# COURSE AND COMPLICATIONS OF INFLUENZA A IN SENIORS OVER 65 YEARS OF AGE

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**SUMMARY**

*Objectives:* Influenza A and B viruses cause epidemics every year, with approximately 3–5 million serious cases and about 290,000 to 650,000 deaths worldwide. Most patients die from bacterial complications of influenza. The aim of our study was to describe the clinical pictures of influenza and the development of the complications in seniors over 65 years of age, who were treated in University Hospital Pilsen. The course of the disease and changes in laboratory parameters were evaluated with regard to the method of treatment performed.

*Methods:* A descriptive retrospective study was performed. Clinical and laboratory data of seniors with the diagnosis of influenza were extracted from electronic medical records and later analysed. The data were processed with Excel 2016 and Statistica.

*Results:* A collection of 261 seniors, of whom 218 were hospitalized and 43 treated in an outpatient setting, has been studied. Patients who later developed complications had elevated values of CRP, procalcitonin, urea, and creatinine. The antiviral drug oseltamivir was administered to 226 of 261 seniors. Forty-seven seniors (18.0%) died from influenza and its complications (severe pneumonia with acute respiratory insufficiency or heart failure).

*Conclusions:* The course of influenza in seniors was usually more severe and required hospitalization along with antiviral treatment. The mortality rate in the monitored group exceeded 18%. Annual timely vaccination, but also other preventive measures, and maybe considering other risk groups are methods to prevent severe or even fatal cases of influenza.

*Key words:* influenza, respiratory infections, seniors, complications, vaccination

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## INTRODUCTION

Influenza is an infectious disease caused by influenza viruses A and B, which belong to the family of orthomyxoviruses. The rarer influenza virus C then forms a completely separate special genus. Influenza A and B viruses are responsible for epidemics each year (1). According to the World Health Organization (WHO) there are around a billion cases of seasonal influenza annually, including 3–5 million cases of severe illness and 290,000 to 650,000 respiratory deaths. Ninety-nine percent of deaths are associated with influenza-related lower respiratory tract infections in children under 5 years of age living in developing countries (2, 3).

It is estimated that each year influenza viruses infect approximately ten to thirty per cent of European population, and cause hundreds of thousands of hospitalizations, and 15,000–17,000 deaths across Europe each year (3).

Mortality is not significantly different when affected by both influenza A and B (4). The average annual excess respiratory and cardiovascular mortality rates attributed to influenza A (H3N2), B/Yamagata, B/Victoria, and A (H1N1) were 8.47 (95% eCI: 6.60–10.30), 5.81 (95% eCI: 3.35–8.25), 3.68 (95% eCI: 0.81–6.49), and 2.83 (95% eCI: −1.26–6.71), respectively, where eCI means confidence interval obtained empirically through simulations (5).

The cause of death from influenza is typically complication affecting the lungs and heart. The most common complication of influenza is bacterial pneumonia. Rare, but severe extrapulmonary complications of influenza, like myocarditis and pericarditis, may occur. Furthermore, exacerbations of various chronic diseases (chronic obstructive pulmonary disease, bronchial asthma, chronic heart failure and others) can be observed as complications (6).

The impacts of influenza on public health are evident in several key areas. Influenza occurs seasonally, usually during the winter months. The consequence of annual epidemics is an extreme burden on health systems due to the high number of cases of the disease. However, influenza also has significant economic impacts in the form of treatment and hospitalization costs, and productivity losses occur in various sectors of the economy as a result of incapacity for work.

Preventive measures include monitoring the emergence and circulation of new strains of influenza viruses, consistent anti-epidemic measures such as regular hand washing and the use of disinfectants, public information campaigns and regular training for medical staff. However, the most effective way to prevent influenza is vaccination. Vaccines are updated annually to match the current strains of the virus. Vaccination is especially recom-

mended for risk groups such as the elderly, pregnant women, young children, and people with chronic diseases.

Vaccination coverage against influenza is very low in the Czech Republic. Vaccination with a combined tetravalent vaccine against two influenza A and two influenza B subtypes of virus should be widely recommended to the population (1).

## MATERIALS AND METHODS

A retrospective data analysis of the electronic medical record using M4 software (Medicalc Software, s.r.o., Pilsen, Czech Republic) was performed. The collection consisted of patients over 65 years of age (seniors), who were diagnosed with influenza in the period between 1 January 2018 and 31 December 2020 at the University Hospital in Pilsen on the basis of anamnesis, clinical picture and subsequent virologic examination. We studied the history and nature of the symptoms, clinical observations and signs at the initial examination, results of hematologic, biochemical and microbiological examinations, complications, and the final clinical condition of the patient. We also recorded flu vaccination status where available. Prior to processing, seniors' data were protected by anonymization in compliance with the GDPR. The data were processed using Excel 2016 (Microsoft Corporation, Redmond, USA) and Statistica (StatSoft CR, s.r.o., Prague, Czech Republic). Continuous data are characterized by means and medians, categorical data by counts and percentages. Between-groups comparisons of continuous variables were performed using a two-sample t-test. Results with p-values less than 0.05 were considered statistically significant. The local Ethics Committee was consulted prior to the start of data collection, and it was determined that no approval or informed consent of seniors was required for this study.

## RESULTS

The diagnosis of influenza A was confirmed in 602 patients at the respective hospital in the study period. Of these, 261 (43.4%) were seniors, 286 (47.5%) patients were 19–65 years old, and 55 (9.1%) were children aged up to 18 years. Among seniors (the group of interest), there were 143 (54.8%) women and 118 (45.2%) men. The average age was 77.5 years (range 65–99 years, median 76 years). By month, the most cases were reported in February.

The first meeting of patients with a physician took place within five days from onset of symptoms, most often on the third day (Fig. 1).

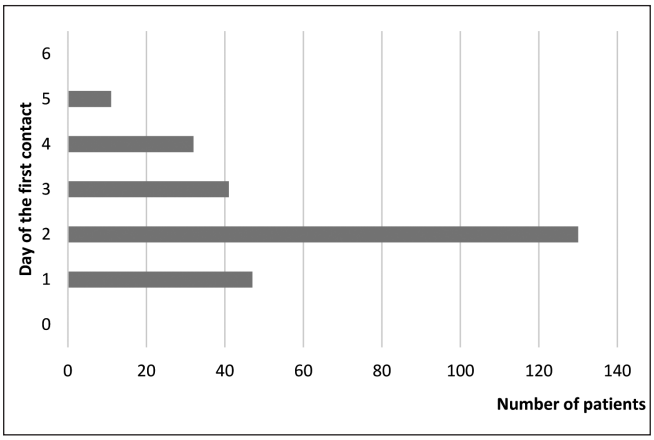


***Fig. 1.*** *Initial doctor visit by seniors following onset of influenza symptoms.*

Most of the patients of interest developed severe pneumonia with acute respiratory failure. Severe heart failure in the senior group was noted to occur in patients with or without respiratory complications. One patient developed acute colitis complicated by ileus. Decompensation of other chronic diseases in seniors was also observed. Only 43 (16.5%) seniors were treated on an outpatient basis, all without risk factors and complications. The other 218 (83.5%) seniors were hospitalized. Of those hospitalized, 163 (74.8%) were treated in a standard bed, 40 (18.4%) required a stay in a first- or second-degree intensive care bed, and 15 patients (6.9%) required higher-level resuscitation care in a third-degree intensive care bed. Forty-seven seniors (18.0%) died from influenza and its complications (Table 1).

The most common symptom of influenza was fever detected in 218 (83.5%) seniors. Cough occurred in 189 seniors (72.4%). The combination of fever and cough occurred in 160 cases (61.3%), general weakness in 182 (69.7%), and fatigue in 166 (63.6%) cases (Table 2).

In 192 (73.6%) patients a diverse range of complications were observed. Pneumonia was confirmed in 114 (43.7%) seniors, the aetiology of which was demonstrated only in 48 cases. *Klebsiella pneumoniae* in 22 cases (45.8%) *Streptococcus pneumoniae* in 14 cases (29.2%), in the remaining 12 cases *Hemophilus influenzae*, *Chlamydia pneumoniae* and *Pseudomonas aeruginosa* were confirmed as the aetiological pathogens. Acute respiratory insufficiency was diagnosed in 72 (27.6%) seniors. Of these, 49 received sufficient oxygen therapy with a mask or nasal spikes with a higher oxygen flow, 8 were connected to the high flow nasal oxygen therapy (HFNO), 5 temporarily required non-invasive lung ventilation in an intensive care bed, and another

***Table 1.*** *Different care needs for seniors over 65 years of age with diagnosis of influenza, admitted to hospital in 2018–2020*

| | All seniors | Hospitalization | | Standard bed | | ICU grade I. and II. | | ICU grade III. | | Death | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | n | % | n | % | n | % | n | % | n | % |
| Vaccinated | 11 | 6 | 54.6 | 6 | 100.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Unvaccinated | 105 | 88 | 83.8 | 62 | 70.5 | 17 | 19.3 | 9 | 10.2 | 19 | 18.1 |
| Unknown history of vaccination | 145 | 124 | 85.5 | 95 | 76.6 | 23 | 18.6 | 6 | 4.8 | 28 | 19.3 |
| Altogether | 261 | 218 | 83.5 | 163 | 74.8 | 40 | 18.4 | 15 | 6.9 | 47 | 18.0 |

ICU – intensive care unit

***Table 2.*** *Symptoms of influenza A in seniors admitted to hospital in 2018–2020 (N = 261)*

| Symptom | Cases | |
|---|---|---|
| | n | % |
| Fever | 218 | 83.5 |
| Cough | 189 | 72.4 |
| Infirmity | 182 | 69.7 |
| Fatigue | 166 | 63.6 |
| Myalgia | 106 | 40.6 |
| Arthralgia | 101 | 38.7 |
| Chills | 41 | 15.7 |
| Nausea | 37 | 14.2 |
| Diarrhoea | 33 | 12.6 |
| Nasal congestion | 30 | 11.5 |
| Sore throat | 23 | 8.8 |
| Headache | 21 | 8.1 |
| Chest pain | 20 | 7.7 |
| Vomiting | 19 | 7.3 |
| Flatulence | 19 | 7.3 |
| Pleuritic pain | 14 | 5.4 |
| Rhinorrhoea | 11 | 4.2 |
| Abdominal pain | 11 | 4.2 |
| Hoarseness | 9 | 3.5 |
| Haemoptysis | 5 | 1.9 |

***Table 3.*** *Complications of influenza A in seniors admitted to hospital in 2018–2020 (N = 261)*

| Complications | Cases | |
|---|---|---|
| | n | % |
| Pneumonia | 114 | 43.7 |
| Acute respiratory insufficiency | 72 | 27.6 |
| Heart failure | 69 | 26.4 |
| Acute renal failure | 41 | 15.7 |
| Acute bronchitis | 37 | 14.2 |
| Urinary tract infection | 20 | 7.7 |
| Chronic obstructive pulmonary disease exacerbation | 14 | 5.4 |
| Acute sinusitis | 10 | 3.8 |
| Encephalopathy | 7 | 2.7 |
| Acute tonsillitis | 5 | 1.9 |
| Myocarditis | 4 | 1.5 |
| Encephalitis | 2 | 0.8 |
| Myositis | 2 | 0.8 |
| Ileus | 1 | 0.4 |

10 required secured airways by tracheal intubation and artificial lung ventilation. Exacerbation of chronic obstructive pulmonary disease occurred in 14 patients, and a urinary tract infection was diagnosed in 20 patients (7.7%) (Table 3).

The mean leukocyte count at the first blood draw was $9.2 \times 10^9$/L, erythrocytes $4.3 \times 10^{12}$/L and platelets $188.1 \times 10^9$/L. The mean C-reactive protein (CRP) value in seniors with an uncomplicated course was 51 mg/L, in patients with complications 91 mg/L; the difference was not statistically significant (p = 0.37). The mean procalcitonin level (n = 147) in uncomplicated influenza cases was 0.33 μg/L, in those with complications 1.73 μg/L, which was statistically significant (p = 0.048). Renal function deteriorated in seniors with influenza complications. The mean values of urea were 11.2 mmol/L and creatinine was 127 μmol/L. In the whole set, the average serum electrolyte values were sodium 139 mmol/L, chloride 102 mmol/L and potassium 4.0 mmol/L (Table 4).

Antiviral treatment with oseltamivir was indicated in 226 (86.6%) patients. The medicine was well tolerated in all seniors. The vaccination status was available in 116 (44.4%) cases. Only 11 patients in this group were vaccinated in the preceding autumn (vaccination coverage 9.5%). There were no mortalities in the six patients from this group that required hospitalization for respiratory complications. Among those unvaccinated, 26 (24.8%) patients had to be admitted to the intensive care unit (ICU) and 19 (18.1%) died as a result of complications of influenza. Twenty-eight deaths were recorded in the group of patients where the vaccine history was not known (Table 1).

***Table 4.*** *Laboratory values obtained during the first blood draw of seniors admitted to hospital for influenza A in 2018–2020*

| | Mean | Mean uncomplicated | Mean complicated | p-value |
|---|---|---|---|---|
| Leukocyte count | $9.2 \times 10^9$/L | | | |
| Erythrocytes | $4.3 \times 10^{12}$/L | | | |
| Platelets | $188.1 \times 10^9$/L | | | |
| CRP | | 51 mg/L | 91 mg/L | 0.37 |
| PCT | | 0.33 μg/L | 1.73 μg/L | 0.048* |
| Urea | 11.2 mmol/L | | | |
| Creatinine | 127 μmol/L | | | |
| Sodium | 139 mmol/L | | | |
| Chloride | 102 mmol/L | | | |
| Potassium | 4.0 mmol/L | | | |

Mean – from all obtained values; mean un/complicated – values in seniors with an un/complicated courses; CRP – C-reactive protein; PCT – procalcitonin
*Significant difference

## DISCUSSION

We have conducted a descriptive retrospective study of 261 seniors over 65 years of age, diagnosed with influenza. Our findings were not surprising. We conclude, in accordance with other scientific data, that seniors remain at high risk for complications of influenza, especially if not previously vaccinated (7, 8).

The clinical course influenza in the elderly can affect multiple systems including the respiratory, digestive and musculoskeletal systems. The general symptoms of a viral disease, such as fever, cough, myalgia, breathing-dependent chest pain, headache, sore throat, and chills were observed in cases within our study, as well as by other authors (1, 3, 5). Fever occurred in 83.5% and cough in 72.4% of cases, jointly these symptoms occurred in 61.3% of patients. Chronic diseases, as risk factors for the course of influenza, include cardiovascular diseases, chronic respiratory diseases, renal, hepatic and haematological diseases (9–12). In our study we identified pneumonia (43.7%) and heart failure (26.4%) as the most common complications of influenza in seniors. Similar data have been published by other authors (5, 11, 13). Pneumonia as a serious complication of influenza was observed mainly in unvaccinated patients. Pneumonia with acute respiratory insufficiency, was a common indication for admission to an intensive care unit and also the most common cause of death.

Influenza viruses themselves can cause severe pneumonia, however, secondary bacterial pneumonia is the significant contributor to mortality (14). The most commonly described pathogen causing bacterial pneumonia in influenza is *Streptococcus pneumoniae* (15), similar to findings in our study. *Staphylococcus aureus*, including MRSA (16), is also frequently reported. In our study, we detected *Klebsiella pneumoniae* and *Streptococcus pneumoniae* as the most common pathogens causing secondary bacterial pneumonia in our patients. Among the most common complications we observed were acute bronchitis, exacerbation of chronic respiratory diseases and acute respiratory insufficiency. Acute cardiac decompensation also occurred frequently as a complication. We also often observed acute kidney injury, occasionally of a high degree, which is a commonly described complication of influenza (17).

Laboratory findings were in no way out of line with common findings in respiratory viral diseases. Leucocytosis was commonly observed in the blood count. The level of CRP was also consistent with known findings in common viral infections. Procalcitonin reliably indicated possible bacterial complications of influenza. A side finding of our study is the fact that interleukin-6 is not commonly measured in hospitalized patients suffering from influenza, despite the fact that it is a significant predictor of severity of influenza disease and its evolution (18), as is the case, for example, of COVID-19 (19, 20).

The interval of the first contact with the doctor from symptoms to onset of the disease was often decisive for the prognosis of the patient. On the first day of symptoms no patient sought medical intervention. There were 96.4% of patients presented to the University Hospital between 2–5 days post symptom onset; the rest presented on the 6th day reporting persistent difficulties. Lam et al. (9) report that in the group of elderly patients studied, 54% visited the emergency department 2–5 days after the onset of symptoms. Twenty-nine percent of elderly patients presented after 5 days of symptoms. We consider important to note that all patients over 65 who died of influenza and its complications in the study period came into contact with the doctor after 3 days of symptoms. We have published some of the results elsewhere (21). In our group, 226 out of 261 seniors (86.6%) were treated with oseltamivir. It was usually administered twice daily, orally, at a dose of 75 mg. The oseltamivir resistance development in course of the prophylaxis or therapy is not usual, but it has been described in the literature (22, 23). Patients usually were not treated with corticosteroids, as many studies have shown an increase in mortality (24, 25), a greater number of complications (26, 27), and a prolonged release of the influenza virus (28).

Coleman at al. evaluated a possible correlation between vaccination coverage rates in adults ≥65 years in EU countries and the influenza-associated mortality rates in the 65+ age group. They found that 88% of deaths were among people 65 years and older, and the rate of influenza-associated mortality in this age group was roughly 35 times higher than that of those under 65. Their data highlight the importance of targeting prevention and control interventions at this age group (12).

In the Czech Republic, the annual seasonal flu vaccination is recommended for adults over 50 years, children over 6 months of age, and special at-risk groups such as pregnant women, those who are immunocompromised, and healthcare workers (29, 30).

## CONCLUSIONS

Seniors are a group of fragile patients with many chronic diseases and smaller functional reserves. The most common symptoms, and thus the predictors of disease, during flu season are mainly the rapid onset of fever and dry cough. Influenza in the elderly is often accompanied by many complications. Pneumonia was the most common complication in our group of seniors. Determining the level of PCT could help in estimating the severity of the course of influenza and thus the prognosis for the elderly. Acute heart failure and impaired renal function were also noted more often. Mortality rate in studied seniors reached 18.0%. In a group of 11 vaccinated seniors, no death from influenza was recorded. However, the results are burdened with the error of small numbers in our study. Influenza poses a significant health risk with wide-ranging public health and economic implications. Preventive measures such as vaccination and hygiene practices are key to minimizing these impacts. Early monitoring of influenza incidence and the introduction of anti-epidemic measures significantly contributes to the protection of public health. Early initiation of vaccination campaigns must be preceded by intensive transmission of information on the importance of influenza vaccination, especially among people at risk in the categories of older age people, pregnant women, children, and immunocompromised persons. These measures can reduce the incidence of influenza in the population, and also reduce the risk of severe or fatal outcomes in a high-risk group of patients.

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**Conflicts of Interest**

None declared

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