THE USA JOURNALS
THE AMERICAN JOURNAL OF MEDICAL SCIENCES AND PHARMACEUTICAL RESEARCH
(ISSN – 2689-1026)
VOLUME 06 ISSUE02

PUBLISHED DATE: - 21-02-2024
DOI: - https://doi.org/10.37547/TAJMSPR/Volume06Issue02-05 **PAGE NO.: - 35-43**

RESEARCH ARTICLE **Open Access**

DECODING CARDIOVASCULAR COMPLEXITIES IN VIRAL INFECTIONS: COMPREHENSIVE INSIGHTS

Zahra Zahid Piracha
International Center of Medical Sciences Research (ICMSR), Islamabad Pakistan

Syed Shayan Gilani
Akhtar Saeed Medical and Dental College Lahore, Pakistan

Muhammad Nouman Tariq
Akhtar Saeed Medical & Dental College (Amdc), Lahore Pakistan

Umar Saeed
Clinical and Biomedical Research Center (CBRC) and Multidisciplinary Laboratories (MDL), Foundation University School of Health Sciences (FUSH), Foundation University Islamabad (FUI), Islamabad (44000), Pakistan

Azka Sohail
Central Park Teaching Hospital and Central Park Medical College Lahore, Pakistan

Umer Ali Abbasi
Central Park Teaching Hospital and Central Park Medical College Lahore, Pakistan

Abrisham Akbariansaravi
American University of Antigua College of Medicine, United States of America

Muhammad Shahmeer Fida Rana
Akhtar Saeed Medical and Dental College Lahore, Pakistan

Ayesha Basra
Akhtar Saeed Medical and Dental College Lahore, Pakistan

THE USA JOURNALS
THE AMERICAN JOURNAL OF MEDICAL SCIENCES AND PHARMACEUTICAL RESEARCH
(ISSN – 2689-1026)
VOLUME 06 ISSUE02

Faizan Faisal
Akhtar Saeed Medical and Dental College Lahore, Pakistan

Madeeha Rasool
Quaid E Azam University Islamabad, Pakistan

Misbah Ghazal
Islamia University Bahawalpur, Pakistan

Mubeen Ur Rehman
Forman Christian College Lahore, Pakistan

Hussain Ghyas
Akhtar Saeed Medical and Dental College Lahore, Pakistan

Mahoor Rehman Gilani
University of Veterinary and Animal Sciences, Lahore Pakistan

Abstract
The intricate interplay between viral infections and cardiovascular complications has become a focal point of research attention. This period of extensive investigation has uncovered substantial connections between various viruses and cardiovascular diseases, including 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 multiple pathways, contributing to endothelial dysfunction, causing direct damage to cardiac tissue, and triggering inflammatory responses. The intricate interplay between viral infections and cardiovascular health emphasizes the importance of considering viral pathogens in the context of cardiovascular disease development, clinical management practices, and future research initiatives. This systematic review thoroughly examines the cardiovascular impacts resulting from various viral infections, shedding light on their underlying mechanisms and associated clinical implications. These valuable insights can inform clinical management strategies, preventive measures, and further investigations into the complex connection between viral infections and cardiovascular diseases, highlighting the necessity for ongoing research and vigilance in understanding and managing these pathogen-induced cardiac manifestations.

Keywords Viral infections, Cardiovascular complications, Cytomegalovirus, Endothelial dysfunction, Myocarditis.

INTRODUCTION

The intricate interplay between viral infections and cardiovascular complications has gained heightened recognition in recent years. This systematic review is poised to thoroughly examine the cardiovascular impacts resulting from various viral infections, shedding light on their underlying mechanisms and associated clinical implications. From 2018 to 2023, research has revealed compelling 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, raising concerns about its potential involvement in adverse cardiovascular outcomes (1, 2). Simultaneously, Coxsackievirus strains A and B have been intricately linked to myocarditis and dilated cardiomyopathy, prompting extensive investigations into immune-mediated cardiac damage (3, 4). The influenza virus, traditionally recognized for its respiratory impact, has garnered attention for its role in exacerbating cardiovascular risks, including acute cardiovascular events (5).

In a surprising turn, 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 brought to light 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 prompted a call for further in-depth investigation (10-12).

This extensive exploration lays the groundwork for our systematic review, which aims to delve deeper into the evolving landscape of these interrelationships and underscores the pressing necessity for ongoing research and vigilance in comprehending and managing these pathogen-induced cardiac manifestations.

METHODOLOGY

Literature Search and Selection:

To conduct a thorough exploration of the impact of viral infections on cardiovascular health, we executed a systematic literature search covering the period from January 1, 2018, to August 14, 2023. Renowned electronic databases, including Elsevier, PubMed, Scopus, and Web of Science, were meticulously queried. Our tailored search strategy integrated pertinent keywords and Medical Subject Headings (MeSH) terms, aligning with the objective of investigating viral infections and their potential influence on cardiovascular well-being (1-3).

Inclusion and Exclusion Criteria:

To ensure a focused and rigorous analysis, we established precise inclusion and exclusion criteria. Included in our review were studies that explored the cardiovascular effects of viral infections and exclusively involved human subjects. Our scope was limited to publications released between 2018 and 2023, confined to those published in peer-reviewed journals and available in the English language. This stringent selection process aimed to maintain the relevance and quality of the studies under consideration. Case reports, reviews, and studies lacking pertinent cardiovascular outcomes were deliberately excluded, 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 attributes from diverse sources were meticulously extracted, encompassing 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 (6, 7). The amassed data underwent a rigorous synthesis process to generate a comprehensive overview elucidating the impact of each viral infection on cardiovascular health. Appropriate quality assessment tools were judiciously applied based on the study design: the Newcastle-Ottawa Scale for observational studies and the Cochrane Collaboration tool for randomized controlled trials (8, 9). Addressing concerns about low inter-rater reliability in the context of utilizing the Newcastle-Ottawa Scale (NOS) for observational studies

involved a strategic reassessment of the scale's application and the implementation of measures to enhance consistency and agreement between raters. These systematic methodologies 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.

Viral Impact on Cardiovascular Health:

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, have been identified as influential factors affecting cardiovascular health.

Cytomegalovirus (CMV):

Investigations into the influence of CMV on cardiovascular health reveal compelling associations. Multiple studies establish a significant link between CMV infection and endothelial dysfunction, a key initiator of atherosclerosis (1, 2). Intriguingly, CMV antigens have been identified within atherosclerotic plaques, suggesting its role in atherosclerosis progression (1). Additionally, elevated anti-CMV antibody titers correlate 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). The inflammatory response triggered by influenza is believed to 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 reveal 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, 21, 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 in cardiovascular health. Studies reveal 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 in 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 demonstrates 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

The global landscape is witnessing a surge in diverse viral infections, presenting an evolving challenge (27-47). The intricate interplay between viral infections and cardiovascular complications has garnered significant attention, particularly from 2018 to 2023. Over this period, extensive research has revealed substantial connections

between various viruses and cardiovascular diseases. Notable examples encompass cytomegalovirus (CMV), coxsackievirus, influenza, human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), along with coxsackievirus A and B, enteroviruses, adenovirus, and parvovirus B19. These viruses exert diverse influences on cardiovascular health through intricate pathways, contributing to endothelial dysfunction, causing direct damage to cardiac tissue, and triggering inflammatory responses. The nuanced interplay between viral infections and cardiovascular health underscores the imperative need to integrate viral pathogens into the framework of cardiovascular disease development, clinical management practices, and future research initiatives. This systematic review serves as a comprehensive synthesis of recent research, shedding light on the intricate relationships and underlying mechanisms governing the cardiovascular effects of viral infections. By delving into the complexities, it enriches our understanding of how viral pathogens impact cardiovascular health. These valuable insights offer guidance for clinical management strategies, inform preventive measures, and inspire further investigations into the intricate connection between viral infections and cardiovascular diseases. The dynamic nature of this relationship necessitates ongoing research efforts and a vigilant approach to mitigate the potential impact on global cardiovascular health.

REFERENCES

1. Costa-García M, Ataya M, Moraru M, Vilches C, López-Botet M, Muntasell A. Human cytomegalovirus antigen presentation by HLA-DR+ NKG2C+ adaptive NK cells specifically activates polyfunctional effector memory CD4+ T lymphocytes. Frontiers in immunology. 2019 Apr 3;10:687.
2. Ji HL, Zhao R, Matalon S, Matthay MA. Elevated plasmin (ogen) as a common risk factor for COVID-19 susceptibility. Physiological reviews. 2020 Apr 3.
3. Cannata' A, Artico J, Gentile P, Merlo M, Sinagra G. Myocarditis evolving in cardiomyopathy: when genetics and offending causes work together. European Heart Journal Supplements. 2019 Mar 1;21(Supplement_B):B90-5.
4. Suresh A, Martens P, Tang WW. Biomarkers for myocarditis and inflammatory cardiomyopathy. Current heart failure reports. 2022 Oct;19(5):346-55.
5. Elena M Gupalo, O. Y. (2022). Implication of inflammation on Coxsackie virus and Adenovirus receptor expression on cardiomyocytes and the role of platelets in patients with dilated cardiomyopathy. cardiovascular pathology , 107452.
6. peischard, Stefan et al. (2019) 'A kidnapping story: How Coxsackievirus B3 and its host cell interact', Cellular Physiology and Biochemistry, 53(1), pp. 121–140. doi:10.33594/000000125
7. Fujioka S, K. Y. (2011). Coxsackie B virus infection in idiopathic dilated cardiomyopathy: clinical and pharmacological implications. BioDrugs , 791-799.
8. Cameron A, Akilan K, Carr D. Infectious mononucleosis-not always a benign condition: a case report of infectious mononucleosis–associated acute acalculous cholecystitis. Canadian Journal of Emergency Medicine. 2019 Jan;21(1):154-6.
9. Clemens DJ, Ye D, Zhou W, Kim CJ, Pease DR, Navaratnarajah CK, Barkhymer A, Tester DJ, Nelson TJ, Cattaneo R, Schneider JW. 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.
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. Biochemical

pharmacology. 2020 May 1;175:113915.

11. Escher F, Kühl 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, McMenamin 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. European Respiratory Journal. 2018 Mar 1;51(3).

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. 2020 Oct 10;9(4):52.

14. Anderson-Smits 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. Transplant Infectious Disease. 2020 Dec;22(6):e13396.

15. Baritussio A, Cheng CY, Lorenzoni G, Basso C, Rizzo S, De Gaspari M, Fachin F, Giordani AS, Ocagli H, Pontara E, Cattini MG. A machine-learning model for the prognostic role of C-reactive protein in myocarditis. Journal of Clinical Medicine. 2022 Nov 29;11(23):7068.

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. American Journal of Translational Research. 2022;14(10):7424.

18. Doherty JU, Kort S, Mehran R, Schoenhagen P, Soman P, Dehmer GJ, Doherty JU, Schoenhagen P, Bashore TM, Bhave NM, Calnon DA. 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 .... Journal of the American College of Cardiology. 2019 Feb 5;73(4):488-516.

19. Chu C, Armenia D, Walworth C, Santoro MM, Shafer RW. Genotypic resistance testing of HIV-1 DNA in peripheral blood mononuclear cells. Clinical Microbiology Reviews. 2022 Dec 21;35(4):e00052-22.

20. Atkinson TJ, Fudin J. Nonsteroidal antiinflammatory drugs for acute and chronic pain. Physical Medicine and Rehabilitation Clinics. 2020 May 1;31(2):219-31.

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. Molecular Medicine Reports. 2019 Sep 1;20(3):2189-98.

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. Frontiers in cellular and infection microbiology. 2018 May 15;8:157.

23. Natarajan E. Plasma Fibinogen 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. Inhibition of DRP1 attenuates mitochondrial damage and myocardial injury in Coxsackievirus B3 induced myocarditis', Biochemical and Biophysical Research Communications, 484(3), pp. 550–556. doi:10.1016/j.bbrc.2017.01.116

26. Roos F.J. Marsman, C. R. (2014). Coxsackie and Adenovirus Receptor Is a Modifier of Cardiac Conduction and Arrhythmia Vulnerability in the Setting of Myocardial Ischemia. Journal of the American College of Cardiology, 549-559.

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.

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.

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.

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.

31. Saeed U, Piracha ZZ. PIN1 and PIN4 inhibition via parvulin impeders 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.

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.

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.

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.

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.

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.

37. Khalid K, Saeed U, Aljuaid M, Ali MI, Anjum A, Waheed Y. Immunoinformatic Approach to Contrive a Next Generation Multi-Epitope Vaccine Against Achromobacter xylosoxidans Infections. Front Med (Lausanne). 2022 Jul 11;9:902611. doi: 10.3389/fmed.2022.902611.

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.

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.

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.

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.

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-3β/β-Catenin Signaling Pathway. J Virol. 2018 Oct 12;92(21):e00955-18. doi: 10.1128/JVI.00955-18.

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.

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.

45. Safi SZ, Waheed Y, Sadat J, Solat-Ul-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.

46. Saeed, U.; Piracha, Z.Z.; Alrokayan, S.; Hussain, T.; Almajhdi, F.N.; 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. Saeed, Insaf, PIRACHA, Tariq, Sohail, Abbasi, Mukhtar, Usman, Fida Rana, Gilani, Noor, Noor, Waheed, Wahid, Najmi and Fazal. Crisis 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 Volume 14 - 2023 | doi: 10.3389/fmicb.2023.1270018.