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Challenges in Influenza Control and Surveillance in the Republic of Kazakhstan

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ABSTRACT

The COVID-19 pandemic has significantly disrupted the circulation of influenza viruses in Kazakhstan, highlighting the vulnerabilities in the country's public health infrastructure. This review critically examines the challenges faced in infiltrating and controlling influenza in Kazakhstan, particularly in light of the shifting epidemiological landscape post-pandemic. Key issues include the decline in influenza cases during the pandemic, which complicates the assessment of influenza epidemiology, vaccine effectiveness, and planning of vaccination campaigns. Although part of the Global Influenza Hospital Surveillance Network (GIHSN), Kazakhstan's surveillance systems face data collection, coordination, and public awareness gaps. The review discusses the prevalence of various influenza strains, the impact of zoonotic infections, and the necessity for improved monitoring frameworks. Additionally, the historical context of infectious disease control in Kazakhstan is explored, emphasising the need for enhanced international collaboration and targeted public health strategies. The findings underscore the importance of vaccination and robust surveillance to mitigate the risks of seasonal and pandemic influenza, advocating for a comprehensive approach to safeguard public health in Kazakhstan.

***Keywords*-** Influenza, COVID-19, Kazakhstan, surveillance, public health, vaccination, zoonotic infections, epidemiology, Global Influenza Hospital Surveillance Network, public awareness, health infrastructure.

I. INTRODUCTION

The circulation of respiratory viruses, mainly the influenza virus, has been disrupted by the emergence of the COVID-19 pandemic and SARS-CoV-2 [1]. The emergence of SARS-CoV-2, the resulting COVID-19 pandemic, and the public health measures put in place to contain the spread of SARS-CoV-2 caused significant disruptions to the circulation of influenza and other respiratory viruses. Early in the COVID-19 pandemic, there was a drastic reduction in the circulation of seasonal influenza viruses, with most countries reporting a marked decline in influenza positivity rates [2]. Respiratory pathogens can inflict a considerable burden on public health; in 2018, before the COVID-19 pandemic, 6.1% of total deaths in the UK were attributable to respiratory

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infections. Though capable of causing substantial mortality, infection by respiratory pathogens can often result in differing severity among the population [3]. The high mortality rate was very concerning and attracted significant media attention, and the disease was dubbed "bird flu" [4]. Although influenza A viruses have caused pandemics for centuries, future pandemics cannot be predicted with our current understanding and resources. Concern about an H5N1 avian influenza pandemic has caused alarm since 1997, but there are many other possible routes to pandemic influenza [5]. A consistent globally negative correlation exists between influenza A/H3N2 and A/H1N1.

Meanwhile, interactions between influenza A (A/H3N2, A/H1N1) and B show significant differences across countries, primarily influenced by population-related factors [6]. The Global Influenza Hospital Surveillance Network (GIHSN) has since 2012 provided patient-level data on severe influenza-like illnesses from >100 participating clinical sites worldwide based on a core protocol and consistent case definitions [7]. Influenza is a leading cause of morbidity and mortality globally. Little is known about the actual burden and epidemiology of influenza in Africa. Nigeria has a sentinel surveillance system for influenza virus (IFV). Respiratory infections like influenza remain one of the leading causes of illness and death in people of all ages. Globally, influenza is estimated to cause 3–5 million severe illnesses and about half a million deaths annually, with children under the age of 5, adults over 65 years of age, pregnant women and those with co-morbidities being at higher risk for severe disease [8]. It remains uncertain whether influenza and other respiratory viruses will return to their typical circulation patterns or adapt to a new normality. Foreseeing when respiratory virus epidemics will occur is crucial in public health; for example, planning when to run influenza vaccination campaigns depends on the expected timing patterns of when the virus is spreading the most [9]. Viruses circulating among wild and domestic animal populations are potentially risky to animal and human health. Epizootic infections cause economic damage to agriculture and related industries every year. Zoonotic infections carry a high risk of pandemics, as seen in the historical examples from 1918 (H1N1), 2009-2010 (H1N1pdm 2009), and the recent SARS-CoV-2 pandemic [10]. In pre-revolutionary Kazakhstan, infectious disease control was episodic owing to limited resources and insufficient well-trained and experienced doctors, paramedics, and nurses. Despite the post-civil war complexities of rebuilding the economy, the Soviet Union has prioritised the prevention of epidemics [12]. Diagnosing acute respiratory infections (ARIs) is challenging due to the diversity of potential microbial causes [13]. Influenza is a seasonal, highly contagious infectious disease and one of the most essential respiratory tract infections from a public health point of view. Influenza outbreaks have a seasonal distribution and typically peak in the northern hemisphere between December and March. The World Health Organization (WHO) estimate that approximately 5–15% of the population will be infected each year, putting the annual global number of severe infections at 3–5 million. Therefore, influenza's medical and economic burden was estimated in elderly populations in the Czech Republic, Hungary, Kazakhstan, Poland, Romania, and Ukraine [14]. This review aims to critically assess Kazakhstan's challenges in controlling and surveilling influenza viruses. It explores the country's epidemiological landscape, including the prevalence of various influenza strains, the effectiveness of existing surveillance systems, and public health responses. The review highlights gaps in data collection, coordination among health agencies, and public awareness, emphasising the need for enhanced monitoring frameworks and international collaboration. Ultimately, the article advocates for targeted strategies to improve influenza preparedness and response in Kazakhstan, thereby safeguarding public health.

II. RESULT AND DISCUSSION

Influenza surveillance is essential for determining the timing and spread of influenza, tracking changes in circulating influenza viruses to inform seasonal influenza vaccine composition, and as an alert mechanism for potential pandemic viruses. One of the gaps in influenza surveillance highlighted during the 2009 pandemic was the lack of routine systems monitoring severe influenza [15]. The Global Influenza Hospital Surveillance Network (GIHSN) aims to determine the burden of severe influenza disease and Influenza Vaccine Effectiveness (IVE). This is a prospective, active surveillance and hospital-based epidemiological study to collect epidemiological data in the GIHSN [16]. Until recently, four foreign seasonal influenza vaccines were registered in Kazakhstan, the purchase of which for risk groups cost the state budget a considerable amount. The most available has been the VAXIGRIP® vaccine (Sanofi Pasteur, France). To ensure the prevention of seasonal influenza in the Republic of Kazakhstan (RK), the Research Institute for Biological Safety Problems of the RK has developed an allantoic split inactivated seasonal influenza vaccine (RIBSP vaccine) containing influenza viruses of subtypes A (H1N1pdm09 and H3N2) and type B [17]. Influenza viruses cause seasonal epidemics with high burden and severity, as well as pandemics. Representing a threat to public health, influenza is one of the most thoroughly monitored diseases globally [18]. Addressing the need for raising additional healthcare funds, Kazakhstan's government has decided to introduce national mandatory health insurance system starting 2017 [19]. Influenza viruses (IVs) are widespread pathogens worldwide that infect humans and a wide range of animals. Since the emergence of pandemic IAV A(H1N1)pdm09 in Kazakhstan in 2009–2010, this subtype almost every year caused a large number of

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Volume-3 Issue-5 || October 2024 || PP. 160-165

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human infection cases, being the dominant agent in the structure of the aetiology of ARVI [11].

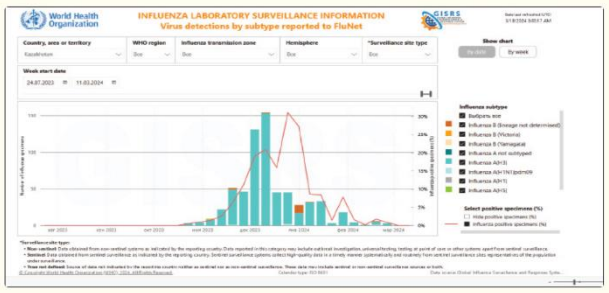

Fig. 1: Identification of influenza virus subtypes in Kazakhstan during the 2023–2024 epidemic season, FluNet data [11].

Influenza pandemics, distinguished from epidemics based on their geographical spread, have caused significant illness, death, and disruption for centuries. The Asian flu was the first pandemic to occur in an environment with global surveillance systems and laboratory capabilities in place to study it [20]. Influenza is an acute respiratory infectious disease caused by influenza viruses, which pose a severe health risk to humans. Influenza viruses have variable antigenic properties and spread rapidly, causing seasonal epidemics every year. Outbreaks are easy to occur in places where people gather, such as schools, childcare institutions, and nursing homes [21].

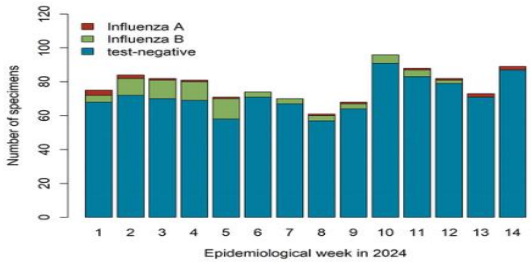

Figure 2: Weekly recruited individuals were tested negative or tested positive for influenza virus in Ili Kazakh autonomous prefecture, Xinjiang Uygur autonomous region, China (n = 1094) [21].

Vaccination is the most effective method to control the prevalence of seasonal influenza, and the most widely used influenza vaccine is the inactivated influenza vaccine (IIV). The influenza vaccine must be updated each season to be most effective against current circulating variants [22]. The recurrent outbursts and fast spillover differing genetically and antigenically IAVs pose a severe problem for pig production and public health. Genetic analysis of the H1N1 IAV strain, isolated in Kazakhstan in 2020, showed that it belongs to clade 1A.3.2.2 lineage 1A. This clade has a broad global distribution, which includes the 2009 H1N1 pandemic strains [23]. The rapid spread and extensive impact of influenza epidemics pose significant threats to public health and societal stability2. According to World Health Organization (WHO) data, approximately 10% of the global population is affected by influenza annually, leading to many cases and around 500,000 deaths3, thereby imposing a substantial disease burden and economic losses. Hotspot analysis indicated a progressive rise in influenza incidence hotspots, primarily concentrated in northern Xinjiang, particularly in Urumqi, Ili Kazakh Autonomous Prefecture, and Hotan Prefecture [24]. The results of determining hemagglutinin subtypes of the new influenza virus in the HAI assay are presented in Table 3. As seen from table 3, hemagglutinating activity of four isolates from humans (04/18, 05/18, 14/18, and 15/18) was inhibited by immune serums against A/H1N1 and A/H1N1pdm viruses (from 1/4 to homologous titer), that of three viruses (06/18, 07/18, and 08/18) by serum against influenza type B virus (from 1/2 to homologous titer) [25].

Table 1: Identification of hemagglutinin subtypes in influenza virus isolates obtained from humans and swine during 2017-2018 in the HAI assay [25].

Isolate	Antihemagglutinin titer with diagnostic serums against reference strains			
	A/H1N1	A/H1N1pdm	A/H3N2	type B
Almaty/04/18	40	80	< 20	< 20
Almaty /05/18	80	< 20	< 20	< 20
Almaty /06/18	< 20	< 20	< 20	160
Almaty /07/18	< 20	< 20	< 20	80
Almaty /08/18	< 20	< 20	< 20	80
Karaganda/14/18	40	160	< 20	< 20
Karaganda/15/18	40	80	< 20	< 20
Karaganda/16/18	< 20	< 20	80	< 20
swine/Kostanay/471/18	40	20	< 20	< 20
swine/Kostanay/522/18	80	20	< 20	< 20
Homologous titer of serums against reference viruses	160	160	160	160

Note. The reciprocals of antibody titers are presented here and in table 3.

Kazakhstan is a central transit corridor for the passage of epidemic variants of the influenza virus, reinforcing its geopolitical importance in global influenza surveillance. In addition to everyday preventive actions, fall influenza vaccination campaigns were considered an essential component of prevention [26].

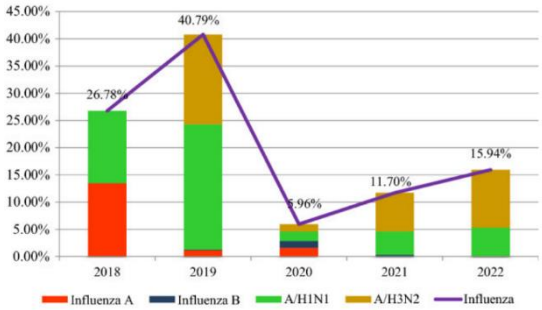

Figure 4: Dynamics of prevalence of different influenza types

Influenza A viruses (IAVs) are found worldwide and cause frequent epidemics in humans and domestic animal species, including poultry, pigs, and horses (1). The IAV genome consists of eight segments of negative-stranded RNA, which codes for at least ten proteins. IAVs

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are classified based on two highly variable glycoproteins, hemagglutinin (HA) and neuraminidase (NA), expressed inside the host cell and assembled on the surface of the virus particles [27]. The high pathogenic strains of the avian influenza H5N1 virus isolated in Kazakhstan have NS of different genotypes. The influenza virus strains isolated in 2005 are of the NS1E Qinghai genotype. A/swan/Mangystau/3/2006 strain is of NS2A genotype typical for Gs/Gd-like strains [28]. Large poultry die-offs happened in Kazakhstan during the autumn of 2020. Phylogenetic trees for hemagglutinin and neuraminidase show that viruses from Kazakhstan belong to the A/H5N8 subtype and the hemagglutinin H5 clade 2.3.4.4b. Surface proteins hemagglutinin (HA) and neuraminidase (NA) determine the antigenic properties of the virus [29]. While developing and introducing effective vaccines is essential for suppressing influenza pandemics, the current production capacity cannot fully meet the world's demand for pandemic vaccines [6]. As part of a strategic plan to provide the population of Kazakhstan with sufficient stocks of vaccines against pandemic influenza, within the limits of the national scientific program for 2009-2011, the country has developed the first Kazakhstan egg-derived, inactivated, whole-virion adjuvanted vaccine Refluvac® against influenza strain A (H1N1) pdm09.

III. CONCLUSION

The review highlights the significant challenges faced by Kazakhstan in controlling and surveilling influenza viruses, particularly in the context of the disruptions caused by the COVID-19 pandemic. The emergence of SARS-CoV-2 has led to a notable decline in the circulation of seasonal influenza viruses, raising concerns about the potential return and evolution of these pathogens. Important points include COVID-19's effects: Evaluating influenza epidemiology and vaccination efficacy became more challenging due to the pandemic's significant decrease in influenza cases. The conventional patterns of respiratory virus circulation were also upset by public health initiatives intended to suppress COVID-19. The state of epidemiology Influenza viruses are a significant cause of morbidity and mortality globally, making them a substantial health risk. Young children, older people, expectant mothers, and people with comorbidities are among the high-risk groups. The assessment emphasizes the necessity of efficient surveillance systems to track influenza activity and guide immunization plans. Influenza Surveillance Systems: Kazakhstan's surveillance infrastructure still has deficiencies, even after the Global Influenza Hospital Surveillance Network (GIHSN) was established to gather information on severe influenza cases. Problems like ineffective data collecting, poor cooperation between health organizations, and low public knowledge hamper effective influenza control. Development and Availability of Vaccines: The review emphasizes how crucial immunization is to controlling influenza outbreaks. Although Kazakhstan has created its vaccine to prevent seasonal influenza, production capacity issues and the need for updated vaccines against circulating strains still exist. Zoonotic Threats: Due to its geographic location, Kazakhstan is a transit corridor for influenza pandemic types, which raises the possibility of zoonotic transmissions. The assessment recommends improved monitoring mechanisms, international cooperation, and focused public health initiatives to increase influenza preparedness and response in Kazakhstan. Protecting the public from future influenza outbreaks requires bolstering vaccination programs and enhancing the healthcare system. In conclusion, Kazakhstan's complex influenza surveillance and control issues require a comprehensive approach that includes increasing epidemiological surveillance, increasing public awareness, and ensuring vaccine availability to reduce the impact of influenza viruses on public health. Examples from history show how zoonotic illnesses can lead to pandemics, highlighting the importance of thorough surveillance of both human and animal populations.

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