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RESEARCH ARTICLE

Symptoms and Outcomes of COVID-19 in Elderly Recipients of Influenza and COVID-19 Vaccines

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Abstract:

Background:

Health providers and policymakers aim to prevent or reduce the severity of disease outcomes globally.

Objective:

The present study aimed to explore the outcomes and common symptoms of COVID-19 in the elderly population vaccinated against influenza and COVID-19 in hospitals of Ramsar and Tonekabon cities in Iran.

Methods:

To participate in the present cross-sectional descriptive study, 11 qualified subjects were selected through a census. The data collection instruments included the “Demographic and clinical questionnaire” and “Registration form of sampled patients with acute disease syndrome”. The data were analyzed in SPSS 24 using descriptive statistics (frequency).

Results:

The average age of the participants was 70.63±5.85 years. As the results showed, mild cardiovascular symptoms were found in 6 participants (54.5%), lower respiratory system symptoms in 5 (45.5%), nervous system symptoms in 4 (36.4%), and auxiliary symptoms in 4 (36.4%). No cardiac, renal, blood or central nervous system outcomes were observed in the elderly, and the mortality rate was 0%. The findings also showed a reduction in clinical symptoms and severity of outcomes, an improvement in clinical findings, and no mortality among the elderly.

Conclusion:

The present findings supported measures aimed at increasing the coverage of influenza and COVID-19 vaccination in people, especially the elderly.

Keywords: COVID-19, Influenza vaccines, COVID-19 vaccines, Symptoms, Patient outcome assessment, Influenza.

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1. INTRODUCTION

COVID-19 has turned into a global issue. Until 19 November 2021, a total number of 254,847,065 people had been infected with COVID-19, and 5,120,712 died as a result in the world. In Iran, 6,057,893 people were infected with the disease, and 128,531 died of the infection [1, 2]. Thus, health providers and policymakers attempt to prevent or reduce the severity of the disease outcomes on a global scale [3 - 6]. One way to prevent or reduce the severity of disease outcomes is vaccination. COVID-19 vaccination for high-risk groups has already begun in many countries [7], but still COVID-19 inflicts many people worldwide [1, 8]. Many countries have

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prioritized vaccinating high-risk populations, such as the elderly and those at a greater risk of infection, such as the medical staff [7]. There are concerns that the confluence of COVID-19 and seasonal influenza in autumn and winter may lead to a high mortality rate and challenge the health system [9]. Therefore, it is necessary to identify factors that may increase the burden of disease in society and take measures in this field [10 - 13]. Influenza vaccination for high-risk populations has raised concerns about the coincidence of vaccination with the spread of COVID-19 and its clinical outcomes and the resultant mortalities [14]. However, studies in recent months evidenced the reduced clinical outcomes of COVID-19 in influenza vaccine recipients [15 - 19]. Several researchers believe that high vaccine coverage will reduce the spread of influenza and improve the efficiency and performance of the health system to provide services to control COVID-19 [20 - 22]. Preventive vaccines are the most effective countermeasure against influenza virus infection and its pandemic [23, 24]. In Iran, there were concerns about the possibility of influenza spreading simultaneously with the spread of COVID-19. On 3 October 2020, Iran Ministry of Health and Medical Education (MOHME) announced the influenza vaccination guidelines to the affiliated organizations. Due to the limited supply of influenza vaccine and the allocated human influenza vaccine quota, this guideline gives instructions on prioritizing the recipients of the seasonal influenza vaccine [25 - 28]. Then, the question raised was whether the use of the flu vaccine reduced the common symptoms and severity of the outcomes of COVID-19. It is necessary to conduct more research on healthcare systems and different communities to explore the prevalence of the outcomes of COVID-19 in recipients of trivalent influenza and COVID-19 vaccines. In their research, Ruscio *et al.* showed that simultaneous vaccination against COVID-19 and influenza could help prevent respiratory and cardiovascular diseases and reduce mortalities [29, 30]. In another study, Ragni *et al.* found a significant negative relationship between receiving the influenza vaccine and COVID-19 diagnosis. Yet, receiving the influenza vaccine was ineffective in improving the outcomes of COVID-19 [18, 19, 31 - 33].

Then, the question raised was whether the influenza vaccine could reduce the typical symptoms and severity of the outcomes of COVID-19 in the elderly. The immune system undergoes many changes through ageing, known as immune aging. These changes affect many cellular and molecular elements of both the innate and acquired immune systems and their coordination in response to infections. These make the elderly population particularly vulnerable to new infectious diseases. Immune aging, characterized by a decrease in the ability to develop an adequate immune response to infection and sustainability to pro-inflammatory diseases, is a major factor in the elderly's susceptibility to COVID-19 [34 - 36]. The elderly over 65 years of age are known as the high-risk groups. They are more vulnerable than other age groups and need special care and attention. Social isolation, social distance, and quarantine measures to prevent the spread of COVID-19 raised concerns about the elderly's general health [37]. This disease adversely affects the physical and social health of the elderly, who already suffer immunodeficiency, low activity, and improper nutrition. Nurses play an important role in preventing the virus infection, treating and caring for the elderly, and providing rehabilitation after discharge [38, 39]. The outcomes of COVID-19 in the elderly include neurological, cardiovascular, respiratory, digestive, skeletal-muscular, behavioral, and mental-psychological changes, changes in nutritional status, pain, lung involvement, and mortality [36, 40].

There are contradictory findings in the existing literature in different countries and different service providers. In Iran, there is a lack of similar research on the prevalent outcomes of COVID-19 in recipients of trivalent inactivated influenza and COVID-19 vaccines. Most of the 60 to 80-year-old residents of Ramsar were vaccinated against both influenza and COVID-19 in health centers. Thus, the present study aimed to explore the outcomes and typical symptoms of COVID-19 in the elderly recipients of influenza and COVID-19 vaccines in Ramsar and Tonekabon cities in Iran.

2. METHODS AND MATERIALS

2.1. Design of Study and Sample Selection

The present research was cross-sectional and descriptive in type. The case study included the hospitals of Ramsar and Tonekabon cities in Iran. The research population consisted of all hospitalized patients aged 60-80 years in Ramsar and Tonekabon hospitals. The data collection began after the project was approved by the Research Council of Babol University of Medical Sciences and the research ethics committee. A census sampling method was used in this study. The inclusion criteria were: having visited the hospital due to COVID-19 infection, the age of 60-80 years, having received trivalent influenza and COVID-19 vaccines, having received two doses of COVID-19 vaccine, a proper interval between receiving two COVID-19 vaccinations (21 days for Spontik, 28 days for Sinopharm, and 3 months for Estrazinka), and entrance to the study two weeks after the second vaccination. The exclusion criterion was the incompleteness of more than two-thirds of the records and registration forms of patients hospitalized with COVID-19.

The necessary data were then extracted from the registration forms of the sample suffering from an acute respiratory disease in hospitals. The necessary information about the history of receiving the COVID-19 vaccine was collected from the health headquarters of Ramsar and Tonekabon. The census included the time span between the beginning of the national vaccination program (3 October) in health centers and hospitals until the sampling (26 May 2022). Since the majority of elderly residents of Ramsar (aged 60 to 80) were vaccinated against influenza and COVID-19 in health centers, the research population included all elderly residents (60-80 years) of Ramsar and Tonekabon. The data were collected using the information registration form of sampled patients suffering from acute respiratory distress syndrome (ARDS) (for COVID-19 patients) in Ramsar and Tonekabon hospitals. This study form was completed when the COVID-19 patients were admitted to hospitals.

2.2. Instrumentation

There were two data collection instruments: "The Demographic and Clinical Questionnaire" and "The Registration Form of Sampled Patients with Acute Respiratory Disease" as described below:

2.2.1. Demographic and Clinical Questionnaire

It includes information about age, sex, job, education level, place of residence, marital status, type of influenza vaccine, and type of COVID-19 vaccine.

2.2.2. Registration form of Sampled Patients with Acute Respiratory Disease

It includes information about receiving the influenza vaccine, receiving the COVID-19 vaccine, history of comorbidities, outcomes of COVID-19 (respiratory support, central nervous outcomes, cardiovascular outcome, renal and blood outcomes [*e.g.*, polynephritis/cystitis, ATN, uremia, DIC, bleeding (due to thrombocytopenia)], pulmonary outcome, determination of lung involvement, duration of hospitalization, and mortality rate), clinical symptoms of COVID-19 [(*e.g.*, typical symptoms, lower respiratory tract symptoms, cardio-respiratory symptoms), and auxiliary symptoms (*e.g.*, muscle pain-cramping, anorexia, chilling, skin bruising, joint pain, headache, nausea and vomiting, runny nose/sneezing, red eyes, diarrhea, fever and cough, abnormal hearing, conjunctival redness, radiological signs)].

2.3. Data Analysis

The data were analyzed using relevant descriptive statistics (frequency). A multivariate regression model was used to test the relationship between trivalent influenza and COVID-19 vaccination with the prevalence of typical symptoms and outcomes of COVID-19. However, the multivariate regression analysis was not applicable due to the small number of eligible subjects and the limited number of those in the statistical columns, and the results were not reported. SPSS 24 was used for data analysis.

3. RESULTS

A total of 11 elderly people with a mean age of 70.63±5.85 years in the age range of 60-78 years were examined in the study. All the elderly had no history of traveling in the past two weeks. 90.9% (n=10) of patients were hospitalized during the sampling (Table **1**).

Table 1. Demographic characteristics of the elderly who received influenza and COVID-19 vaccines in Ramsar and Tonekabon cities.

Demographic Variable	Levels	Number	Percent(%)
gender	men	7	63.6
	women	4	36.4
Level of Education	Under high school diploma	7	63.6
	High school diploma	3	27.3
	Academic	1	9/1
place of residence	City	7	63.6
	Village	4	36.4
marital status	Single	2	18.2
	married	9	81/8
Underlying disease	yes	11	100
	no	0	0
The frequency of infection with COVID-19	1	9	81.8
	2	2	18.2
Type of influenza vaccine received	Trivalent	10	90.9
	Quadrivalent	1	9.1
Type of COVID-19 vaccine received	AstraZeneca	1	9.1
	Sputnik	1	9.1
	Sinopharm	9	81.8
Patient's status during sampling	Hospitalized	10	90.9
	Outpatient	1	9.1
History of travel in the last two weeks	yes	0	0
	no	11	100
age (years); mean(SD)	70.63±5.85		

Table 2. Determining the clinical symptoms of COVID-19 infection in the elderly who received influenza and COVID-19 vaccines in Ramsar and Tonekabon cities.

Clinical Symptoms Of Covid	Levels	Number	Percent(%)
Key symptoms	no	4	36.4
	Cough	3	27.3
	Fever and cough	4	36.4

(Table 2) contd.....

Clinical Symptoms Of Covid	Levels	Number	Percent(%)
Lower respiratory tract symptoms	no	6	54.5
	Shortness of breath	2	18.2
	Difficult breathing	3	27.3
Cardiovascular symptoms	No	5	45.5
	Chest discomfort	6	54.5
Nervous system symptoms	No	7	63.6
	The feeling of confused/dizzy	2	18.2
	Sleepiness	2	18.2
Auxiliary symptoms	No	7	63.6
	Muscle pain and bruising	3	27.3
	Muscle pain, joint pain, and runny nose	1	9.1

The results showed that key symptoms (63.6 percent), cardiovascular symptoms (54.5 percent), lower respiratory tract symptoms (45.5 percent), nervous system symptoms (36.4 percent), and auxiliary symptoms (4 The highest prevalence of key symptoms of covid-19 is among the elderly. So that in the key symptoms, 27.3 percent of the elderly had cough symptoms and 36.4 percent had fever and cough symptoms (Table **2**).

36.4% of the elderly needed respiratory support; Also, the results showed that heart, kidney, blood and central nervous system complications were not observed in the elderly with covid-19 who received influenza vaccine and covid vaccine. Also, the results show that 9.1% of the elderly with covid had pulmonary ARDS (Table **3**).

The results showed that in terms of previous disease history, 45.4% of the elderly had one disease. Also, the results show that 54.5% of the elderly had a long history of aspirin use and all the elderly had no history of prophylaxis. Corona disease was detected in 27.3% of the elderly through CT scan findings (Table **4**).

Table 3. Determining the outcome of infection with COVID-19 in the elderly who received influenza and COVID-19 vaccines in Ramsar and Tonekabon cities.

Outcome Of COVID-19	Levels	Number	Percent(%)
Respiratory support	yes	4	36.4
	no	7	63.6
Cardiac outcome	no	11	100
	yes	0	0
kidney and blood outcome	no	11	100
	yes	0	0
Central nervous system outcome	no	11	100
	yes	0	0
Pulmonary outcome	no	10	90.9
	ARDS	1	9.1

Table 4. Determining the imaging findings, previous disease history, drug use history, and death and discharge information of elderly people who received influenza and COVID-19 vaccines in Ramsar and Tonekabon cities.

Variables	Levels	Number	Percent (%)
History of previous diseases	One disease	5	45.4
	Two diseases	4	36.3
	More than two diseases	2	18.3
History of prophylaxis	yes	11	100
	no	0	0
History of drug use	no	5	45.5
	Long-term consumption of aspirin	6	54.5
Imaging findings	no	8	72.7
	CT Scan	3	27.3
Discharge Status	yes	11	100
	no	0	0

(Table 4) contd.....

Variables	Levels	Number	Percent (%)
Patient status at discharge	Relative improved	5	45.5
	Improved	6	54.5
Death	yes	0	0
	no	11	100
Number of hospitalization days	Less than 3	3	27.3
	3-5	5	45.4
	More than 5	3	27.3

4. DISCUSSION

The present study aimed to explore the outcomes and common symptoms of COVID-19 in the elderly recipients of influenza and COVID-19 vaccines in Ramsar and Tonekabon. As the results showed, cardiovascular, lower respiratory system, nervous system, and auxiliary symptoms were, respectively, observed in the participants at the rates of 27.3 and 54.5 percent.

The involvement of several organs, including the liver, digestive system, and kidney, was reported in SARS in 2003 and recently in patients with COVID-19 [31]. Even though the respiratory and immune systems are the main targets of COVID-19, there is also acute kidney damage and protein excretion in the urine [31]. As the literature shows, neurological, cardiovascular, and respiratory outcomes have been observed in the elderly with COVID-19 [41 - 43]. This contradictory finding shows that it may be possible to reduce the severity of symptoms and the involvement of vital organs in patients with COVID-19 by vaccinating them with two vaccines, influenza and COVID-19.

In light of the present findings, the clinical symptoms in the elderly included mild symptoms such as fever, cough, shortness of breath, difficulty breathing, chest discomfort, confusion/dizziness, sleepiness, muscle pain and bruises, joint pain, and runny nose. Similar studies during the pandemic in 2019-2020 and before vaccination for COVID-19 showed that besides the symptoms mentioned above, there were more extensive and severe symptoms such as smell and hearing disorders, digestive disorders (*e.g.*, nausea and vomiting, diarrhea, stomachache, taste and smell disorders), anxiety and poor quality of sleep, low lymphocytes, skin rashes, abnormality in chest CT scan images and even death [34, 41]. Liu *et al.* reported that the most common symptoms of COVID-19 in the elderly were fever, cough, sputum, involvement of the lung lobes, and decreased lymphocytes [41]. These findings suggest that more research is needed to answer the question of whether it is possible to prevent the severity of symptoms of these two diseases (influenza and COVID-19) by vaccinating the elderly against the two diseases.

The frequency of COVID-19 outcomes in the elderly recipients of influenza and COVID-19 vaccines in Ramsar showed that a few elderly participants needed respiratory support. This result was consistent with another study by Fink *et al.* (2020). This study clinically examined subjects with a history of inactivated trivalent influenza vaccination, hospitalized with a definite diagnosis of COVID-19, and having received the influenza vaccine. The research findings indicated that vaccinated subjects needed invasive respiratory services less than the control [34]. In a study by Lee *et al.*, the mortality rate, severity of symptoms, and the need for respiratory aids were higher in the elderly over 65 years of age [45]. However, in another study by Hosseini Damiri *et al.*, fewer patients needed respiratory support. The statistical difference might be due to the different research populations, sample size, study time, and different history of chronic diseases [46].

The results also showed that cardiac, renal, blood and central nervous system outcomes were not observed in the elderly recipients of influenza and COVID-19 vaccines, and only 1 participant had the pulmonary outcome of acute respiratory distress syndrome (ARDS). These findings are consistent with a body of research [47 - 51]. This disease has numerous short-term or long-term complications in different body organs. Lung involvement is suggested as the main cause of mortality, and complications are frequently reported, such as lung fibrosis, secondary bacterial or fungal infections, cardiac involvement (myocarditis and pericarditis), and vascular complications such as pulmonary embolism [46]. The results of other studies have reported the COVID-19 outcomes in the elderly, including neurological, cardiovascular, respiratory, and renal-blood outcomes [41, 52, 53]. In light of the present findings and the existing literature, vaccination can be a useful method to prevent many complications of COVID-19.

The present study showed that the mortality rate was 0% in patients with a history of comorbidities (one disease, two, and more than two diseases). Furthermore, the results of studies by Arab *et al.* [54], Salari *et al.* and Firouzi *et al.* indicated an increase in the mortality outcome in people with a history of chronic disease and COVID-19, probably due to the different sample size, research population, and the history of vaccination [55, 56]. Daoust reported that the mortality rate of COVID-19 was higher in the elderly [57]. As reported by Zaki *et al.*, the severity of symptoms and mortality of COVID-19 were higher in the elderly with a history of chronic diseases [58]. The inconsistent findings of these studies show that vaccination against COVID-19 and influenza can help prevent the severe outcomes of the disease, including mortality in patients with comorbidities.

As the present findings showed, COVID-19 was diagnosed in 27.3% of the elderly through CT scan findings. Another study by Sun *et al.* found abnormalities in the chest CT scan images of 96% of patients infected with COVID-19, probably due to the different history of vaccination and the time setting of research [59]. In another study by Alian *et al.*, the percentage of lung involvement was 75.6% (within a range of 0-25%), 29.22% (within a range of 25-50%), and 27.20% (within a range of more than 75%) [60]. In a study by Shafiei *et al.*, per broncho vascular features were significantly observed in hospitalized patients with COVID-19. Furthermore, an increase in patient age increased the number of lobes involved in the lung. The consolidation level was significantly higher in

hospitalized patients with fever or myalgia. A significant increase was observed in linear opacities of hospitalized patients with diarrhea or nausea, indicating the high and severe involvement of lungs in COVID-19 patients in 2020 and before the national vaccination in Iran [61]. These data indicated the lung involvement in hospitalized patients before vaccination against COVID-19 and the usefulness of COVID-19 vaccination in preventing lung involvement.

As the results showed, more than half of the elderly had a complete recovery at discharge, and the other half had a partial recovery. In a study by Fink *et al.*, COVID-19 patients with a recent experience of inactivated influenza vaccination had significantly better clinical outcomes than unvaccinated patients in Brazil [61]. In a study by Caspi *et al.*, the severity of disease and mortality were lower in the elderly vaccinated against COVID-19 [62]; hence, it may be possible to take effective steps to improve the clinical findings of hospitalized patients by vaccinating the elderly against the two diseases, influenza and COVID-19.

Many studies have focused on the clinical characteristics of Covid-19 patients, and information about the factors affecting the severity and lethality of the disease among the elderly is still limited [63] According to the findings, the duration of hospitalization decreased, and the mortality rate was 0% in patients. The results are consistent with a study by Fang *et al.* (2020), which showed a lower mortality rate of COVID-19 patients vaccinated with Brazil's trivalent inactivated influenza vaccine. The vaccinated subjects had a 16% lower mortality rate than the control group [64]. In another study, Marín-Hernández *et al.* (2020) showed a significant negative relationship between the mortality rate induced by COVID-19 and receiving the influenza vaccine in the elderly [41]. The mortality rate of the elderly recipients of the COVID-19 vaccine was lower in the study conducted by Parra *et al.* [65].

The usefulness of vaccination against influenza and COVID-19 to prevent the mortality of the elderly with COVID-19 should be taken seriously according to the present findings because age is a risk factor for COVID-19 and mortality in the elderly [61].

4.1. Limitations

The limitations of the study include the limited sample size and the impossibility of generalizing the results. It was impossible to test the regression of the symptoms and outcomes of COVID-19 on the participants' demographic variables due to the limited sample size. The study was descriptive and it was impossible to control all the results' determinants.

4.2. Suggestions

It is suggested to conduct further research on healthcare systems and different populations to answer the question about the prevalence of symptoms and outcomes of COVID-19 in recipients of trivalent influenza and COVID-19 vaccines. It is also suggested to test the relationship between the regression of symptoms and the outcome of COVID-19 on participants' demographic variables.

CONCLUSION

There are always concerns that the confluence of COVID-19 and seasonal influenza in the fall and winter may lead to significant mortality and impose high costs on the health system. Therefore, it is necessary to explore the relevant factors that may increase the disease burden on society and take the required measures. Health providers and policymakers in the world aim to prevent or reduce the severity of disease outcomes. The most effective countermeasure against influenza virus and COVID-19 infection is to use preventive vaccines. The results of the present study showed reduced clinical symptoms and less severe outcomes, improved clinical results, and less mortality in the elderly with a history of vaccination against influenza and COVID-19. Therefore, the present findings support measures taken to increase the coverage of vaccination against influenza and COVID-19 in the public, especially the elderly population.

LIST OF ABBREVIATIONS

COVID-19	=	Corona Virus-19
ARDS	=	Acute Respiratory Distress Syndrome

AUTHORS' CONTRIBUTION

All authors participated and approved the study design. FM, ZF, and FC contributed to the design study, AZ, SAM, and FL collected the data and analyzed it by KHA and HRE. The final report and manuscript were developed by FM, ZF, and AZ. All authors read and approved the final draft.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Research Ethics Committee of Babol University of Medical Sciences (#IR.MUBABOL.HRI.REC.140.178). Written informed consent was obtained from all group members. Consent to submission was all co-authors, as well as the corresponding author - tacitly or explicitly - at the institute/organization where the work has been carried out before the work was submitted.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human participants were used in accordance with the ethical standards of the committee in charge of human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Consent was obtained from all participants of this study.

STANDARDS OF REPORTING

STROBE Guidelines were followed in this study

AVAILABILITY OF DATA AND MATERIALS

The datasets used in the study are available from the corresponding author [Z.F] upon reasonable request.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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