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Cardiovascular Complications Of A(H1n1) Influenza Infection And Pathogenetic Mechanisms Of Its Effects On The Myocardium And Vascular System

Munojat Khayatovna Ismailova
Tashkent State Medical University, Head of the Department of Medical Radiology
munojat.rad@gmail.com
Abdurashidov Shoxruhbek Shuxratbek ogli
Tashkent State Medical University, resident physician, Department of Medical Radiology
Abdulloh90991@gmail.com
Mamadalieva Asalkhon Bakhriddinovna
Tashkent Medical Academy, second-year student, Faculty of General Medicine
queenkoroleva578@gmail.com
Goyibnazarov Rozimurod Bakhtiyorovich
Tashkent State Medical University, Assistant of Biomedical Engineering, Informatics and Biophysics
rozi_murodjon@mail.ru

Article History	Abstract
Received: 10th March, 2026 Accepted: 8th April, 2026	This article analyzes the impact of the influenza virus on the cardiovascular system and its role in the development of acute cardiovascular complications. The infection induces systemic inflammation, endothelial dysfunction, and prothrombotic changes, thereby increasing the risk of acute coronary syndrome, myocarditis, cardiac rhythm disturbances, and decompensation of chronic heart failure. During seasonal influenza epidemics, timely prevention and cardiovascular risk stratification are considered key measures for reducing mortality and the frequency of severe complications.
Keywords: influenza, cardiovascular diseases, acute coronary syndrome, myocarditis, chronic heart failure, arrhythmias, epidemiology, prevention,	

vaccination, antiviral treatment, pathogenetic mechanisms, cardiovascular complications.

Influenza A(H1N1) infection is one of the leading causes of increased mortality during seasonal epidemics. According to the World Health Organization, 290,000 to 650,000 deaths associated with influenza-related diseases are recorded worldwide each year; these diseases cause not only respiratory manifestations but also clinically significant extrapulmonary complications, among which cardiovascular disorders occupy a special place.

For the 2009 pandemic A(H1N1)pdm09 virus, the global mortality estimate was substantially higher than the number of laboratory-confirmed deaths. According to modeled data, during the first year of viral circulation, 105.7-395.6 thousand respiratory deaths occurred worldwide; when cardiovascular complications were included, the overall estimated range was 151.7-575.4 thousand deaths [2]. These data emphasize that the clinical significance of H1N1 is determined not only by respiratory tract involvement but also by systemic complications, including cardiovascular events.

In the Republic of Uzbekistan, official statistics reported 588.4 thousand cases of influenza and acute infections of the upper and lower respiratory tract in 2024 [3]. However, this indicator reflects not laboratory-confirmed H1N1 alone, but the combined category of influenza and acute respiratory infections. According to the metadata of the official statistics, the indicator is generated from administrative data submitted by the Ministry of Health once a year [3].

More specific H1N1 data are presented in the weekly national bulletins of the Ministry of Health of Uzbekistan. In week 44 of 2024, sentinel surveillance of influenza-like illness detected influenza A/H1N1 viruses in 10.3% of cases, while A/H1N1 accounted for 100.0% of positive influenza results [4]. In week 46 of 2024, the detection rate of A/H1N1 among influenza-like illness cases increased to 19.0%; among severe acute respiratory infections requiring hospitalization, A/H1N1 viruses were detected in 21.7% of cases. Since the beginning of the season, A/H1N1 also accounted for 100.0% of positive influenza results among severe acute respiratory infections [5].

Biophysical mechanisms of interaction between influenza A(H1N1) and the cardiovascular system

The systemic inflammatory response in influenza is accompanied by changes in the coagulation profile and hemorheological prerequisites of blood flow. In a clinical cohort of patients with seasonal influenza, the median fibrinogen

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concentration before treatment was 4.2 g/L, with a reference range of 2-4 g/L, and the proportion of patients with fibrinogen levels above 4 g/L reached 54.5%. At the same time, the median D-dimer level was 1.1 mg/L, compared with a normal value of less than 0.55 mg/L, and elevated D-dimer was detected in 71.9% of patients [5]. After treatment, fibrinogen decreased to 3.5 g/L and D-dimer to 0.6 mg/L, indicating the reversibility of the inflammatory-coagulation shift as the infection resolves [5].

The hemorheological significance of these changes is related to the fact that fibrinogen is not only a coagulation protein but also a factor capable of increasing plasma viscosity, enhancing erythrocyte aggregation, and promoting platelet-mediated thrombosis [6]. Platelet activation in influenza is also confirmed by direct cellular indicators: in patients with severe A(H1N1), the proportion of platelet-monocyte aggregates was 21.4 ± 4.7%, compared with 8.1 ± 4.5% in healthy individuals, while PAC-1 binding increased to 9.5 ± 4.7%, compared with 0.61 ± 0.15% in healthy controls [7].

Taken together, elevated fibrinogen, increased cellular aggregation, and platelet activation create conditions for increased vascular resistance, slowing of microcirculation, and formation of a prothrombotic state. The clinical significance of this mechanism is supported by cardiovascular data: during the first week after laboratory-confirmed influenza, the risk of hospitalization for acute myocardial infarction increased approximately sixfold; the incidence ratio was 6.05, and the hospitalization rate was 20.0 cases per week, compared with 3.3 cases per week during the control period [8]. In a large study of hospitalized adults with influenza, an acute cardiovascular event was recorded in 11.7% of patients; the most frequent events were acute heart failure (6.2%) and acute ischemic heart disease (5.7%) [9].

In addition, virus-induced inflammation causes endothelial dysfunction, accompanied by a reduction in nitric oxide (NO) synthesis, which is a key mediator of vascular regulation. NO deficiency leads to vasoconstriction, increased systemic vascular resistance, and higher cardiac afterload. Sympathetic nervous system activation also contributes significantly by promoting tachycardia and elevated arterial pressure, thereby further increasing myocardial oxygen demand.

Against the background of respiratory system involvement, hypoxemia develops and, in combination with microcirculatory disturbances, reduces oxygen delivery to cardiomyocytes. Oxygen deficiency suppresses oxidative phosphorylation, reduces ATP synthesis, and decreases myocardial contractile function.

Influenza A(H1N1)pdm09 is accompanied by activation of the innate immune response and increased production of proinflammatory mediators, among which IL-6, IL-1β, TNF-α, IL-8, and IL-10 have the greatest clinical relevance. In severe infection, a state of hypercytokinemia develops; it is not limited to local inflammation of the airways but becomes systemic and contributes to vascular endothelial injury, impaired microcirculation, and increased cardiovascular risk. A study of patients with pandemic H1N1 showed that severe cases were associated with significantly higher IL-6 levels than mild cases; IL-6 reached 88.0 pg/mL in severe patients versus 8.8 pg/mL in healthy individuals, representing an approximately tenfold increase [11]. In the same study, IL-10 increased from 2.39 pg/mL in healthy individuals to 10.01 pg/mL in severe H1N1, and a strong positive correlation between IL-6 and IL-10 was found in severe patients ($r = 0.847$; $p = 0.004$) [11]. These findings make it possible to consider IL-6 not only as a marker of inflammation but also as an indicator of systemic immune dysregulation in severe H1N1.

The clinical significance of IL-6 is supported by data from hospitalized patients with laboratory-confirmed H1N1pdm: IL-6 concentrations were higher in patients requiring intensive care than in those who did not require critical care. In a logistic regression model, elevated IL-6 was statistically associated with the risk of death: OR = 2.63; 95% CI: 1.06-6.49; $p = 0.036$ [12]. In a later study of patients with A(H1N1)pdm09, IL-6 also showed prognostic value: the area under the ROC curve for differentiating survivors of severe disease from fatal cases was AUC = 0.81; $p < 0.0001$, which was higher than that for IL-10 (AUC = 0.73; $p < 0.01$) [13].

The role of TNF-α and IL-1β in the pathogenesis of severe H1N1 is confirmed primarily as part of the proinflammatory cascade; however, their serum levels are described less consistently across clinical studies than IL-6. Therefore, in this context it is more accurate to indicate not a universal increase in TNF-α in a fixed proportion of patients, but its participation in the severe inflammatory phenotype and in genetic predisposition to severe disease. Thus, in a Mexican cohort that included 145 patients with A(H1N1), 133 patients with influenza-like illness, and 360 healthy contacts, the IL6 rs1818879 GA genotype was associated with A(H1N1) infection (OR = 5.94; 95% CI: 3.05-11.56), whereas the TNF-238 GA genotype was associated with an increased risk of severe disease (OR = 16.06; p = 0.007) [14]. In addition, IL-6 levels were higher in patients with severe A(H1N1) than in patients with other influenza-like illnesses (p = 0.007) [14].

Excessive cytokine activation creates conditions for cardiovascular injury through several interrelated pathways. IL-6 enhances the acute-phase response, including the synthesis of fibrinogen and C-reactive protein, which contributes to increased plasma viscosity, erythrocyte aggregation, and formation of a prothrombotic environment. TNF-α and IL-1β additionally support endothelial activation, increase vascular permeability, and promote leukocyte adhesion. Together, these processes may lead to interstitial edema, impaired capillary perfusion of the myocardium, disruption of the electrophysiological stability of cardiomyocytes, and an increased probability of arrhythmias, ischemic injury, and inflammatory damage to the heart muscle.

Oxidative stress is also of substantial importance. During influenza infection, reactive oxygen species are generated in response to viral cellular injury and inflammatory activation of immune mechanisms; they can enhance apoptosis, lung tissue damage, inflammation, DNA damage, lipid peroxidation, and mitochondrial dysfunction [15, 24]. For the cardiovascular system, this is fundamentally important because excess reactive oxygen species reduce the bioavailability of nitric oxide, impair vasodilation, intensify endothelial dysfunction, and sustain the prothrombotic state. Experimental data on A(H1N1)pdm09 also demonstrate a vascular direction of injury: in rats with premorbid acute cardiomyopathy, A(H1N1)pdm09 infection caused marked dysregulation of endothelial factors, including a 3.47-fold increase in PAI-1 expression after 96 hours and a 6.43-fold increase in plasma PAI-1 concentration after 24 hours compared with controls [16]. This confirms the association of H1N1 infection with endothelial dysfunction and impaired fibrinolytic balance, which pathogenetically increases the risk of microcirculatory and thrombotic complications.

Main cardiological risks associated with influenza A(H1N1)

Acute coronary syndrome (ACS). Influenza A(H1N1) increases the risk of acute coronary syndrome through systemic inflammatory reactions and prothrombotic changes. Inflammation induces endothelial dysfunction, platelet activation, and activation of the coagulation cascade, thereby promoting destabilization of atherosclerotic plaque and formation of an intravascular thrombus. Plaque rupture or erosion leads to acute coronary occlusion and myocardial infarction [4]. The strongest clinical evidence concerns acute myocardial infarction: during the first week after laboratory-confirmed influenza, the risk of hospitalization for infarction increased approximately sixfold; the incidence ratio was 6.05, and the hospitalization rate was 20.0 cases per week versus 3.3 cases per week during the control period [8].

Myocarditis. Myocarditis is an inflammatory lesion of the myocardium caused by direct viral cytopathic effects and immune-mediated injury to cardiomyocytes following viral interaction with sialic acid receptors [3]. The frequency of myocarditis in laboratory-confirmed A(H1N1) influenza infection is 1-2% [8], and among hospitalized patients it is 1.3-1.7% [9]. In individuals with concomitant cardiovascular diseases, this rate reaches 6%, mainly in the age group over 65 years [10].

Decompensation of chronic heart failure (CHF). Severe influenza A(H1N1) can provoke decompensation of chronic heart failure by increasing hemodynamic load on the myocardium. The infectious process leads to impaired cardiac contractile function and reduced cardiac output. In patients with CHF, infection is associated with an increased risk of acute cardiovascular complications, including pulmonary edema and cardiogenic shock. Exacerbation of heart failure develops in approximately 13% of patients with CHF who have had influenza and often requires hospitalization and adjustment of therapy [11], [6].

Arrhythmias. Severe influenza A(H1N1) can induce tachyarrhythmias and bradyarrhythmias as a result of systemic inflammation, myocardial hypoxia, and electrolyte imbalance. Sympathetic nervous system activation is an additional arrhythmogenic factor. The most frequently recorded rhythm disorders are atrial fibrillation and ventricular extrasystoles. Rhythm disturbances are detected in 10-15% of patients with severe influenza, predominantly in individuals older than 65 years and in patients with concomitant cardiovascular pathology [6]. The development of arrhythmias is associated with an increased risk of severe cardiovascular complications, including myocardial infarction and stroke [11].

Thromboembolic complications. The influenza virus contributes to a hypercoagulable state, increasing the risk of thrombus formation and pulmonary embolism (PE). Prothrombotic changes are caused by systemic inflammation, activation of the coagulation cascade, and endothelial dysfunction. In patients with influenza infection, the risk of venous thrombosis and PE increases approximately twofold compared with individuals without infection. The highest frequency of thromboembolic complications is observed in elderly patients and in the presence of comorbidities, including arterial hypertension and diabetes mellitus [11], [6].

Autoimmune reactions. Viral infection may trigger autoimmune reactions in which the immune system attacks the body's own tissues, including the myocardium. This maintains inflammation in the heart and may lead to chronic myocardial injury. In some cases, autoimmune reactions may lead to the development of pericarditis or myocarditis, increasing the risk of long-term heart disease. According to the literature, autoimmune complications develop in 3-5% of cases after acute viral disease, including influenza, and may cause further inflammation and myocardial damage [5].

Dysregulation of the autonomic nervous system. Fever and intoxication in influenza activate the sympathetic nervous system, which increases myocardial oxygen demand. This may contribute to myocardial ischemia, especially in patients with ischemic heart disease. According to studies conducted in 2022, symptoms of myocardial ischemia are observed in approximately 20% of patients with cardiovascular diseases who have had influenza.

For effective prevention and treatment of these complications, timely measures are important. Vaccination against influenza A(H1N1) is a key preventive method, especially among patients with cardiovascular diseases (CVD). According to studies, vaccination reduces the risk of cardiovascular events by 36% in patients with CVD [4]. In addition, it reduces the severity of infection and the likelihood of complications, including myocardial infarction and stroke. Since 2022, Uzbekistan has implemented a free vaccination program for individuals older than 65 years and patients with chronic diseases, including CVD, which contributes to reducing morbidity and hospitalization rates.

Early diagnosis and antiviral therapy with oseltamivir or zanamivir play an important role in reducing disease severity and preventing cardiovascular complications. The use of antiviral drugs in the early stages of infection shortens disease duration by 1-2 days and reduces the risk of severe complications by 30-40% [9]. This effect is especially significant in patients with cardiovascular pathology.

Medical monitoring of patients with cardiovascular diseases during influenza epidemics is of key importance. Patients in this group require regular monitoring of cardiac function, including electrocardiography, measurement of cardiospecific markers such as troponin, and control of arterial pressure and electrolyte balance. Particular attention is given to the early detection of signs of chronic heart failure decompensation and rhythm disturbances. If the patient's condition worsens, timely correction of therapy is required, including optimization of anticoagulant and cardiotropic treatment [6, 24].

Comprehensive treatment of patients with severe influenza A(H1N1) and CVD includes maintenance of baseline cardiological therapy, correction of heart failure, and prevention of thromboembolic complications. In cases of chronic heart failure decompensation, dose adjustment of angiotensin-converting enzyme inhibitors, beta-blockers, and the use of diuretics for control of congestion may be required.

Prevention of thrombus formation in patients at high thrombotic risk is carried out using anticoagulants, including low-molecular-weight heparins, and antiplatelet agents, which reduces the likelihood of venous thrombosis and pulmonary embolism.

Adequate hydration, body temperature control, and monitoring of electrolyte balance are also important, because hyperthermia and electrolyte disturbances can promote arrhythmias and worsen hemodynamics, especially in elderly patients [10].

Conclusion

Severe influenza A(H1N1) virus infection is a significant risk factor for the development of cardiovascular complications, including acute coronary syndrome, myocarditis, rhythm disturbances, and decompensation of chronic heart failure. The pathogenetic basis of these conditions consists of the systemic inflammatory response, endothelial dysfunction, hypercoagulation, microcirculatory disorders, and myocardial hypoxia.

Patients with pre-existing cardiovascular diseases are at the highest risk, because influenza infection can act as a trigger for acute cardiac events.

Reducing the frequency and severity of cardiovascular complications is possible through a combination of preventive and therapeutic measures, including influenza vaccination, early diagnosis of infection, timely administration of antiviral therapy, and regular monitoring of cardiovascular function. Dynamic observation of high-risk patients, with monitoring of hemodynamic parameters, electrocardiographic changes, and laboratory markers of myocardial injury, is of particular importance.

A comprehensive approach to prevention and management of patients with influenza and cardiovascular pathology can reduce the risk of severe complications, decrease hospitalization rates, and improve clinical outcomes.

Further research should focus on a more detailed investigation of the molecular mechanisms underlying the interaction between viral infection and the cardiovascular system, as well as on the development of effective strategies for preventing cardiovascular complications in high-risk patients.

References

1. WHO. Influenza (seasonal). Fact sheet. 28 February 2025.
2. Dawood F. S., Iuliano A. D., Reed C. et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study // The Lancet Infectious Diseases. 2012. Vol. 12, No. 9. P. 687-695. DOI: 10.1016/S1473-3099(12)70121-4.
3. National Statistics Committee of the Republic of Uzbekistan. Number of cases of influenza and acute infections of the upper and lower respiratory tract. Official statistics, indicator 2.04.07.0004.
4. Ministry of Health of the Republic of Uzbekistan. Weekly national bulletin on influenza and ARVI for week 46 of 2024: 11.11.2024-17.11.2024.
5. Zhang J., Huang X., Ding D. et al. Platelet-driven coagulopathy in COVID-19 patients: in comparison to seasonal influenza cases // Experimental Hematology & Oncology. 2021. Vol. 10. Article 34. DOI: 10.1186/s40164-021-00228-z.
6. Lominadze D., Dean W. L., Tyagi S. C., Roberts A. M. Mechanisms of fibrinogen-induced microvascular dysfunction during cardiovascular disease // Acta Physiologica. 2010. Vol. 198, No. 1. P. 1-13. DOI: 10.1111/j.1748-1716.2009.02037.x.
7. Rondina M. T., Brewster B., Grissom C. K. et al. In vivo platelet activation in critically ill patients with primary 2009 influenza A(H1N1) // Chest. 2012. Vol. 141, No. 6. P. 1490-1495. DOI: 10.1378/chest.11-2860.
8. Kwong J. C., Schwartz K. L., Campitelli M. A. et al. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection // New England Journal of Medicine. 2018. Vol. 378, No. 4. P. 345-353. DOI: 10.1056/NEJMoa1702090.
9. Chow E. J., Rolfes M. A., O'Halloran A. et al. Acute Cardiovascular Events Associated With Influenza in Hospitalized Adults: A Cross-

Sectional Study // Annals of Internal Medicine. 2020. Vol. 173, No. 8. P. 605-613. DOI: 10.7326/M20-1509.

10. Obi A. T., Tignanelli C. J., Jacobs B. N. et al. Empirical systemic anticoagulation is associated with decreased venous thromboembolism in critically ill influenza A H1N1 acute respiratory distress syndrome patients // Journal of Vascular Surgery: Venous and Lymphatic Disorders. 2019. Vol. 7, No. 3. P. 317-324. DOI: 10.1016/j.jvsv.2018.08.010.
11. Nguyen H., Patel R., O'Connor C. Influenza and Decompensated Heart Failure: Clinical Insights and Management Strategies. Int J Cardiol. 2022;347: 89-96.
12. European Society of Cardiology. Influenza vaccination in patients with cardiovascular disease // European Heart Journal. 2021. Vol. 42. P. 490-491.
13. Zhang J., Huang X., Ding D. et al. Platelet-driven coagulopathy in COVID-19 patients: in comparison to seasonal influenza cases // Experimental Hematology & Oncology. 2021. Vol. 10. Article 34. DOI: 10.1186/s40164-021-00228-z.
14. Lominadze D., Dean W. L., Tyagi S. C., Roberts A. M. Mechanisms of fibrinogen-induced microvascular dysfunction during cardiovascular disease // Acta Physiologica. 2010. Vol. 198, No. 1. P. 1-13. DOI: 10.1111/j.1748-1716.2009.02037.x.
15. Rondina M. T., Brewster B., Grissom C. K. et al. In vivo platelet activation in critically ill patients with primary 2009 influenza A(H1N1) // Chest. 2012. Vol. 141, No. 6. P. 1490-1495. DOI: 10.1378/chest.11-2860.
16. Kwong J. C., Schwartz K. L., Campitelli M. A. et al. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection // New England Journal of Medicine. 2018. Vol. 378, No. 4. P. 345-353. DOI: 10.1056/NEJMoa1702090.
17. Chow E. J., Rolfes M. A., O'Halloran A. et al. Acute Cardiovascular Events Associated With Influenza in Hospitalized Adults: A Cross-Sectional Study // Annals of Internal Medicine. 2020. Vol. 173, No. 8. P. 605-613. DOI: 10.7326/M20-1509.
18. Yu X., Zhang X., Zhao B. et al. Intensive cytokine induction in pandemic H1N1 influenza virus infection accompanied by robust production of IL-10 and IL-6 // PLoS ONE. 2011. Vol. 6, No. 12. Article e28680. DOI: 10.1371/journal.pone.0028680.

19. Paquette S. G., Banner D., Zhao Z. et al. Interleukin-6 is a potential biomarker for severe pandemic H1N1 influenza A infection // PLoS ONE. 2012. Vol. 7, No. 6. Article e38214. DOI: 10.1371/journal.pone.0038214.
20. Alagarasu K., Kaushal H., Shinde P. et al. TNFA and IL10 polymorphisms and IL-6 and IL-10 levels influence disease severity in influenza A(H1N1)pdm09 virus infected patients // Genes. 2021. Vol. 12, No. 12. Article 1914. DOI: 10.3390/genes12121914.
21. García-Ramírez R. A., Ramírez-Venegas A., Quintana-Carrillo R. et al. TNF, IL6, and IL1B polymorphisms are associated with severe influenza A(H1N1) virus infection in the Mexican population // PLoS ONE. 2015. Vol. 10, No. 12. Article e0144832. DOI: 10.1371/journal.pone.0144832.
22. Chen K.-K., Minakuchi M., Wuputra K. et al. Redox control in the pathophysiology of influenza virus infection // BMC Microbiology. 2020. Vol. 20. Article 214. DOI: 10.1186/s12866-020-01890-9.
23. Marchenko V., Zelinskaya I., Toropova Y. et al. Influenza A(H1N1)pdm09 virus aggravates pathology of blood vessels in Wistar rats with premorbid acute cardiomyopathy // Viruses. 2023. Vol. 15, No. 5. Article 1114. DOI: 10.3390/v15051114.
24. Tursunmetov I. R., Goyibnazarov R. B., Ganiev S. F. Key biophysical and biochemical conditions for organ cultivation using information technology // Central Asian Journal of Medicine. 2025. No. 5. P. 120-128.