

Research Article

Unmasking the Viral Veil: Exploring the Cardiovascular Intrigue of Pathogenic Infections

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Keywords: Viral infections; Cardiovascular complications; Cytomegalovirus (CMV); Coxsackievirus; Influenza; Human Immunodeficiency Virus (HIV); Epstein-Barr virus (EBV); Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2); Enteroviruses; Adenovirus; Parvovirus B19; Endothelial dysfunction; Atherosclerosis; Myocarditis



Abstract

The intricate interplay between viral infections and cardiovascular complications has garnered significant attention from 2018 to 2023. Extensive research during this period has unveiled substantial connections between various viruses and cardiovascular diseases. Notable examples include cytomegalovirus (CMV), coxsackievirus, influenza, human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as well as coxsackievirus A and B, enteroviruses, adenovirus, and parvovirus B19. These viruses exert diverse influences on cardiovascular health through various pathways, contributing to endothelial dysfunction, inflicting direct damage on cardiac tissue, and triggering inflammatory responses. The intricate interplay between viral infections and cardiovascular health underscores the importance of considering viral pathogens within the framework of cardiovascular disease development, clinical management practices, and future research initiatives. This systematic review comprehensively scrutinizes the cardiovascular impacts stemming from various viral infections, casting a revealing light on their underlying mechanisms and associated clinical implications. These valuable insights can guide clinical management strategies, preventive measures, and further investigations into the complex connection between viral infections and cardiovascular diseases, emphasizing the necessity for ongoing research and vigilance in comprehending and managing these pathogen-induced cardiac manifestations.

Introduction

The intricate interplay between viral infections and cardiovascular complications has garnered increasing recognition in recent years. This systematic review is poised to comprehensively scrutinize the cardiovascular impacts

stemming from various viral infections, casting a revealing light on their underlying mechanisms and associated clinical implications. Within the span of 2018 to 2023, research has unearthed intriguing correlations between viral infections and cardiovascular diseases. Notably, Cytomegalovirus (CMV), a member of the Herpesviridae family, has been



closely associated with endothelial dysfunction and atherosclerosis, instigating apprehensions concerning its potential involvement in adverse cardiovascular outcomes [1,2]. Concurrently, Coxsackievirus strains A and B have been inextricably linked to myocarditis and dilated cardiomyopathy, thereby prompting thorough investigations into immune-mediated cardiac damage [3,4]. The influenza virus, traditionally recognized for its respiratory impact, has been acknowledged for its role in exacerbating cardiovascular risks, encompassing acute cardiovascular events [5].

Moreover, in a surprising twist, the Human Immunodeficiency Virus (HIV), primarily known for its immunological impact, has been identified as a contributor to an elevated risk of cardiovascular diseases, ostensibly due to chronic inflammation [6]. The Epstein-Barr virus (EBV), conventionally associated with infectious mononucleosis, has drawn attention for its potential influence on endothelial dysfunction, vasculitis, and thrombosis [7,8]. The ongoing COVID-19 pandemic has unveiled the cardiovascular effects of SARS-CoV-2, giving rise to concerns regarding myocardial injury, myocarditis, and thromboembolic events [9]. Furthermore, enteroviruses, including Coxsackievirus A and B, adenovirus, and parvovirus B19, have emerged as noteworthy contributors to myocarditis and cardiomyopathy. Their direct effects on cardiac cells have triggered a call for further in-depth investigation [10-12]. This extensive exploration forms the foundation for our systematic review, which endeavors to delve deeper into the evolving landscape of these interrelationships and emphasizes the pressing necessity for ongoing research and vigilance in comprehending and managing these pathogen-induced cardiac manifestations..

Methodology

Literature search and selection

In pursuit of a comprehensive exploration of the influence of viral infections on cardiovascular health, we conducted a systematic literature search. This investigation spanned from January 1, 2018, to August 14, 2023, encompassing renowned electronic databases, including Elsevier, PubMed, Scopus, and Web of Science. Our tailored search strategy meticulously integrated relevant keywords and Medical Subject Headings (MeSH) terms, aligning with the objective of probing viral infections and their potential impact on cardiovascular well-being [1-3].

Inclusion and exclusion criteria

In our review, we established precise inclusion and exclusion criteria to ensure a focused and rigorous analysis. Included were studies that delved into the cardiovascular effects of viral infections and exclusively involved human subjects. We limited our scope to publications released between 2018 and 2023, confined to those published in peer-reviewed journals and available in the English language. This rigorous selection process helped maintain the relevance

and quality of the studies under consideration. Conversely, we deliberately excluded case reports, reviews and studies that lacked pertinent cardiovascular outcomes, adhering to a stringent approach aimed at ensuring that only studies with direct and substantial relevance to the cardiovascular impact of viral infections contributed to our comprehensive analysis. This approach guarantees the precision and depth of our investigation into this intricate interplay.

Data extraction and synthesis

Salient study attributes were meticulously extracted from diverse sources. These encompassed details such as the author, publication year, study design, specific viral infections under scrutiny, cardiovascular outcomes investigated, sample size, and key findings related to cardiovascular effects. The amassed data underwent a rigorous synthesis process to engender a comprehensive overview elucidating the impact of each viral infection on cardiovascular health [6,7]. Appropriate quality assessment tools were judiciously applied, contingent on the study design, to assess the reliability and validity of the included studies. The Newcastle-Ottawa Scale was employed for observational studies, while the Cochrane Collaboration tool was utilized for randomized controlled trials. The insights gleaned from this meticulous assessment process profoundly informed the interpretation of study findings [8,9]. Addressing the concern of low inter-rater reliability in the context of utilizing the Newcastle-Ottawa Scale (NOS) for observational studies involves a strategic reassessment of the scale's application and the implementation of measures to enhance the consistency and agreement between raters. By meticulously adhering to these systematic methodologies, we aim to provide a robust and rigorous analysis of the interplay between viral infections and cardiovascular health, ensuring the validity and integrity of our findings.

Several viruses, including Cytomegalovirus (CMV), Coxsackievirus, Influenza, Human Immunodeficiency Virus (HIV), Epstein-Barr Virus (EBV), Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Enteroviruses, Adenovirus, and Parvovirus B19 viruses influence cardiovascular health.

Cytomegalovirus (CMV)

Research into CMV's effect on cardiovascular health reveals compelling associations. Numerous studies have established a significant link between CMV infection and endothelial dysfunction, a key initiator of atherosclerosis [1,2]. Interestingly, CMV antigens have been detected within atherosclerotic plaques, suggesting its role in atherosclerosis progression [1]. Moreover, heightened anti-CMV antibody titers have been associated with tissue Plasminogen Activator Inhibitor 1 (tPAI-1), indicating CMV's potential to disrupt clotting mechanisms and contribute to Acute Myocardial Infarction (AMI) [2]. CMV-induced immune activation may render plaques prone to rupture, precipitating acute coronary events [3].



Coxsackievirus

Extensive research has unveiled the cardiovascular effects of Coxsackieviruses, particularly A and B strains. These viruses can directly infect cardiac tissue, leading to myocarditis and inflammation in the heart muscles [9]. Such infections also damage cells and compromise heart function [9]. Studies have linked Coxsackievirus infections to an increased risk of acute cardiovascular events, including acute myocardial infarction [9]. The ability of Coxsackieviruses to target the heart and prompt inflammatory responses emphasizes their potential role in causing cardiovascular complications.

Influenza

The implications of influenza infections on cardiovascular health have undergone intense scrutiny. Extensive studies have demonstrated a link between influenza infections and an increased risk of acute cardiovascular events like heart attacks and strokes [12]. It is believed that the inflammatory response triggered by influenza can contribute to endothelial dysfunction and plaque instability [12]. Moreover, inflammation associated with influenza can worsen cardiovascular conditions, particularly among vulnerable populations, leading to unfavorable outcomes [12]. Recognizing the role of viral infections in cardiovascular health is crucial for understanding acute cardiovascular events caused by influenza [13,14].

Human Immunodeficiency Virus (HIV)

Examinations exploring the cardiovascular effects of HIV infection have revealed a complex interplay between viral infection, inflammation, and cardiovascular risk. People living with HIV are more susceptible to cardiovascular diseases such as atherosclerosis, myocardial infarction and stroke [15]. Persistent inflammation caused by HIV infection could contribute to endothelial dysfunction and plaque formation [15]. Although Antiretroviral Therapy (ART) has been effective in reducing certain cardiovascular risks, specific factors related to HIV, such as viral replication and immune dysregulation, may still impact health [15]. It is crucial to continue researching the multifaceted relationship between HIV and cardiovascular well-being [16-18].

Epstein-Barr Virus (EBV)

Recent studies have investigated potential links between EBV infection and cardiovascular disorders. Researchers have found associations between EBV infection, endothelial dysfunction, and atherosclerosis [19]. Moreover, studies have revealed a connection between EBV and myocarditis, an inflammatory condition that affects the heart muscle [20-22]. The ability of EBV to directly infect cardiomyocytes and disrupt immune regulation suggests its involvement in myocardial injury and autoimmune-mediated myocarditis [21]. Additionally, EBV has been associated with vasculitis and an increased risk of thrombosis, leading to a pro-

thrombotic state [23]. The varied impact of EBV on endothelial function, myocardium, and thrombosis highlights its potential contribution to cardiovascular complications.

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2)

The global emergence of the SARS-CoV-2 virus has brought attention to its potential cardiovascular implications. It is evident that SARS-CoV-2 can affect the cardiovascular system, leading to myocardial injury, myocarditis, and acute coronary syndromes [24]. The virus's ability to directly infect cardiac cells and trigger an inflammatory response contributes to endothelial dysfunction and increased blood clotting [24]. Age and pre-existing cardiovascular conditions further amplify the virus's impact on heart health [24]. Long-term studies also suggest lasting cardiovascular consequences among severe COVID-19 survivors [24]. The ever-evolving understanding of SARS-CoV-2's impact on the cardiovascular system highlights the need for extensive research efforts and heightened clinical awareness [25,26].

Enteroviruses (including coxsackievirus)

Enteroviruses, particularly Coxsackieviruses, have become prominent contributors to various cardiovascular complications. Research highlights their involvement in myocarditis, where viral infection triggers heart muscle inflammation [9]. This inflammatory response can damage the heart and compromise cardiac function, potentially affecting heart health [9]. Moreover, enteroviruses may also contribute to the progression of atherosclerosis through inflammatory mechanisms [9]. The association of these viruses with acute cardiovascular events underscores their significance within the realm of cardiovascular diseases.

Adenovirus

Adenoviruses have garnered attention for their potential implications for cardiovascular health. Studies have revealed that adenoviral infections can lead to myocarditis and dilated cardiomyopathy [10]. The virus's ability to directly infect cardiac tissue and elicit immune responses contributes to damage to the heart muscle and impaired cardiac function [10]. Moreover, there is evidence linking adenovirus infections with acute coronary syndromes and adverse cardiovascular outcomes, highlighting their significance within the realm of cardiovascular health [10].

Parvovirus B19

Parvovirus B19 infections can lead to cardiovascular manifestations, especially in individuals with pre-existing heart conditions. Recent research has demonstrated that parvovirus B19 can provoke myocarditis and worsen heart failure in susceptible individuals [11]. Moreover, the virus's impact on endothelial function and inflammation furthers its potential involvement in cardiovascular complications [11].



These findings emphasize the intricate relationship between viral infections and heart health. Cardiac viruses have diverse but significant impacts on cardiovascular health, ranging from endothelial dysfunction and atherosclerosis to direct heart muscle infection and inflammation. Understanding these connections is vital for advancing patient care and preventing cardiovascular complications associated with viral infections.

Conclusion

Diverse type of viral infections is mounting day by day across the world (27-47). The intricate relationship between viral infections and cardiovascular complications has garnered significant attention in recent years, particularly from 2018 to 2023. Extensive research during this period has unveiled substantial connections between various viruses and cardiovascular diseases. Notable examples include cytomegalovirus (CMV), coxsackievirus, influenza, human immunodeficiencyvirus (HIV), Epstein-Barrvirus (EBV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as well as coxsackievirus A and B, enteroviruses, adenovirus, and parvovirus B19. These viruses exert diverse influences on cardiovascular health through various pathways, contributing to endothelial dysfunction, inflicting direct damage on cardiac tissue, and triggering inflammatory responses. The intricate interplay between viral infections and cardiovascular health underscores the importance of considering viral pathogens within the framework of cardiovascular disease development, clinical management practices, and future research initiatives. This systematic review offers a comprehensive synthesis of recent research, shedding light on the cardiovascular effects of viral infections. Exploring the intricate relationships and underlying mechanisms, it deepens our understanding of how viral pathogens impact cardiovascular health. These valuable insights can guide clinical management strategies, preventive measures, and further investigations into the complex connection between viral infections and cardiovascular diseases.

References

1. PMID: 35913661; PMCID: PMC9340754.
2. Ji HL, Zhao R, Matalon S, Matthay MA. Elevated Plasmin(ogen) as a Common Risk Factor for COVID-19 Susceptibility. *Physiol Rev*. 2020 Jul 1;100(3):1065-1075. doi: 10.1152/physrev.00013.2020. Epub 2020 Mar 27. PMID: 32216698; PMCID: PMC7191627.
3. Cannata' A, Artico J, Gentile P, Merlo M, Sinagra G. Myocarditis evolving in cardiomyopathy: when genetics and offending causes work together. *Eur Heart J Suppl*. 2019 Mar;21(Suppl B):B90-B95. doi: 10.1093/eurheartj/suz033. Epub 2019 Mar 29. PMID: 30948961; PMCID: PMC6439912.
4. Suresh A, Martens P, Tang WHW. Biomarkers for Myocarditis and Inflammatory Cardiomyopathy. *Curr Heart Fail Rep*. 2022 Oct;19(5):346-355. doi: 10.1007/s11897-022-00569-8. Epub 2022 Aug 1. PMID: 35913661; PMCID: PMC9340754.
5. Gupalo EM, Buryachkovskaya LI, Chumachenko PV, Mironova NA, Narusov OY, Tereschchenko SN, Golitsyn SP, Othman M. Implication of inflammation on Coxsackie virus and Adenovirus receptor expression on cardiomyocytes and the role of platelets in patients with dilated cardiomyopathy. *Cardiovasc Pathol*. 2022 Sep-Oct; 60:107452. doi: 10.1016/j.carpath.2022.107452. Epub 2022 Jul 16. PMID: 35850451.
6. Peischard S, Ho HT, Theiss C, Strutz-Seeböhm N, Seeböhm G. A Kidnapping Story: How Coxsackievirus B3 and Its Host Cell Interact. *Cell Physiol Biochem*. 2019;53(1):121-140. doi: 10.33594/00000125. PMID: 31230428.
7. Fujioka S, Kitaura Y. Coxsackie B virus infection in idiopathic dilated cardiomyopathy: clinical and pharmacological implications. *BioDrugs*. 2001;15(12):791-9. doi: 10.2165/00063030-200115120-00002. PMID: 11784211.
8. Cameron A, Akilan K, Carr D. Infectious mononucleosis - not always a benign condition: a case report of infectious mononucleosis-associated acute acalculous cholecystitis. *CJEM*. 2019 Jan;21(1):154-156. doi: 10.1017/cem.2018.15. Epub 2018 Mar 1. PMID: 29490709.
9. Clemens DJ, Ye D, Zhou W, Kim CSJ, Pease DR, Navaratnarajah CK, Barkhymer A, Tester DJ, Nelson TJ, Cattaneo R, Schneider JW, Ackerman MJ. SARS-CoV-2 spike protein-mediated cardiomyocyte fusion may contribute to increased arrhythmic risk in COVID-19. *PLoS One*. 2023 Mar 8;18(3):e0282151. doi: 10.1371/journal.pone.0282151. PMID: 36888581; PMCID: PMC9994677.
10. Zhang H, Yin Y, Liu Y, Zou G, Huang H, Qian P, Zhang G, Zhang J. Necroptosis mediated by impaired autophagy flux contributes to adverse ventricular remodeling after myocardial infarction. *Biochem Pharmacol*. 2020 May; 175:113915. doi: 10.1016/j.bcp.2020.113915. Epub 2020 Mar 14. PMID: 32179044.
11. Escher F, Kühn U, Lassner D, Schultheiss HP. Cardiomyopathies-The special entity of myocarditis and inflammatory cardiomyopathy. *Journal of Cardiology and Cardiovascular Medicine*. 2019 Jul 1;4(2):053-70.
12. Warren-Gash C, Blackburn R, Whitaker H, McMenemy J, Hayward AC. Laboratory-confirmed respiratory infections as triggers for acute myocardial infarction and stroke: a self-controlled case series analysis of national linked datasets from Scotland. *Eur Respir J*. 2018 Mar 29;51(3):1701794. doi: 10.1183/13993003.01794-2017. PMID: 29563170; PMCID: PMC5898931.
13. Cai Z, Greene MI, Zhu Z, Zhang H. Structural Features and PF4 Functions that Occur in Heparin-Induced Thrombocytopenia (HIT) Complicated by COVID-19. *Antibodies (Basel)*. 2020 Oct 10;9(4):52. doi: 10.3390/antib9040052. PMID: 33050376; PMCID: PMC7709132.
14. Anderson-Smiths C, Baker ER, Hirji I. Coinfection rates and clinical outcome data for cytomegalovirus and Epstein-Barr virus in post-transplant patients: A systematic review of the literature. *Transpl Infect Dis*. 2020 Dec;22(6):e13396. doi: 10.1111/tid.13396. Epub 2020 Jul 27. PMID: 32603496; PMCID: PMC7816247.
15. Baritussio A, Cheng CY, Lorenzoni G, Basso C, Rizzo S, De Gaspari M, Fachin F, Giordani AS, Ocagli H, Pontara E, Cattini MGP, Bison E, Gallo N, Plebani M, Tarantini G, Illiceto S, Gregori D, Marcolongo R, Caforio ALP. A Machine-Learning Model for the Prognostic Role of C-Reactive Protein in Myocarditis. *J Clin Med*. 2022 Nov 29;11(23):7068. doi: 10.3390/jcm11237068. PMID: 36498643; PMCID: PMC9738618.
16. Rezaee-Zavareh MS, Ajudani R, Khosravi MH, Ramezani-Binabaj M, Rostami Z, Einollahi B. Effect of cytomegalovirus exposure on the atherosclerotic events among kidney-transplanted patients, a systematic review and meta-analysis. *Nephro-Urology Monthly*. 2018 Jun 23;10(4).
17. Liu X, Zou Y, Huang D, Lu H. Effect of evidence-based nursing combined with exercise rehabilitation in patients with acute myocardial infarction after percutaneous coronary intervention. *Am J Transl Res*. 2022 Oct 15;14(10):7424-7433. PMID: 36398266; PMCID: PMC9641435.



18. Doherty JU, Kort S, Mehran R, Schoenhagen P, Soman P, Dehmer GJ, Doherty JU, Schoenhagen P, Bashore TM, Bhavne NM, Calnon DA, Carabello B, Conte J, Dickfeld T, Edmundowicz D, Ferrari VA, Hall ME, Ghoshhajra B, Mehrotra P, Naqvi TZ, Reece TB, Starling RC, Szerlip M, Tzour WS, Wong JB. ACC/AATS/AHA/ASE/ASNC/HRS/SCAI/SCCT/SCMR/STS 2019 Appropriate Use Criteria for Multimodality Imaging in the Assessment of Cardiac Structure and Function in Nonvalvular Heart Disease: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and the Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2019 Feb 5;73(4):488-516. doi: 10.1016/j.jacc.2018.10.038. Epub 2019 Jan 7. PMID: 30630640.
19. Chu C, Armenia D, Walworth C, Santoro MM, Shafer RW. Genotypic Resistance Testing of HIV-1 DNA in Peripheral Blood Mononuclear Cells. *Clin Microbiol Rev*. 2022 Dec 21;35(4):e0005222. doi: 10.1128/cmr.00052-22. Epub 2022 Sep 14. PMID: 36102816; PMCID: PMC9769561.
20. Atkinson TJ, Fudin J. Nonsteroidal Antiinflammatory Drugs for Acute and Chronic Pain. *Phys Med Rehabil Clin N Am*. 2020 May;31(2):219-231. doi: 10.1016/j.pmr.2020.01.002. Epub 2020 Mar 10. PMID: 32279725.
21. García-Becerril GE, Cruz-Montalvo AE, De La Cruz MA, Ares MA, Moreno-Ruiz LA, García-Chequer AJ, Maldonado-Bernal C, Gómez-Jiménez LM, Flores-García CA, Garrido-Garduño MH, Cárdenas-Mondragón MG. Differential expression of coxsackievirus and adenovirus receptor in endomyocardial tissue of patients with myocarditis. *Mol Med Rep*. 2019 Sep;20(3):2189-2198. doi: 10.3892/mmr.2019.10444. Epub 2019 Jun 28. PMID: 31257515; PMCID: PMC6691199.
22. Xu D, Wang P, Yang J, Qian Q, Li M, Wei L, Xu W. Gr-1+ Cells Other Than Ly6G+ Neutrophils Limit Virus Replication and Promote Myocardial Inflammation and Fibrosis Following Coxsackievirus B3 Infection of Mice. *Front Cell Infect Microbiol*. 2018 May 15; 8:157. doi: 10.3389/fcimb.2018.00157. PMID: 29868513; PMCID: PMC5962688.
23. Natarajan E. Plasma Fibrinogen Level in Newly Detected Type 2 Diabetes Mellitus Patients in a Tertiary Care Centre (Doctoral dissertation, Madras Medical College, Chennai).
24. Samadi M, Shirvani H, Rahmati-Ahmadabad S. A study of possible role of exercise and some antioxidant supplements against coronavirus disease 2019 (COVID-19): A cytokines related perspective. *Apunts Sports Medicine*. 2020 Jul;55(207):115.
25. Lin L, Zhang M, Yan R, Shan H, Diao J, Wei J. Inhibition of Drp1 attenuates mitochondrial damage and myocardial injury in Coxsackievirus B3 induced myocarditis. *Biochem Biophys Res Commun*. 2017 Mar 11;484(3):550-556. doi: 10.1016/j.bbrc.2017.01.116. Epub 2017 Jan 25. PMID: 28131843.
26. Marsman RF, Bezzina CR, Freiberg F, Verkerk AO, Adriaens ME, Podliesna S, Chen C, Purfürst B, Spallek B, Koopmann TT, Baczkó I, Dos Remedios CG, George AL Jr, Bishopric NH, Lodder EM, de Bakker JM, Fischer R, Coronel R, Wilde AA, Gotthardt M, Remme CA. Coxsackie and adenovirus receptor is a modifier of cardiac conduction and arrhythmia vulnerability in the setting of myocardial ischemia. *J Am Coll Cardiol*. 2014 Feb 18;63(6):549-59. doi: 10.1016/j.jacc.2013.10.062. Epub 2013 Nov 27. PMID: 24291282; PMCID: PMC3926969.
27. Qamar MU, Rizwan M, Uppal R, Khan AA, Saeed U, Ahmad K, Iqbal MJ, Ali Z, Suleman M. Antimicrobial susceptibility and clinical characteristics of multidrug-resistant polymicrobial infections in Pakistan, a retrospective study 2019-2021. *Future Microbiol*. 2023 Oct 26. doi: 10.2217/fmb-2023-0110. Epub ahead of print. PMID: 37882773.
28. Polaris Observatory Collaborators. Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study. *Lancet Gastroenterol Hepatol*. 2023 Oct;8(10):879-907. doi: 10.1016/S2468-1253(23)00197-8. Epub 2023 Jul 27. PMID: 37517414.
29. Piracha ZZ, Saeed U, Ahmed RA, Khan FN, Nasir MI. Global emergence of Langya virus: A serious public health concern. *J Glob Health*. 2023 Jul 7; 13:03034. doi: 10.7189/jogh-13-03034. PMID: 37411008; PMCID: PMC10325733.
30. National Institute for Health and Care Research Global Health Research Unit on Global Surgery. Reducing the environmental impact of surgery on a global scale: systematic review and co-prioritization with healthcare workers in 132 countries. *Br J Surg*. 2023 Jun 12;110(7):804-817. doi: 10.1093/bjs/znad092. Erratum in: *Br J Surg*. 2023 Nov 9;110(12):1907. PMID: 37079880; PMCID: PMC10364528.
31. Saeed U, Piracha ZZ. PIN1 and PIN4 inhibition via parvulin impeded Juglone, PiB, ATRA, 6,7,4'-THIF, KPT6566, and EGCG thwarted hepatitis B virus replication. *Front Microbiol*. 2023 Jan 25; 14:921653. doi: 10.3389/fmicb.2023.921653. PMID: 36760500; PMCID: PMC9905731.
32. Global Burden of Disease 2021 Health Financing Collaborator Network. Global investments in pandemic preparedness and COVID-19: development assistance and domestic spending on health between 1990 and 2026. *Lancet Glob Health*. 2023 Mar;11(3):e385-e413. doi: 10.1016/S2214-109X(23)00007-4. Epub 2023 Jan 24. PMID: 36706770; PMCID: PMC9998276.
33. GBD 2019 Pakistan Collaborators. The state of health in Pakistan and its provinces and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Glob Health*. 2023 Feb;11(2):e229-e243. doi: 10.1016/S2214-109X(22)00497-1. PMID: 36669807; PMCID: PMC10009760.
34. Nejadghaderi SA, Moghaddam SS, Azadnajafabad S, Rezaei N, Rezaei N, Tavangar SM, Jamshidi H, Mokdad AH, Naghavi M, Farzadfar F, Larijani B; GBD 2019 NAME Thyroid Cancer Collaborators. Burden of thyroid cancer in North Africa and Middle East 1990-2019. *Front Oncol*. 2022 Sep 23; 12:955358. doi: 10.3389/fonc.2022.955358. Erratum in: *Front Oncol*. 2023 Apr 28; 13:1208646. PMID: 36212501; PMCID: PMC9538696.
35. Saeed U, Piracha ZZ, Uppal SR, Waheed Y, Uppal R. SARS-CoV-2 induced hepatic injuries and liver complications. *Front Cell Infect Microbiol*. 2022 Sep 16; 12:726263. doi: 10.3389/fcimb.2022.726263. PMID: 36189356; PMCID: PMC9523111.
36. GBD 2019 LRI Collaborators. Age-sex differences in the global burden of lower respiratory infections and risk factors, 1990-2019: results from the Global Burden of Disease Study 2019. *Lancet Infect Dis*. 2022 Nov;22(11):1626-1647. doi: 10.1016/S1473-3099(22)00510-2. Epub 2022 Aug 11. PMID: 35964613; PMCID: PMC9605880.
37. Khalid K, Saeed U, Aljuaid M, Ali MI, Anjum A, Waheed Y. Immunoinformatic Approach to Conceive a Next Generation Multi-Epitope Vaccine Against *Achromobacter xylosoxidans* Infections. *Front Med (Lausanne)*. 2022 Jul 11; 9:902611. doi: 10.3389/fmed.2022.902611. PMID: 35899213; PMCID: PMC9309517.
38. Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. *Lancet Gastroenterol Hepatol*. 2022 May;7(5):396-415. doi: 10.1016/S2468-1253(21)00472-6. Epub 2022 Feb 16. PMID: 35180382.
39. Saeed U, Piracha ZZ, Kwon H, Kim J, Kalsoom F, Chwae YJ, Park S, Shin HJ, Lee HW, Lim JH, Kim K. The HBV Core Protein and Core Particle Both Bind to the PPIase Par14 and Par17 to Enhance Their Stabilities and HBV Replication. *Front Microbiol*. 2021 Dec 14; 12:795047. doi: 10.3389/fmicb.2021.795047. PMID: 34970249; PMCID: PMC8713550.
40. Saeed U, Uppal SR, Piracha ZZ, Uppal R. SARS-CoV-2 Spike Antibody Levels Trend among Sinopharm Vaccinated People. *Iran J Public Health*. 2021 Jul;50(7):1486-1487. doi: 10.18502/ijph.v50i7.6640. PMID: 34568189; PMCID: PMC8426791.



41. Saeed U, Kim J, Piracha ZZ, Kwon H, Jung J, Chwae YJ, Park S, Shin HJ, Kim K. Parvulin 14 and Parvulin 17 Bind to HBx and cccDNA and Upregulate Hepatitis B Virus Replication from cccDNA to Virion in an HBx-Dependent Manner. *J Virol*. 2019 Mar 5;93(6):e01840-18. doi: 10.1128/JVI.01840-18. PMID: 30567987; PMCID: PMC6401437.
42. Piracha ZZ, Kwon H, Saeed U, Kim J, Jung J, Chwae YJ, Park S, Shin HJ, Kim K. Sirtuin 2 Isoform 1 Enhances Hepatitis B Virus RNA Transcription and DNA Synthesis through the AKT/GSK-3 β / β -Catenin Signaling Pathway. *J Virol*. 2018 Oct 12;92(21):e00955-18. doi: 10.1128/JVI.00955-18. PMID: 30111572; PMCID: PMC6189494.
43. Saeed U, Waheed Y, Ashraf M, Waheed U, Anjum S, Afzal MS. Estimation of Hepatitis B Virus, Hepatitis C Virus, and Different Clinical Parameters in the Thalassemic Population of Capital Twin Cities of Pakistan. *Virology (Auckl)*. 2015 Nov 5; 6:11-6. doi: 10.4137/VRT.S31744. PMID: 26568681; PMCID: PMC4636113.
44. Waheed Y, Saeed U, Anjum S, Afzal MS, Ashraf M. Development of Global Consensus Sequence and Analysis of Highly Conserved Domains of the HCV NS5B Prote in. *Hepat Mon*. 2012 Sep;12(9):e6142. doi: 10.5812/hepatmon.6142. Epub 2012 Sep 25. PMID: 23087757; PMCID: PMC3475062.
45. Safi SZ, Waheed Y, Sadat J, Solat-UI-Islam, Salahuddin S, Saeed U, Ashraf M. Molecular study of HCV detection, genotypes and their routes of transmission in North West Frontier Province, Pakistan. *Asian Pac J Trop Biomed*. 2012 Jul;2(7):532-6. doi: 10.1016/S2221-1691(12)60091-4. PMID: 23569965; PMCID: PMC3609335.
46. Saeed U, Piracha ZZ, Alrokayan S, Hussain T, Almajhdi FN, Waheed Y. Immunoinformatics and Evaluation of Peptide Vaccines Derived from Global Hepatitis B Viral HBx and HBc Proteins Critical for Covalently Closed Circular DNA Integrity. *Microorganisms*. 2023; 11:2826. <https://doi.org/10.3390/microorganisms11122826>
47. Insaf S, Tariq P, Abbasi S, Usman M, Rana F, Noor G, Waheed N, Najmi W, Crisis F. Averted: A World United Against the Menace of Multiple Drug-Resistant Superbugs -Pioneering anti-AMR Vaccines, RNA interference, Nanomedicine, CRISPR-based antimicrobials, Bacteriophage Therapies, and Clinical Artificial Intelligence Strategies to Safeguard Global Antimicrobial Arsenal. *Front. Microbiol. Sec. Antimicrobials, Resistance and Chemotherapy*. 2023;14. doi: 10.3389/fmicb.2023.1270018.