OH&RM ONE HEALTH & RISK MANAGEMENT

VOL. 5, ISSUE 3
2024

RESEARCH ARTICLE – ARTICLES DE RECHERCHE

MEDICAL SCIENCES

OPEN ACCESS

# EVOLUTION OF INFLUENZA AND ACUTE RESPIRATORY INFECTIONS IN THE REPUBLIC OF MOLDOVA DURING THE 2014/15 TO 2022/23 EPIDEMIC SEASONS

Alina DRUC

National Agency for Public Health, Chisinau, Republic of Moldova

*Corresponding author*: Alina Druc, e-mail: druc.alina@gmail.com

DOI: 10.38045/ohrm.2024.3.02 CZU: [616.921.5+616.21-022](478)

***Keywords:*** *influenza, acute respiratory infections, severe acute respiratory infections.*

***Introduction.*** *Influenza-like illness (ILI), Acute Respiratory Infections (ARI), and Severe Acute Respiratory Infections (SARI) are the most common infectious diseases globally, causing severe forms annually, especially in at-risk groups. The aim of this paper is to analyse the epidemiological and virological data on ILI, ARI, and SARI in the Republic of Moldova during the 2014/2015 to 2022/2023 epidemic seasons.*

***Material and methods.*** *The descriptive-retrospective epidemiological study analysed morbidity due to ILI, ARI, and SARI, as well as laboratory results for the presence of influenza viruses during the 2014/2015 to 2022/2023 epidemic seasons.*

***Results.*** *ILI has been of low to medium intensity except for two seasons, while ARI has been of very high intensity in one season. ILI, ARI, and SARI primarily affected children aged 0-14 years. During the nine seasons (except 2020/2021), influenza virus types A(H1N1) pdm09, A(H3N2), and B have been identified, with the percentage of positives decreasing considerably in the last two seasons. During the period under review, each influenza virus type dominated, and in three seasons, two to three virus types co-dominated. Genetic characterization of the identified strains demonstrated that influenza viruses fully fit the phylogenetic tree constructed for the nominated period, do not differ antigenically from strains identified in other regions of the northern hemisphere, and are susceptible to antivirals.*

***Conclusions.*** *The national surveillance system for ILI, ARI, and SARI makes it possible to monitor the evolution of the epidemic process in real time and geographic space, facilitating prompt intervention with control and response measures.*

***Cuvinte-cheie:*** *gripa, infecții acute ale căilor respiratorii superioare, infecții respiratorii acute severe.*

***EVOLUȚIA GRIPEI ȘI A INFECȚIILOR RESPIRATORII ACUTE ÎN REPUBLICA MOLDOVA ÎN PERIOADA SEZOANELOR 2014/2015-2022/2023***

***Introducere.*** *Gripa, infecțiile acute ale căilor respiratorii superioare (IACRS) și infecțiile respiratorii acute severe (SARI) sunt cele mai răspândite boli infecțioase la nivel global, provocând anual forme severe în special la grupele de risc. Scopul lucrării este de a analiza datele epidemiologice și virologice privind gripa, IACRS și SARI în Republica Moldova, în perioada sezoanelor 2014/2015 – 2022/2023.*

***Material și metode.*** *În studiul epidemiologic descriptiv-retrospectiv a fost analizată morbiditatea prin gripă, IACRS și SARI și rezultatele de laborator la prezența virusurilor gripali în perioada sezoanelor 2014/2015-2022/2023.*

***Rezultate.*** *Gripa a avut o intensitate de nivel jos și mediu cu excepția a 2 sezoane, iar IACRS a înregistrat într-un sezon un nivel de intensitate foarte înaltă. Gripa, IACRS și SARI a afectat primordial copii de 0-14 ani. Pe parcursul celor 9 sezoane (excepție 2020/2021) au fost identificate tipurile de virusuri gripale: A(H1N1) pdm09, A(H3N2) și B, procentul pozitivității reducându-se considerabil în ultimele 2 sezoane. În perioada analizată a dominat unul dintre virusurile gripale, iar în 3 sezoane au dominat concomitent 2-3 tipuri de virusuri. Profilul genetic al tulpinilor identificate a demonstrat că virusurile gripale se încadrează totalmente în arborele filogenetic construit în perioada nominalizată, nediferențiindu-se antigenic de tulpinile identificate în alte regiuni ale emisferei de nord și fiind sensibile la antivirale.*

***Concluzii.*** *Sistemul național de supraveghere a gripei, IACRS și SARI face posibilă monitorizarea eficientă a evoluției procesului epidemic în timp real și spațiu geografic, favorizând o intervenție promptă cu măsuri de control și răspuns.*

## INTRODUCTION

Influenza-like illness (ILI), as well as acute and severe viral respiratory infections, are among the most widespread infectious diseases worldwide, accounting for up to 95% of infectious diseases in some countries (in the Republic of Moldova), they account for up to 89.7% of infectious diseases). Due to the level of morbidity and mortality they cause, these infections have a negative impact on the health of the population, the health system, and the national economy. Experts estimate that the costs associated with acute respiratory infections worldwide amount to about $25 billion (1).

Seasonal influenza viruses are continuously evolving and cause severe illness every year, especially in older adults, children, pregnant women, and individuals with chronic health issues. From 2002 to 2011, approximately 389,000 respiratory deaths linked to influenza occurred annually worldwide (uncertainty range of 294,000 to 518,000) (2–5). Among these, persons aged 65 and above accounted for 67% (2, 3). The World Health Organization (WHO) in 2019 declared influenza and potential pandemic influenza strains as one of the most important threats to global health (6).

WHO has implemented the Global Influenza Strategy (2019-2030) to strengthen country capacity and preparedness for future pandemics by improving seasonal influenza prevention, surveillance, and control (7). Enhancing surveillance, monitoring, and utilization of global influenza data, alongside promoting research and innovation, are two core objectives of this strategy.

Currently, about 200 antigenically distinct viruses from 10 genera are known to cause acute respiratory illness, but the most dangerous, the most studied, and, at the same time, the most unknown and unpredictable remain the influenza viruses (1).

In this context, WHO recommends that all National Influenza Centers conduct surveillance for ILI, acute respiratory infections (ARI), and severe acute respiratory infections (SARI) according to geographical spread, intensity and trend of the epidemic process, epidemic threshold, dominant/co-dominant influenza virus strains, antiviral resistance, and influence on the health system in order to reduce the socio-economic impact caused by morbidity and mortality from these infections and improve surveillance and respons measures (8).

*The aim* of this paper is to analyze the epidemiological and virological situation of ILI, ARI, and SARI morbidity in the Republic of Moldova during the 2014/2015 to 2022/2023 epidemic seasons.

## MATERIAL AND METHODS

A descriptive analysis of the annual evolution of epidemiological and virological data for ILI, ARI, and SARI was performed. Data collection was carried out through the national surveillance and monitoring system of ILI, ARI, and SARI in all administrative territories of the Republic of Moldova according to Annex No. 2 (Reporting form on cases of ILI, ARI, and SARI in the district) of the Ministry of Health Order No. 792/2023 (11,063 annexes) (9). The epidemic threshold for ILI and ARI, as well as the medium, high, and very high thresholds, were calculated by ECDC and WHO specialists based on data uploaded weekly to the European surveillance portal for infectious diseases (EpiPulse) by the National Influenza Centre of Moldova.

Detection of influenza viruses in nasopharyngeal exudate samples from individuals with a presumeptive diagnosis of influenza, ARI, or SARI was performed using molecular biology techniques (rRT-PCR).

Isolation of influenza viruses was performed in MDCK and MDCK-SIAT1 cell cultures according to WHO-recommended methodology. Identification of isolated strains was performed by hemagglutination-inhibition assay with reference antisera to influenza A(H1N1) pdm09, A(H3N2), and B viruses. Genetic characterization of influenza virus strains was performed using molecular biology techniques (PCR-real time, sequencing), and the susceptibility of isolated strains to anti-influenza remedies (oseltamivir, zanamivir) was determined by the neuraminidase inhibition test, following the method recommended by the World Health Organization in collaboration with the Francis Crick National Institute for Health Research in London, UK.

Statistical data processing was performed using Microsoft Excel 365 and Epi Info 7.2. Descriptive statistics, including incidence rates and proportions, were calculated for the variables of interest. The data were presented as percentages, accompanied by 95% confidence intervals (CI) for proportions.

## RESULTS

During the 2014/2015 to 2022/2023 epidemic seasons, a total of 13,074 cases of ILI were registered, of which 75.9±0.7% were hospitalized. The highest percentage (24.9±0.7%) of the total number of registered ILI cases was in the 2019/2020 season, followed by the 2018/2019 season with 16.8±0.6%, the 2014/2015 season with 15.3±0.6%, and the 2022/2023 season with 15.1±0.6%. In the 2020/2021 season, no influenza cases were recorded.

The calculation of the ILI epidemic threshold started in the 2018/2019 season, initially being 2.09$\%_{000}$ cases of ILI, and then increased to 5.72$\%_{000}$ cases from the 2020/2021 season. Analyzing the evolution of ILI morbidity in these seasons (fig. 1), it is highlighted that the 2019/2020 season is the only season that exceeded the mid-level epidemic threshold for ILI (14.22$\%_{000}$) during weeks 08/2020 to 09/2020, reaching the highest incidence in the last nine seasons of 16.5$\%_{000}$ ILI cases.

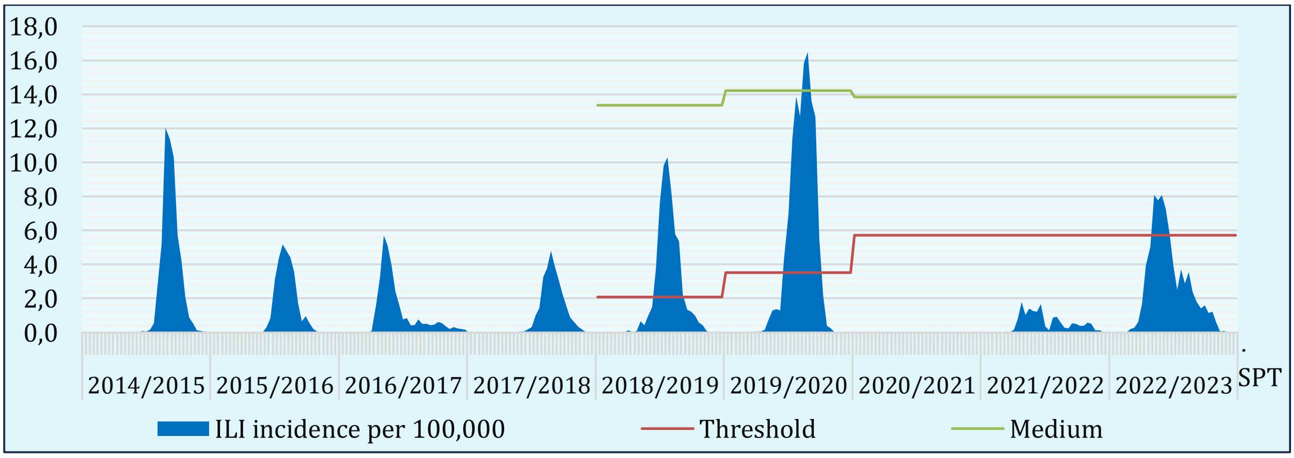


Figure 1. Evolution of ILI morbidity during the 2014/2015 to 2022/2023 epidemic seasons, per 100,000 population.

Only in two seasons (2016/2017 and 2022/2023), the maximum weekly incidence was recorded at the beginning of December in week 51 of 2017 and 2023, with 5.1$\%_{000}$ and 8.1$\%_{000}$ ILI cases respectively. In two seasons (2020/2021 and 2021/2022), the evolution of ILI remained below the epidemic threshold. In the other seasons, the maximum weekly incidence was recorded during weeks 06-09 (February).

In five of the seasons analyzed, ILI predominantly affected children in the 0-14 age group, ranging from 54.4±3.1% (2017/2018) to 64.4±4.5% (2021/2022). The 2014/2015 season was the only one in which the 30+ age group had a proportion of 53.0±2.2% (fig. 2). The fewest cases were recorded in the 65+ age group, ranging from 3.3±0.7% in the 2019/2020 season to 8.9±1.3% in the 2014/2015 season.

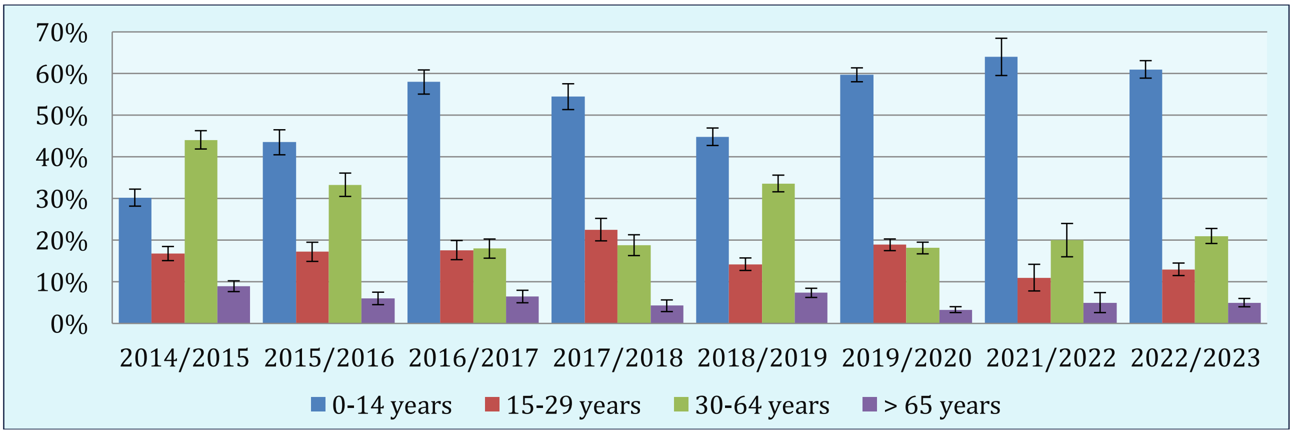


Figure 2. Percentage of ILI cases by age, 2014/2015 to 2022/2023 epidemic seasons.

In total, 2,120,942 cases of ARI were recorded in the RM over nine seasons, ranging from 6.8±0.03% (2020/2021) to 13.7±0.04% (2018/2019) of the total per season. Of the total number of cases, only 3.7±0.03% were hospitalized. Acute respiratory infections were recorded in all administrative territories.

As in the case of ILI, the maximum weekly incidence of ARI in two seasons was recorded in early December, specifically in week 51 of 2017 and 2023, with 447.5‱ and 636.3‱ cases respectively. In the 2020/2021 season, the evolution of ARI remained below the epidemic threshold of 283.63‱, and in the 2021/2022 season, the maximum weekly incidence was recorded in week 03 with 443.96‱. In the other five seasons, the maximum weekly incidence was recorded during weeks 06-09 (February). Only in the last season, 2022/2023, a very high ARI intensity level of 636.29‱ was recorded (fig. 3).

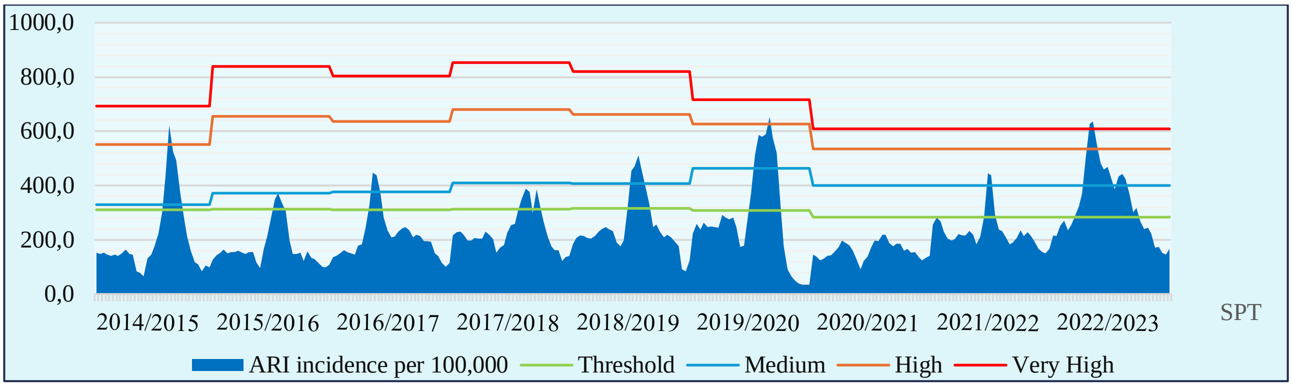


Figure 3. Evolution of ARI morbidity during the 2014/2015 to 2022/2023 epidemic seasons, per 100,000 population.

In the case of acute respiratory infections, each season saw the highest proportion of cases in children aged 0-14 years, ranging from 50.6±0.3% in the 2020/2021 season to 69.1±0.2% in the 2016/2017 season (fig. 4). In the age group 65+ years, the lowest proportion of cases was recorded, ranging from 2.6±0.1% in the 2016/2017 season to a maximum of 7.5±0.1% in the 2020/2021 season.

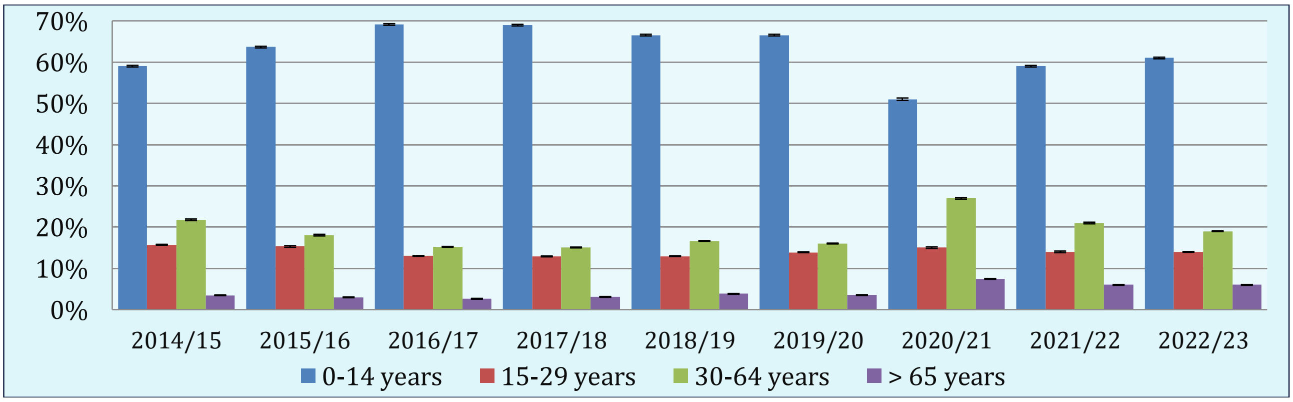


Figure 4. Percentage of ARI cases by age, 2014/2015 to 2022/2023 epidemic seasons.

A total of 157,441 cases of severe acute respiratory infections (SARI) were recorded during the 2014/2015 to 2022/2023 epidemic seasons, all of which were hospitalized according to the case definition. The highest proportion (17.9±0.2%) of all SARI cases occurred in the 2016/2017 season, followed by the 2015/2016 season with 16.8±0.2% and the 2014/2015 season with 14.4±0.2%. The lowest proportion was recorded in the 2019/2020 season with 6.2±0.1%.

In the 2020/2021 influenza season alone, the peak of 40.2‱ SARI cases was reached in week 08, while the season before that had the lowest rate of all seasons, with 2.6‱ SARI cases in week 18 (fig. 5).

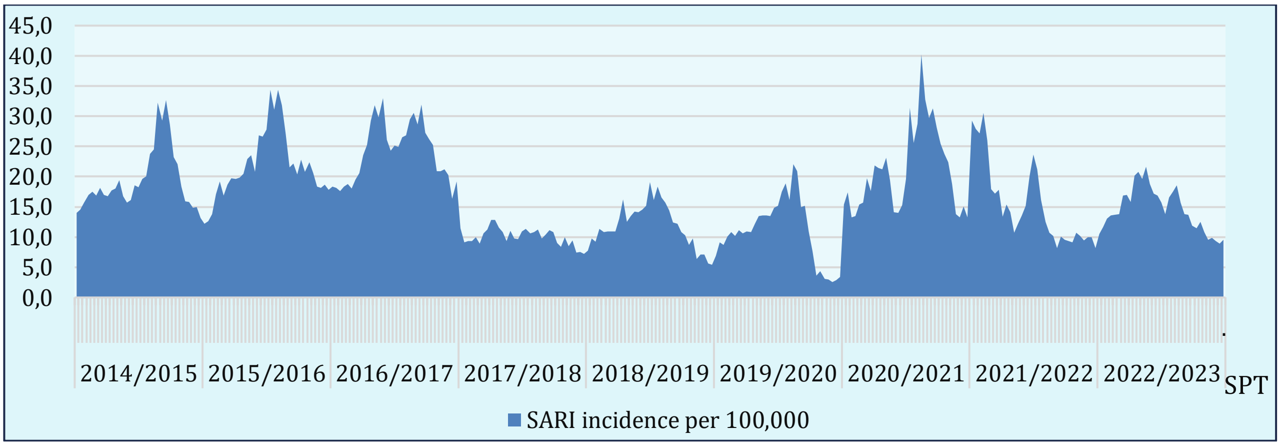


Figure 5. Evolution of SARI morbidity during 2014/2015 to 2022/2023 epidemic seasons, per 100,000 population.

The age group 0-4 years was the most affected by severe acute respiratory infections among all age groups, with a proportion ranging from 39.7±0.9% in the 2022/2023 season to 59.3±0.6% in the 2015/2016 season. Exceptions occurred in the 2020/2021 season, when the 30-64 years age group had the highest share at 49.3±0.7%, and in the 2021/2022 season, when the 30-64 years age group also had the highest share at 29.9±0.8% (fig. 6). SARI cases in the last three seasons have practically doubled in the 65+ age group compared to previous seasons, with percentages increasing from 11.6±0.4%-15.5±0.7% to 22.6±0.7%-31.8±0.7%.

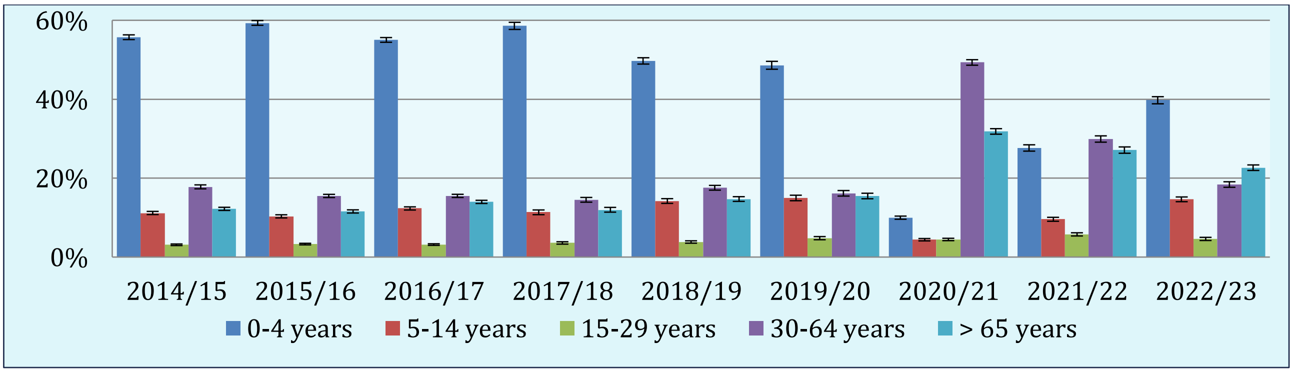


Figure 6. Percentage of SARI cases by age, 2014/2015 to 2022/2023 epidemic seasons.

During the 2014/2015 to 2022/2023 epidemic seasons, no major gender difference was observed in the registration of cases of ILI (women – 50.3±0.9%), acute respiratory infections (women – 2.5±0.07%), and severe acute respiratory infections (women – 49.0±0.2%).

During the 2014/2015 to 2022/2023 epidemic seasons, a total of 17,194 nasopharyngeal exudate samples were investigated for the presence of influenza viruses, of which 12.7±0.5% (2,178 samples) were positive for influenza viruses A(H1N1) pdm09, A(H3N2), and B. In the first six seasons analyzed, the proportion of negative results ranged from 62.5±2.7% (2018/2019 season) to 80.0±2.5% (2017/2018 season) (fig. 7). After the 2020/2021 influenza season, when no influenza virus was detected in 682 samples, the share of negative results increased to 96.8±0.4% and 91.2±0.8% in the following seasons, respectively.

Analyzing this period in terms of dominance and co-dominance of influenza virus strains, three seasons were marked by the co-dominance of two to three virus types: the 2014/2015 season with co-dominance of A(H1N1)pdm09 (47%) and type B (48%) influenza viruses, the 2019/2020 season with co-dominance of A(H1N1)pdm09 (39%), type B (27%), and A(H3N2) (22%) influenza viruses, and the 2022/2023 season with co-dominance of A(H3N2) (35%), A(H1N1)pdm09 (31%), and type B (30%) influenza viruses. In the 2015/2016 and 2018/2019 seasons, the A(H1N1)pdm09 influenza virus strain was dominant with 85% and 80%, respectively. In the other two seasons, the influenza A(H3N2) virus strain dominated with 62% and 64% respectively (2016/2017 and 2021/2022). The type B strain was dominant only in the 2017/2018, with 81%.

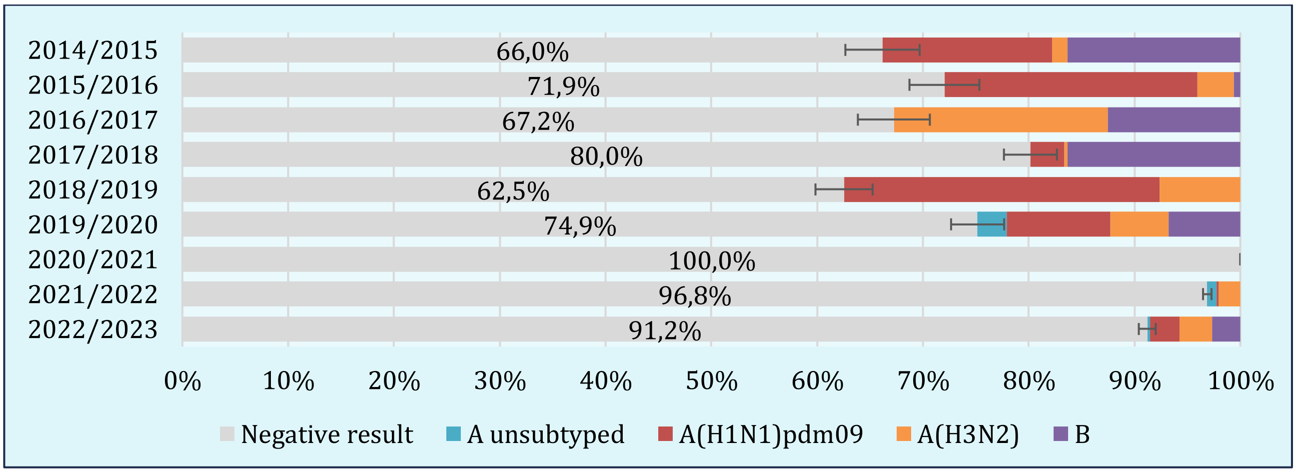


Figure 7. Percentage of influenza viruses identified during the 2014/2015 to 2022/2023 epidemic seasons.

Apart from the 2020/2021 season, the A(H1N1)pdm09 virus was not detected in the 2016/2017 season, and the type B virus was not detected in the 2018/2019 and 2021/2022 seasons.

Of the total 17,194 nasopharyngeal exudate samples investigated, 1,706 (9.9%) samples were from patients with the presumptive diagnosis "ILI," 13,215 (76.9%) samples from patients with the presumptive diagnosis "ARI," and 2,273 (13.2%) samples from patients with the presumptive diagnosis "SARI" (tab. 1).

During the 2014/2015 to 2022/2023 epidemic seasons, of the 1,706 samples from patients with the presumptive diagnosis "ILI," influenza A and B viruses were detected in 44.7%. Out of 13,215 samples of nasopharyngeal exudates from patients with the presumptive diagnosis "ARI," influenza viruses type A and B were identified in 7.4%, and out of 2,273 samples from patients with the presumptive diagnosis "SARI," these influenza viruses were detected in 19.2%.

During the 2014/2015 to 2022/2023 epidemic seasons, 176 strains of influenza viruses were isolated and identified in MDCK cell cultures and shown to fit the phylogenetic tree constructed during the nominated period. All viruses identified and subsequently tested had sufficient sialidase activity to assess resistance to oseltamivir and zanamivir inhibitors in sialidase inhibition assays. All were sensitive to both inhibitors.

## DISCUSSIONS

Since the 2017/2018 season, the SARI case definition was implemented according to WHO recommendations, which caused a 2.4-fold decrease in the number of cases compared to the previous season. Although the SARI case definition was changed, the age group 0-4 years remained the most affected.

As a result of the implementation of strict public health measures during the initial year of the COVID-19 pandemic, no influenza virus was detected in the investigated samples in the 2020/2021 season in the Republic of Moldova. This phenomenon was also observed in the European Region of the World Health Organization, which recorded a 99.8% reduction in positive detections of influenza virus in the sentinel system (33 out of 25,606 tested; 0.1%) (10).

Since the last two seasons, multiplex RT-PCR tests have been included in the laboratory system. This combined test detects three types of viruses simultaneously: SARS-CoV-2, influenza A, and influenza B viruses. As a result, the number of tests has increased considerably, accounting for 77% of the total number of tests in these nine epidemic seasons.

Genetic characterization of the identified strains demonstrated that the influenza viruses fully fit into the phylogenetic tree constructed during the nominated period, do not differ antigenically

Table 1. Results of laboratory investigations of samples from patients with a presumptive clinical diagnosis of ILI, ARI, or SARI for the presence of influenza viruses during the 2014/2015 to 2022/2023 epidemic seasons.

| *Diagnosis* | *Season* | *No. of samples examined* | *Influenza viruses detected* | | | | |
|---|---|---|---|---|---|---|---|
| | | | **A Un-sub-typed** N. (% (95%CI)) | **A(H1N1) pdm09** N. (% (95%CI)) | **A(H3N2)** N. (% (95%CI)) | **B** N. (% (95%CI)) | **A + B** N. (% (95%CI)) |
| ***ILI*** | **2014/15** | 98 | - | 22 (22.4±9.0%) | 3 (3.1±5.0%) | 38 (38.8±9.9%) | - |
| | **2015/16** | 124 | - | 55 (44.4±8.8%) | 5 (4.0±4.7%) | 2 (1.6±3.6%) | 1 (0.8±3.1%) |
| | **2016/17** | 133 | - | - | 51 (38.3±8.5%) | 21 (15.8±6.9%) | - |
| | **2017/18** | 134 | - | 8 (6.0±5.05%) | 1 (0.7±2.9%) | 54 (40.3±8.5%) | - |
| | **2018/19** | 400 | - | 199 (49.7±4.9%) | 33 (8.2±3.0%) | - | - |
| | **2019/20** | 349 | 23 (6.6±3.0%) | 52 (14.9±4.0%) | 25 (7.2±3.1%) | 37 (10.6±3.6%) | 1 (0. ±1.1%) |
| | **2020/21** | 60 | - | - | - | - | - |
| | **2021/22** | 121 | - | - | 19 (15.7±7.3%) | - | - |
| | **2022/23** | 287 | 3 (1.0±1.8%) | 47 (16.4±4.6%) | 25 (8.7±3.7%) | 37 (12.9±4.3%) | - |
| ***ARI*** | **2014/15** | 342 | - | 31 (9.1±3.4%) | 5 (1.5±1.7%) | 45 (13.2±3.9%) | - |
| | **2015/16** | 291 | - | 38 (13.1±4.2%) | 11 (3.8±2.7%) | 1 (0.3±1.3%) | - |
| | **2016/17** | 285 | - | - | 52 (18.2±4.8%) | 41 (14.4±4.4%) | - |
| | **2017/18** | 448 | - | 11 (2.5±1.8%) | 2 (0.4±1.0%) | 63 (14.1±3.5%) | 1 (0.2±0.9%) |
| | **2018/19** | 526 | - | 104 (19.8±3.6%) | 47 (8.9±2.7%) | - | - |
| | **2019/20** | 509 | 6 (1.2±0.6%) | 29 (5.7±2.3%) | 28 (5.5±2.2%) | 28 (5.5±2.2%) | 3 (0.6±1.0%) |
| | **2020/21** | 420 | - | - | - | - | - |
| | **2021/22** | 6194 | 60 (1.0±0.3%) | 9 (0.1±0.1%) | 92 (1.5±0.3%) | - | 8 (0.1±0.1%) |
| | **2022/23** | 4200 | 9 (0.2±0.2%) | 75 (1.8±0.4%) | 102 (2.4±0.5%) | 77 (1.8±0.4%) | 1 (0.02±0.1%) |
| ***SARI*** | **2014/15** | 242 | - | 56 (23.1±5.6%) | 2 (0.8±1.9%) | 28 (11.6±4.7%) | 2 (0.8±1.9%) |
| | **2015/16** | 251 | - | 66 (26.3±5.7%) | 7 (2.8±2.6%) | 1 (0.4±1.6) | - |
| | **2016/17** | 269 | - | - | 36 (13.4±4.5%) | 24 (8.9±3.9%) | - |
| | **2017/18** | 297 | - | 9 (3.0±2.5%) | - | 26 (8.8±3.6%) | 1 (0.3±1.3%) |
| | **2018/19** | 310 | - | 66 (21.3±13.8%) | 14 (4.5±2.8%) | - | - |
| | **2019/20** | 197 | - | 22 (11.2±5.0%) | 5 (2.5±3.0%) | 6 (3.0±3.2%) | - |
| | **2020/21** | 202 | - | - | - | - | - |
| | **2021/22** | 284 | - | 1 (0.4±1.4%) | 25 (8.8±3.7%) | - | - |
| | **2022/23** | 221 | 1 (0.5±1.8%) | 9 (4.1±3.3%) | 17 (7.7±4.1%) | 12 (5.4±3.6%) | 1 (0.5±1.8%) |

from strains identified in other regions of the northern hemisphere, and are sensitive to antivirals (oseltamivir and zanamivir). These phylogenetic analyses have been essential for understanding the evolution and diversity of influenza viruses. This information has also been used to guide the selection of strains included in the influenza vaccine for the northern hemisphere each influenza season.

Continuous epidemiological and virological surveillance provides crucial information for the control of the epidemiological situation at the national level and allows prompt and targeted interventions if needed. In this way, health authorities can implement public health measures adapted to the situation, helping to limit the spread of infections and protect public health.

Currently, the health system of the Republic of Moldova has a routine and sentinel surveillance system for ILI, ARI, and SARI, adjusted to WHO, ECDC, and CDC requirements, which is linked to the European surveillance portal for infectious diseases and the WHO FluNet global network with weekly reporting year-round. This system also includes the National Influenza Centre of the Republic of Moldova, which was recognized and approved in 2013 by WHO and is certified as a member of the Global Influenza Surveillance and Response System (GISRS).

## CONCLUSIONS

1. During the 2014/2015 to 2022/2023 epidemic seasons, ILI exhibited low to medium intensity in the epidemiological process, while ARI displayed all levels of intensity from low to very high. Influenza-like illness, acute respiratory infections, and severe acute respiratory infections predominantly affected children in the 0-14 age group.
2. Over the last nine epidemic seasons, a large number of nasopharyngeal exudate samples have been investigated for influenza viruses, of which 12.7% were positive for influenza viruses A(H1N1) pdm09, A(H3N2), and B. There were no positive results for influenza in the 2020/2021 season.
3. According to the antigenic structure, the isolated influenza viruses are similar to the influenza virus strains that fit the phylogenetic tree constructed during the nominated period. The isolated influenza virus strains were susceptible to the antiviral drugs oseltamivir and zanamivir.
4. The results demonstrate the need to strengthen the system of epidemiological surveillance and response to ILI, acute respiratory infections, and severe acute respiratory infections existing in the republic in order to mitigate the socio-economic impact on the health system and the national economy.
5. Continuous epidemiological and virological surveillance provides crucial information for interventions depending on epidemiological evolution at the national level and allows prompt and targeted interventions if needed. In this way, health authorities can implement public health measures adapted to the situation, helping to limit the spread of infections and protect public health.

## CONFLICT OF INTEREST

The author does not declare any conflict of interest.

## ETHICAL APPROVAL

The article was not approved by the Ethics Committee because it does not contain ethical risks.

## ACKNOWLEDGEMENT

We would like to thank the WHO Collaborating Center for Reference and Research on Influenza, The Francis Crick Institute, London, for the professional support given in studying the strains of influenza viruses isolated in the Republic of Moldova using the latest generation molecular biology techniques.

## REFERENCES

1. Spinu C, Pinzaru I, Gheorghita S, Spinu I, Donos A, Druc A, et al. *Influenza: surveillance, control and response measures*. Chișinău: Tipografia AȘM, 2018. https://library.usmf.md/sites/default/files/2023-02/Gripa%20masuri%20de%20supraveghere%20control%20si%20raspuns.pdf [Accessed January 09, 2024].

2. Sominina A, Danilenko D, Komissarov AB, et al. Assessing the Intense Influenza A(H1N1) pdm09 Epidemic and Vaccine Effectiveness in the Post-COVID Season in the Russian Federation. *Viruses*. 2023;15(8):1780. doi:10.3390/v15081780
3. Paget J, Spreeuwenberg P, Charu V, et al. Global mortality associated with seasonal influenza epidemics: New burden estimates and predictors from the GLaMOR Project. *J Glob Health*. 2019; 9(2):020421. doi:10.7189/jogh.09.020421
4. Li L, Liu Y, Wu P, et al. Influenza-associated excess respiratory mortality in China, 2010-15: a population-based study. *Lancet Public Health*. 2019; 4(9):e473-e481. doi:10.1016/S2468-2667(19)30163-X
5. Li L, Wong JY, Wu P, et al. Heterogeneity in Estimates of the Impact of Influenza on Population Mortality: A Systematic Review. *Am J Epidemiol*. 2018;187(2):378-388. doi:10.1093/aje/kwx270
6. Ten threats to global health in 2019. World Health Organization. https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019 [Accessed January 12, 2024].
7. Global Influenza Strategy 2019-2030. World Health Organization; Geneva, Switzerland: 2019. https://www.who.int/publications/i/item/9789241515320 [Accessed January 9, 2024].
8. National Influenza Centres. World Health Organization. https://www.who.int/initiatives/global-influenza-surveillance-and-response-system/national-influenza-centres [Accessed January 11, 2024].
9. *Order of the Ministry of Health no. 792 of 26.09. 2023 regarding the epidemiological and virological surveillance of influenza, acute upper respiratory tract infections and severe acute respiratory infections in the Republic of Moldova.* Ministry of Health. https://ms.gov.md/wp-content/uploads/2023/09/Ordin-792-2023.pdf [Accessed January 16, 2024].
10. Adlhoch C, Mook P, Lamb F, et al. Very little influenza in the WHO European Region during the 2020/21 season, weeks 40 2020 to 8 2021. Euro Surveill. 2021;26(11):2100221. doi:10.2807/1560-7917.ES.2021.26.11.2100221.

**Date of receipt of the manuscript: 13/02/2024**
**Date of acceptance for publication: 15/06/2024**

Alina DRUC, Web of Science Researcher ID HRE-3363-2023, SCOPUS Author ID 57222617229