its potential as both a preventive and therapeutic strategy for HIV/SIV-associated pulmonary vascular disease.	11 of 21 animals developed SIV-associated pulmonary arterial hypertension (SIV-PAH). PAH-positive animals demonstrated increased frequencies of proinflammatory CD14^dimCD16^+ monocytes compared with PAH-negative animals, although this difference showed a trend toward significance ($p = 0.06$).

Table 9. Case reports and case series describing virus-associated pulmonary hypertension.

Zhao Yan-Nan, et al.[35]	Tsuchiya H, et al.[34]	Ba H, et al.[33]	Hashimoto T, et al.[31]	**Author**
2023	2017	2019	2011	**Date**
Pulmonary hypertension, nephrotic syndrome, and polymyositis due to hepatitis C virus infection: A case report	Interferon Therapy Exacerbated Pulmonary Hypertension in a Patient with Hepatitis C Virus Infection: Pathogenic Interplay among Multiple Risk Factors	Chronic Active Epstein-Barr Virus Infection With Systemic Vasculitis and Pulmonary Arterial Hypertension in a Child	Pulmonary arterial hypertension associated with chronic active Epstein-Barr virus infection	**Purpose of Study**
57-year-old woman with a complex medical history, including chronic hepatitis C infection, nephrotic syndrome, polymyositis, and pulmonary hypertension (PH).	27-year-old woman with chronic hepatitis C virus (HCV) infection developed severe PAH after interferon (IFN) therapy.	A 9-year-old boy with chronic active Epstein-Barr virus (CAEBV) developed pulmonary arterial hypertension (PAH) and systemic vasculitis.	Case report describes the first documented instance of pulmonary arterial hypertension (PAH) associated with chronic active Epstein–Barr virus (CAEBV) infection in an adult.	**Study Design**
Hepatitis C should be regarded as a systemic disease capable of causing multiple extrahepatic complications. While extrahepatic manifestations occur in up to 80% of HCV-infected patients, the coexistence of PH, nephrotic syndrome, and polymyositis in one individual is exceptionally rare.	It is possible that the patient's long-standing chronic HCV infection had already led to the development of asymptomatic pulmonary arterial hypertension (PAH) before interferon (IFN) therapy.	CAEBV should be considered in pediatric patients presenting with secondary PAH.	The temporal progression—heart failure developing within a year of CAEBV onset, supports a possible association.	**Results/Conclusion**

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Akagi S, et al.[32]	Cruz-Utrila Alejandro, et al.[38]	Cueto-Robeldo G, et al.[37]
2020	2020	2021
Chemotherapy Improved Pulmonary Arterial Hypertension in a Patient with Chronic-Active Epstein-Barr Virus Infection	Pulmonary embolism and coronavirus disease 2019: persistent pulmonary hypertension?	Severe Pulmonary Hypertension: An Important Sequel After Severe Post-Acute COVID-19 Pneumonia
A 44-year-old man was admitted after abnormalities were identified on an electrocardiogram and liver function tests during a routine health screening. Transthoracic echocardiography demonstrated right ventricular enlargement with an estimated right ventricular systolic pressure of 92 mmHg. Hemodynamic assessment by right heart catheterization showed a mean pulmonary arterial pressure of 45 mmHg and a pulmonary vascular resistance of 9.8 Wood units. Peripheral blood analysis revealed the presence of granular lymphocytes, with natural killer cells accounting for 91% of the lymphocyte population. Based on these findings, a diagnosis of CAEBV-associated PAH was made.	47-year-old man was admitted to the emergency department with a 10-day history of fever, cough, dyspnea, and loss of taste.	58-year-old woman with a history of well-controlled systemic hypertension presented with progressively worsening exertional dyspnea three months after recovering from severe COVID-19 pneumonia.
After two cycles of chemotherapy, treatment with cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) was administered without the use of PAH-specific agents. Follow-up echocardiography demonstrated an improvement in right ventricular enlargement, with a reduction in estimated right ventricular systolic pressure to 59 mmHg. Hemodynamic reassessment by right heart catheterization showed significant improvement, with the mean pulmonary arterial pressure decreasing to 27 mmHg and pulmonary vascular resistance falling to 2.4 Wood units.	Persistent PH after COVID-19 may stem from several potential mechanisms, including unresolved thromboembolic disease leading to chronic thromboembolic pulmonary hypertension (Group IV), pulmonary parenchymal damage resulting in Group III PH, or pulmonary arterial hypertension (Group 1) secondary to endothelial injury and dysfunction.	Right heart catheterization confirmed severe precapillary pulmonary arterial hypertension (PAH) with markedly elevated mean pulmonary arterial pressure (>35 mmHg), increased pulmonary vascular resistance, and a low cardiac index.

Rossi R, et al.[39]	Walter-Nicolet E, et al.[36]	
2022	2011	
Pulmonary arterial hypertension and right ventricular systolic dysfunction in COVID-19 survivors	Congenital Cytomegalovirus Infection Manifesting as Neonatal Persistent Pulmonary Hypertension: Report of Two Cases	
The study group consisted of 25 consecutive patients, COVID-19 survivors, referred to our divisional outpatient clinic for the cluster of signs and symptoms described above. All patients were hospitalized between March 2020 and February 2021. In all these patients we performed a RHC and a 6-minute walking test (6MWT). The obtained results were compared with those of a control group, which comprised 25 gender- and age-matched patients, COVID-19 survivors who were asymptomatic.	Two cases of persistent pulmonary hypertension in relation with congenital CMV infection following maternal primary infection and reinfection, respectively.	
A post-discharge phase of COVID-19 may be characterized by PAH and RV systolic dysfunction. As long as this state persists, patients suffer from a specific cluster of symptoms and signs.	Neonatal persistent pulmonary hypertension can be the consequence of congenital CMV infection. Intensive respiratory support and IV ganciclovir are indicated in case of life-threatening condition.	

Discussion

This systematic review with mechanistic synthesis integrates heterogeneous evidence from observational studies, animal models, case reports, and narrative literature. While all included studies contributed to the overall synthesis, primary clinical conclusions are based predominantly on observational and hemodynamic data, with narrative evidence supporting mechanistic interpretation. Findings should be interpreted in the context of differing levels of evidence strength and are therefore presented as a structured qualitative synthesis rather than a purely quantitative systematic review. Across diverse viral pathogens, including SARS-CoV-2, HIV, herpesviruses (EBV, CMV), respiratory syncytial virus (RSV), and hepatitis C virus (HCV), recurrent patterns emerge suggesting associations between viral disease and pulmonary vascular dysfunction, elevated pulmonary pressures, and adverse clinical outcomes.

While causality cannot be established from much of the available human data, the convergence of epidemiologic, hemodynamic, histopathologic, and experimental findings supports a biologically plausible link between viral infection and pulmonary hypertension. Additionally, most human evidence is

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derived from observational studies using echocardiographic estimates of pulmonary pressure, which may overestimate or variably define pulmonary hypertension compared with invasive hemodynamic assessment.

Pulmonary fibrosis represents one potential intermediate pathway linking viral lung injury to the development of pulmonary hypertension. Fibrotic remodeling is driven by epithelial–fibroblast dysregulation, persistent inflammatory signaling, oxidative stress, chemokine-mediated leukocyte recruitment, epigenetic alterations, and macrophage-derived profibrotic mediators such as transforming growth factor-β and platelet-derived growth factor. Viral infections may promote these processes through sustained interferon signaling, which has been implicated in pulmonary vascular remodeling and subsequent pulmonary hypertension [16].

These mechanisms converge to support a multifactorial model of viral-associated pulmonary vascular injury in which viral infections may act as multi-system vascular stressors capable of initiating or amplifying pulmonary vascular injury through intersecting inflammatory, endothelial, and thrombotic pathways.

Clinical Evidence From Observational Studies

COVID-19–Associated Pulmonary Hypertension

Observational cohorts consistently demonstrate that pulmonary hypertension, predominantly defined by echocardiography, is a frequent finding in hospitalized and critically ill COVID-19 patients, with important prognostic implications. In hospitalized non-ICU patients, echocardiographic PH (esPAP >35 mmHg) was present in 12%, while right ventricular dysfunction (RVD) was observed in 14.5% [17]. Echocardiographic pulmonary hypertension—but not isolated right ventricular dysfunction—was strongly associated with adverse outcomes, including in-hospital death or ICU admission (41.7% vs 8.5%, $p < 0.001$). Importantly, patients with PH demonstrated more severe pulmonary involvement and inflammatory burden, which may suggest that pulmonary vascular load, rather than ventricular dysfunction alone, is an important determinant of outcome [17].
In critically ill ICU cohorts, the burden of pulmonary vascular involvement was substantially higher. Acute pulmonary hypertension (aPH), defined echocardiographically, was detected in 39% of mechanically ventilated patients and was associated with a nearly sevenfold increase in 21-day mortality (46% vs 7%, $p < 0.001$), independent of left ventricular dysfunction or thromboembolic markers [18]. Biomarkers of myocardial injury were significantly higher in the aPH group, whereas D-dimer levels did not differ**,** suggesting mechanisms beyond overt thromboembolism [18].
Long-term follow-up of ICU survivors demonstrated that aPH during acute infection carried sustained prognostic significance**,** with 24-month mortality of 61.5% in aPH patients versus 12.8% in non-aPH patients [13]. These findings suggest that acute pulmonary vascular stress during COVID-19 may be associated with persistent clinical consequences**.**
Post-acute studies further demonstrate persistence of pulmonary vascular abnormalities following COVID-19 infection**.** In previously healthy individuals evaluated 2–3 months after recovery, elevated pulmonary artery pressures and right ventricular enlargement persisted, correlating with the severity of acute lung injury and CT-documented pulmonary involvement [19]. In a symptom-referred post-COVID cohort younger than 55 years, pulmonary hypertension (esPAP >35 mmHg) was identified in 44% of patients and borderline pulmonary hypertension in 56%, with gradual improvement over six months; however, initial esPAP and the extent of CT-defined lung injury independently predicted residual pulmonary pressure elevation (adjusted $R^2 = 0.722$) [20].
Pulmonary embolism represents an additional contributor to post-COVID pulmonary hypertension. In COVID-19 patients with acute pulmonary embolism, persistent echocardiographic pulmonary hypertension at 3 months was significantly more frequent in those with comorbidities, with a relative risk of 4.17 (95% CI 2.45–7.07) for persistent pulmonary hypertension and 1.44 (95% CI 1.15–1.80) for mortality associated with persistent pulmonary hypertension [14]. These findings raise concern for progression toward chronic thromboembolic pulmonary hypertension in susceptible individuals.

HIV-Associated Pulmonary Hypertension
HIV represents one of the most frequently reported viral infections associated with pulmonary hypertension. Pulmonary arterial hypertension (confirmed by invasive hemodynamic assessment) may develop in a subset of individuals with human immunodeficiency virus despite effective antiretroviral therapy, indicating a pathogenesis driven by chronic immune dysregulation rather than direct viral infection of pulmonary endothelial cells. HIV-associated pulmonary vascular injury is mediated by persistent cytokine signaling, viral protein–induced endothelial dysfunction, and a shift toward apoptosis-resistant, hyperproliferative pulmonary vascular phenotypes. Contributing mechanisms include $CD4^+$ T-cell depletion, Th1-to-Th2 immune polarization with increased IL-4, IL-6, and IL-13, oxidative stress, genetic susceptibility, and hepatitis C virus co-infection, collectively promoting pulmonary vascular remodeling and, in a subset of patients, HIV-associated pulmonary arterial hypertension [21].

Cross-sectional echocardiographic studies demonstrate PH prevalence of approximately 12% among people living with HIV, with higher rates in those with advanced immunosuppression. In a cohort of 100 HIV patients, pulmonary hypertension was present in 12%, and cardiac abnormalities were significantly more common among those with lower $CD4^+$ T-cell counts [22].

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Large-scale longitudinal data from the Veterans Aging Cohort Study further confirm these associations. Among 13,028 veterans with baseline PASP ≤35 mmHg, individuals with HIV demonstrated a higher incidence of pulmonary hypertension (28.6 vs 23.4 per 1,000 person-years, p = 0.0004) and an adjusted hazard ratio of 1.18 (95% CI 1.05–1.34) [10]. Risk increased markedly with CD4 T-cell counts <200 cells/μL (HR 1.94) and HIV viral loads ≥500 copies/mL (HR 1.88) [10].

Importantly, invasive hemodynamic studies further corroborate these findings. Among 62 HIV-infected individuals undergoing right heart catheterization, 52% met criteria for pulmonary hypertension, with lower $CD4^+$ T-cell counts and a 12-fold higher odds of detectable viral load among those with pulmonary hypertension [12]. Despite elevated pulmonary pressures, right ventricular-pulmonary artery coupling remained preserved, suggesting an early, compensated hemodynamic phenotype [12].
HIV/hepatitis C virus coinfection further modifies pulmonary hypertension risk. In 6,023 veterans, HIV/hepatitis C virus coinfection was associated with higher pulmonary artery systolic pressure, whereas HIV or hepatitis C virus infection alone was not [23]. Lower $CD4^+$ T-cell counts, but not viral load or antiretroviral regimen, were consistently linked to elevated PASP, emphasizing the role of immune dysregulation rather than direct viral burden [23].

Herpesvirus-Associated Pulmonary Vascular Disease

Herpesviruses have been implicated in pulmonary vascular remodeling, particularly in chronic lung disease. In idiopathic pulmonary fibrosis, herpesvirus-positive patients demonstrated higher mean pulmonary artery pressures (p = 0.01), worse 6-minute walk distance (p = 0.002), and greater intimal arterial thickening (p = 0.002–0.004) compared with virus-negative patients. Viral presence remained independently associated with worse hemodynamics after adjustment [24].
In idiopathic pulmonary arterial hypertension, Epstein–Barr virus DNA was detected in 44% of patients, while all controls were negative. Epstein–Barr virus viral load correlated with WHO functional class and PD-1 expression on $CD4^+$ T cells, linking viral persistence to immune exhaustion and disease severity [25].

Mechanistic Evidence from Animal Models

Animal models provide important mechanistic support for the clinical associations observed in human studies.

RSV Models

Neonatal mice infected with RSV and reinfected in early adulthood developed pulmonary hypertension-like vascular changes in the absence of hypoxemia, confirmed by RVSP elevation (29.6 ± 6.7 vs 15.9 ± 1.5 mmHg, p < 0.01), and increased RV/LV+S ratio. Pulmonary arteries showed increased medial thickness and muscularization, alongside Th2-biased inflammation with elevated IL-4 and IL-13 [26].

ST2-deficient mice were protected from RSV-induced PH, with normal RVSP, preserved PAAT/ET ratios, reduced vascular remodeling, and increased eNOS expression [27]. These findings identify IL-13–arginase–NOS uncoupling as a potential key pathway in virus-mediated pulmonary vascular disease.

SIV Models of HIV-Associated PAH
In rhesus macaques, SIV infection induced pulmonary hypertension with hemodynamic features consistent with pulmonary arterial hypertension in approximately 52% of animals within 6–12 months, independent of viral load or $CD4^+$ T-cell count [28]. PAH was associated with right ventricular fibrosis, increased PET-CT glucose uptake, and pulmonary arterial collagen deposition [29].
Immune profiling demonstrated skewing toward proinflammatory monocytes and macrophages, reduced IL-10–producing cells, and impaired inflammatory resolution in PAH-positive animals [29]. Pharmacologic intervention in animal models further supports a possible mechanistic link. Prophylactic atorvastatin prevented PAH in 85.7% of SIV-infected macaques, reducing mPAP, inflammatory cytokines (TGF-β, TNF-α), and vascular fibrosis without affecting viral replication or CD4 counts [30].

Case Reports and Case Series

Rare but informative clinical reports illustrate severe manifestations of virus-associated pulmonary vascular disease, including pulmonary hypertension. Chronic active EBV infection has been linked to severe PAH with plexogenic arteriopathy, leading to right heart failure despite viral suppression. Elevated IL-6 levels of 4.6 pg/mL vs normal 1.69 ± 0.76 were observed, supporting cytokine-mediated vascular injury [31,32].

Pediatric CAEBV cases demonstrated reversible pulmonary hypertension with combined immunosuppression and PAH-targeted therapy, with reductions in sPAP from 54 to 40 mmHg and marked NT-proBNP improvement [33].
HCV-associated cases highlight interferon-triggered PAH, with dramatic hemodynamic improvement following IFN withdrawal and combination vasodilator therapy (mPAP 63 to 31 mmHg; PVR 11.8 to 2.6 WU) [34]. Other reports describe PH in HCV with nephrotic syndrome and polymyositis, improving with PAH-specific treatment [35].
Congenital CMV infection was associated with refractory neonatal PPH, often requiring ECMO, with divergent outcomes despite antiviral therapy [36]. COVID-19 case reports describe severe PAH disproportionate to lung restriction, persistent PH after pulmonary embolism, and post-discharge PH with gradual spontaneous recovery paralleling right ventricular function [37,38,39].

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The strength of evidence varies across viral pathogens. The most consistent clinical and mechanistic evidence exists for HIV-associated pulmonary hypertension, supported by both observational studies and invasive hemodynamic data. In contrast, evidence for other viral infections is largely observational or experimental and should be interpreted with caution. Viral infections may therefore be best conceptualized as multi-system vascular stressors capable of initiating or amplifying pulmonary vascular injury in susceptible individuals.

Systematic Reviews and Mechanistic Syntheses

Narrative and mechanistic reviews provide integrative conceptual frameworks that help contextualize the clinical and experimental findings. HIV-associated PAH incidence has been reported as up to 2,500-fold higher than in uninfected populations, with poorer survival [40]. Viral proteins, not direct endothelial infection, are implicated in driving vascular remodeling. COVID-19 autopsy studies demonstrate pulmonary arterial wall thickness more than twice that observed in H1N1 influenza, supporting direct vascular involvement [9]. Endothelial injury, ACE2 dysregulation, endothelin signaling, and microthrombosis are repeatedly implicated [11,41–43]. Persistent prothrombotic endothelial activation, with elevated tissue factor, PAR-1, vWF, factor VIII, and microparticles, may sustain pulmonary hypertension after acute infection [44]. Importantly, the predominance of observational data and reliance on echocardiographic assessment rather than invasive hemodynamic confirmation limits both diagnostic precision and causal inference. This distinction is critical when interpreting reported associations, particularly in differentiating pulmonary hypertension from confirmed pulmonary arterial hypertension.

Synthesis and Limitations

Across diverse viral pathogens, pulmonary hypertension emerges as a recurrent vascular phenotype characterized by immune dysregulation, endothelial injury, inflammation, thrombosis, and maladaptive pulmonary vascular remodeling. However, the evidence base remains predominantly observational and largely dependent on echocardiographic assessment rather than right heart catheterization. Heterogeneous diagnostic criteria further limit diagnostic precision, comparability, and causal inference. The single-reviewer workflow represents an additional potential source of bias.

Residual confounding from comorbid lung disease, cardiovascular disease, autoimmune conditions, antiretroviral therapy, and post-thromboembolic states could not be fully accounted for in the included observational studies and may have influenced reported associations. Although PubMed, PubMed Central (PMC), and the Cochrane Library were used to ensure broad biomedical coverage, PMC overlaps substantially with PubMed and MDPI represents a publisher rather than a primary bibliographic database. Major databases such as Embase, Scopus, and Web of Science were not included due to access limitations and resource constraints, which may have limited database coverage and increased the risk of selection and publication bias. Overall, observational studies demonstrated moderate-to-high methodological quality, while animal studies exhibited variable risk of bias, primarily related to lack of randomization and blinding. These methodological limitations were explicitly considered when interpreting both clinical associations and mechanistic conclusions.

Overall, the certainty of evidence was considered low to moderate for human observational studies and moderate for mechanistic conclusions supported by convergent animal data. Methodological heterogeneity across included studies necessitated qualitative rather than quantitative synthesis. Formal GRADE assessment was not applied due to heterogeneity in study design, outcomes, and diagnostic approaches; however, overall certainty of evidence was qualitatively assessed based on study quality, consistency of findings, and biological plausibility.

Despite these limitations, integrated findings from observational studies, animal models, and mechanistic investigations are consistent with a possible association between viral infection and pulmonary vascular disease. Accordingly, this review synthesizes the available evidence into a conceptual framework in **Table 12**, illustrating potential pathways linking viral infection to pulmonary hypertension.

Table 12. Conceptual framework linking viral infection to pulmonary hypertension

Step	Pathophysiological stage	Key mechanisms	Viruses implicated	Key consequences
1	Viral trigger	Acute or chronic viral persistence	SARS-CoV-2, HIV, EBV, RSV, CMV, HCV	Initiation of inflammatory cascade
2	Immune dysregulation	$CD4^+$ T-cell depletion; Th_2 bias; ↑ IL-6, IL-13, TNF-α, TGF-β; PD-1 upregulation	HIV, RSV, SARS-CoV-2	Chronic immune activation and exhaustion
3	Endothelial injury & dysfunction	↓ NO bioavailability; ACE2 depletion; endothelin-1 activation; NOS uncoupling	SARS-CoV-2, HIV	Endothelial dysfunction and vasoconstriction
4	Thrombo-inflammatory state	Microthrombosis; ↑ D-dimer, tissue factor, vWF; platelet–leukocyte activation	SARS-CoV-2, HIV, RSV	Obstructed pulmonary microcirculation

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5	Pulmonary vascular remodeling	Intimal fibrosis; medial hypertrophy; plexiform lesions; ↑ PA wall thickness	SARS-CoV-2, HIV, EBV	Fixed elevation in pulmonary vascular resistance
6	Hemodynamic consequences	↑ mPAP/RVSP; ↑ PVR; RV–PA uncoupling	SARS-CoV-2, HIV	Right ventricular dysfunction and failure

Conclusion

This study integrates clinical and experimental evidence to examine the relationship between viral infections and pulmonary hypertension. Viral infections may contribute to pulmonary vascular disease through multifactorial mechanisms; however, the current evidence base remains largely observational.

The strength of evidence varies across viral pathogens, with the most consistent clinical association observed in HIV, while evidence for other viruses remains more limited or indirect. Future studies incorporating standardized diagnostic criteria, invasive hemodynamic assessment, and longitudinal follow-up are required to strengthen causal inference and clarify disease progression.

Ethics Statement

This study did not involve direct experimentation on human participants or animals.

Funding

No funding was received for this study.

Conflicts of Interest

The author declares no conflicts of interest.

References:

1. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-3731. doi:10.1093/eurheartj/ehac237
2. Hoeper MM, Humbert M, Souza R, et al. A global view of pulmonary hypertension. *Lancet Respir Med*. 2016;4(4):306-322. doi:10.1016/S2213-2600(15)00543-3
3. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019;53(1). doi:10.1183/13993003.01913-2018
4. Mandras SA, Mehta HS, Vaidya A. Pulmonary Hypertension: A Brief Guide for Clinicians. *Mayo Clin Proc*. 2020;95(9):1978-1988. doi:10.1016/j.mayocp.2020.04.039
5. Rose-Jones L, Mclaughlin V. Pulmonary hypertension: types and treatments. *Curr Cardiol Rev*. 2015;11(1):73-79. doi:10.2174/1573403x09666131117164122
6. Hajra A, Safiriyu I, Balasubramanian P, et al. Recent Advances and Future Prospects of Treatment of Pulmonary Hypertension. *Curr Probl Cardiol*. 2023;48(8). doi:10.1016/j.cpcardiol.2022.101236
7. Austin ED, Loyd JE. The Genetics of Pulmonary Arterial Hypertension. *Circ Res*. 2014;115(1):189. doi:10.1161/CIRCRESAHA.115.303404
8. Ma PJ, Wang MM, Wang Y. Gut microbiota: A new insight into lung diseases. *Biomedicine and Pharmacotherapy*. 2022;155. doi:10.1016/j.biopha.2022.113810
9. Suzuki YJ, Nikolaienko SI, Shults N V., Gychka SG. COVID-19 patients may become predisposed to pulmonary arterial hypertension. *Med Hypotheses*. 2021;147. doi:10.1016/j.mehy.2021.110483
10. Duncan MS, Alcorn CW, Freiberg MS, et al. Association between HIV and incident pulmonary hypertension in US Veterans: a retrospective cohort study. *Lancet Healthy Longev*. 2021;2(7):e417-e425. doi:10.1016/S2666-7568(21)00116-1
11. Tian Z, Cen L. Interaction of Biochemical Processes between Chronic Obstructive Pulmonary Disease (COPD), Pulmonary Arterial Hypertension (PAH), and Coronavirus Disease 2019 (COVID-19). *Pol J Microbiol*. 2023;72(2):143-154. doi:10.33073/pjm-2023-015
12. Rajaratnam A, Rehman S, Sharma P, et al. Right ventricular load and contractility in HIV-associated pulmonary hypertension. *PLoS One*. 2021;16(2):e0243274. doi:10.1371/journal.pone.0243274
13. Norderfeldt J, Liliequist A, Eksborg S, et al. Severe Covid-19 and acute pulmonary hypertension: 24-month follow-up regarding

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Accepted: March 24th, 2026.
Published: March 24th, 2026.
Systematic Review

mortality and relationship to initial echocardiographic findings and biomarkers. *Acta Anaesthesiol Scand*. 2023;67(2):206-212. doi:10.1111/aas.14168
14. Mahdi N, Nadeem I, Ur Rasool M, et al. Pulmonary hypertension, pulmonary embolism and COVID-19: A district general hospital experience from the UK. *J R Coll Physicians Edinb*. 2023;53(1):9-12. doi:10.1177/14782715231152677
15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372. doi:10.1136/bmj.n71
16. Atabati E, Dehghani-Samani A, Mortazavimoghaddam SG. Association of COVID-19 and other viral infections with interstitial lung diseases, pulmonary fibrosis, and pulmonary hypertension: A narrative review. *Can J Respir Ther*. 2020;56:70-78. doi:10.29390/CJRT-2020-021
17. Pagnesi M, Baldetti L, Beneduce A, et al. Pulmonary hypertension and right ventricular involvement in hospitalised patients with COVID-19. *Heart*. 2020;106(17):1324. doi:10.1136/heartjnl-2020-317355
18. Norderfeldt J, Liliequist A, Frostell C, et al. Acute pulmonary hypertension and short-term outcomes in severe Covid-19 patients needing intensive care. *Acta Anaesthesiol Scand*. 2021;65(6):761-769. doi:10.1111/aas.13819
19. Erdem K, Duman A. Pulmonary artery pressures and right ventricular dimensions of post-COVID-19 patients without previous significant cardiovascular pathology. *Heart and Lung*. 2023;57:75-79. doi:10.1016/j.hrtlng.2022.08.023
20. Tudoran C, Tudoran M, Lazureanu VE, et al. Factors Influencing the Evolution of Pulmonary Hypertension in Previously Healthy Subjects Recovering from a SARS-CoV-2 Infection. *J Clin Med*. 2021;10(22). doi:10.3390/jcm10225272
21. Palakeel JJ, Ali M, Chaduvula P, et al. An Outlook on the Etiopathogenesis of Pulmonary Hypertension in HIV. *Cureus*. 2022;14(7). doi:10.7759/cureus.27390
22. Singh S, Vatsa D, Tomar S, Aneja G, S. Arya T. Cardiac complications in people living with human immunodeficiency virus/acquired immunodeficiency syndrome and their association with CD4+ T-cell count - A cross sectional study. *Indian J Sex Transm Dis AIDS*. 2018;39(1):23-27. doi:10.4103/ijstd.IJSTD_18_16
23. Zola CE, Duncan MS, So-Armah K, et al. HIV- and HCV-specific markers and echocardiographic pulmonary artery systolic pressure among United States veterans. *Sci Rep*. 2020;10(1). doi:10.1038/s41598-020-75290-4
24. Calabrese F, Kipar A, Lunardi F, et al. Herpes virus infection is associated with vascular remodeling and pulmonary hypertension in idiopathic pulmonary fibrosis. *PLoS One*. 2013;8(2). doi:10.1371/journal.pone.0055715
25. Tomaszewski M, Grywalska E, Tomaszewski A, et al. Overexpression of PD-1 on Peripheral Blood Lymphocytes in Patients with Idiopathic Pulmonary Arterial Hypertension and Its Association with High Viral Loads of Epstein-Barr Virus and Poor Clinical Parameters. *J Clin Med*. 2020;9(6):1966. doi:10.3390/jcm9061966
26. Kimura D, Saravia J, Jaligama S, et al. New mouse model of pulmonary hypertension induced by respiratory syncytial virus bronchiolitis. *Am J Physiol Heart Circ Physiol*. 2018;315(3):H581. doi:10.1152/ajpheart.00627.2017
27. Vu LD, Saravia J, Jaligama S, et al. Deficiency in ST2 signaling ameliorates RSV-associated pulmonary hypertension. *Am J Physiol Heart Circ Physiol*. 2021;321(2):H309. doi:10.1152/ajpheart.00018.2021
28. Schweitzer F, Tarantelli R, Rayens E, Kling HM, Mattila JT, Norris KA. Monocyte and Alveolar Macrophage Skewing Is Associated with the Development of Pulmonary Arterial Hypertension in a Primate Model of HIV Infection. *AIDS Res Hum Retroviruses*. 2019;35(1):63. doi:10.1089/aid.2018.0132
29. Tarantelli RA, Schweitzer F, Simon MA, et al. Longitudinal Evaluation of Pulmonary Arterial Hypertension in a Rhesus Macaque (Macaca mulatta) Model of HIV Infection. *Comp Med*. 2018;68(6):461-473. doi:10.30802/AALAS-CM-18-000012
30. Rabacal W, Schweitzer F, Rayens E, et al. Statin treatment prevents the development of pulmonary arterial hypertension in a nonhuman primate model of HIV-associated PAH. *Sci Rep*. 2019;9(1):19832. doi:10.1038/s41598-019-55301-9
31. Hashimoto T, Sakata Y, Fukushima K, et al. Pulmonary arterial hypertension associated with chronic active Epstein-Barr virus infection. *Intern Med*. 2011;50(2):119-124. doi:10.2169/internalmedicine.50.4143
32. Akagi S, Miki T, Sando Y, et al. Chemotherapy Improved Pulmonary Arterial Hypertension in a Patient with Chronic-Active Epstein-Barr Virus Infection. *Int Heart J*. 2020;61(1):191-194. doi:10.1536/ihj.19-419
33. Ba H, Xu L, Peng H, et al. Chronic Active Epstein-Barr Virus Infection With Systemic Vasculitis and Pulmonary Arterial Hypertension in a Child. *Front Pediatr*. 2019;7(JUN). doi:10.3389/fped.2019.00219
34. Tsuchiya H, Kioka H, Ozu K, et al. Interferon Therapy Exacerbated Pulmonary Hypertension in a Patient with Hepatitis C Virus Infection: Pathogenic Interplay among Multiple Risk Factors. *Intern Med*. 2017;56(9):1061-1065. doi:10.2169/internalmedicine.56.7822

Volume 11 (05)
Accepted: March 24th, 2026.
Published: March 24th, 2026.
Systematic Review

35. Zhao YN, Liu GH, Wang C, Zhang YX, Yang P, Yu M. Pulmonary hypertension, nephrotic syndrome, and polymyositis due to hepatitis C virus infection: A case report. *World J Gastroenterol*. 2023;29(19):3040-3047. doi:10.3748/wjg.v29.i19.3040
36. Walter-Nicolet E, Leblanc M, Leruez-Ville M, Hubert P, Mitanchez D. Congenital cytomegalovirus infection manifesting as neonatal persistent pulmonary hypertension: report of two cases. *Pulm Med*. 2011;2011. doi:10.1155/2011/293285
37. Cueto-Robledo G, Porres-Aguilar M, Puebla-Aldama D, et al. Severe Pulmonary Hypertension: An Important Sequel After Severe Post-Acute COVID-19 Pneumonia. *Curr Probl Cardiol*. 2022;47(3). doi:10.1016/j.cpcardiol.2021.101004
38. Cruz-Utrilla A, Calderón-Flores M, Escribano-Subias MP. Pulmonary embolism and coronavirus disease 2019: persistent pulmonary hypertension? *Kardiol Pol*. 2020;78(9):937-938. doi:10.33963/KP.15436
39. Rossi R, Coppi F, Monopoli DE, Sgura FA, Arrotti S, Boriani G. Pulmonary arterial hypertension and right ventricular systolic dysfunction in COVID-19 survivors. *Cardiol J*. 2022;29(1):163-165. doi:10.5603/CJ.a2021.0159
40. Flores SC, Almodovar S. Human immunodeficiency virus, herpes virus infections, and pulmonary vascular disease. *Pulm Circ*. 2013;3(1):165-170. doi:10.4103/2045-8932.109955
41. Wang D, Gomes MT, Mo Y, et al. Human Endogenous Retrovirus, SARS-CoV-2, and HIV Promote PAH via Inflammation and Growth Stimulation. *Int J Mol Sci*. 2023;24(8). doi:10.3390/ijms24087472
42. Nabeh OA, Matter LM, Khattab MA, Esraa Menshawey. "The possible implication of endothelin in the pathology of COVID-19-induced pulmonary hypertension." *Pulm Pharmacol Ther*. 2021;71:102082. doi:10.1016/j.pupt.2021.102082
43. Cueto-Robledo G, Roldan-Valadez E, Graniel-Palafox LE, et al. Chronic Thromboembolic Pulmonary Hypertension (CTEPH): A Review of Another Sequel of Severe Post-Covid-19 Pneumonia. *Curr Probl Cardiol*. 2023;48(8). doi:10.1016/j.cpcardiol.2022.101187
44. Xiang M, Jing H, Wang C, Novakovic VA, Shi J. Persistent Lung Injury and Prothrombotic State in Long COVID. *Front Immunol*. 2022;13. doi:10.3389/fimmu.2022.862522

From Virus to Vessel: Viral Infections and Pulmonary Hypertension — A Systematic Review and Mechanistic Synthesis

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