Original Research Article

Influenza Vaccination with the Risk of SARS-CoV-2 Infection and Severe Illness at the Al-Wafa House for the Care of the Infirm and the Elderly in Massa, Libya

Salema R. M Qowaider[1], Faraj Sabir Sulayman[2], Rogia A Haduth[3], Marfoua S. Ali[4*] 🆔

[1]Department of Microbiology and Immunology, Faculty of Medicine, Omar Al-Mukhtar University, El-Beyda, Libya
[2]Department of community medicine, Faculty of Medicine, Omar Al-Mukhtar University, El-Beyda, Libya
[3]Department of medicine, Faculty of Medicine, Omar Al-Mukhtar University, El-Beyda, Libya
[4]Department of Zoology, Faculty of Science, Omar Al-Mukhtar University, El-Beyda, Libya

*Corresponding author: Marfoua S. Ali
Department of Zoology, Faculty of Science, Omar Al-Mukhtar University, El-Beyda, Libya,
ORCID: https://orcid.org/0000-0003-0814-8651

Abstract

SARS CoV-2 is a pandemic infection that is associated with a significant mortality rate in elderly patients due to severe acute respiratory SARS-CoV-2 infection. When compared to adults, children had a lesser vulnerability to SARS-CoV-2 infection and a milder severity. This could be due to the large number of vaccines. This study was aimed to investigate whether the influenza vaccine may reduce the susceptibility and severity of SARS-CoV-2 infection. 79 inmates and workers at the Al-Wafa House for the Care of the Infirm and the Elderly in the Massa region was enrolled from November 15th to December first, 2020, and were test for SARS-CoV-2 infection by PCR on an oropharyngeal swab and presence of antibodies IgG/IgM against SARS-CoV-2 infection. Clinical data, outcomes, BCG and influenza vaccination status were collected from the medical records. 3% of all subjects were positive for IgG and 16.7% were positive for both IgM and IgG at the same time. While 16.7% were negative for both antibodies. Only 17 workers were vaccinated against influenza on November 1st, all workers had received the BCG vaccination. 78.4% of all workers were positive for SARS-CoV-2 IgG and 16.2% were positive for both SARS-CoV-2 IgM and IgG. Results from the present study found that 87% of all subjects had BCG vaccination, and this might offer at least partial protection against SARS-CoV-2. Results were also found that a relationship between vaccination against influenza and asymptomatic, mild, moderate, and severe symptoms associated with the SARS-CoV-2 were found at 13.54, 25.64, and 20.14 respectively, at a significant level. However, the relationship between vaccination against influenza and moderate symptoms associated with the SARS-CoV-2 infection was not significant. According to a current study, influenza immunization could lower SARS-CoV-2 mortality. Prospective investigations are required to verify this conclusion.
Keywords: SARS-CoV-2.infiction, influenza vaccination, illness, Al-Wafa House for the Care of the Infirm and the Elderly in Massa, Libya.

INTRODUCTION

The coronavirus disease of 2019 (SARS-CoV-2) was declared a global public health emergency by the World Health Organization (WHO) in January 2020 [1]. As of May 2021, there are still many countries that do not have SARS-CoV-2 vaccines [2]. There was some evidence that an influenza vaccine could elicit nonspecific immune responses in the immune system, lowering the chance of SARS-CoV-2 infection or reducing the severity of SARS-CoV-2 disease following infection [3]. According to certain research, SARS-CoV-2 patients with positive influenza A immunoglobulin M (IgM) had a lower risk of severe SARS-CoV-2 illness and fatality than those with negative influenza A immunoglobulin M [3]. In a Brazilian study, patients who received influenza vaccine had a 17 percent lower mortality rate. Other studies have also confirmed that influenza vaccination is associated with lower risk of hospitalization and mortality between patients diagnosed with SARS-CoV-2 infection [4].

New studies have proposed that previous vaccination to pathogens such as influenza and tuberculosis may cause some protection against SARS-CoV-2 [5]. Although no cross-reactivity between SARS-CoV-2 and influenza-induced immunity or protection has been shown, numerous speculated mechanisms of influenza vaccine's probable defensive impact have been proposed in recent research [6, 7]. The first proposed mechanism was defined in the most recent case-control study of 261 healthcare staffs, they noted a number of previous studies that recommended both influenza and coronaviruses engage with the tetraspanin antibodies and angiotensin-converting enzyme 2 (ACE-2). Therefore, there is confidence that ACE-2 and tetraspanin antibodies may inhibit low-pathogenic influenza A virus and coronavirus infections. Concentrate on the presence of MF59 in the influenza vaccine: an oil-in-water squalene emulsion that has been indicate to help in potentiating an immune response to variants of SARS-CoV-2 [7]. Otherwise, influenza vaccination's likely has protective effect may possibly explained by its capability to stimulate natural killer cells activation [5, 8, 9]. Susceptibility and mortality rates of SARS-CoV-2 patients increase with age even after the correction for comorbidity and gender [10, 11]. From all possible factors which can clarify a lower severity rate of SARS-CoV-2 in children, there is a no specific immune response to previous vaccinations to other pathogens, particularly respiratory viruses [11, 12]. The theory is the vaccine administration possibly will lead to an increase or reduce the risk to gain infections caused by other microorganisms [11, 12]. Flu persuades an increased the expression of ACE2 receptors in alveolar cells and also may increase the severity of a subsequent infection with SARS-CoV-2, whereas preventing influenza by vaccine may decrease the severity of the SARS-CoV-2-related disease [7].

In addition to the influenza vaccine, epidemiological data on the global prevalence of SARS-CoV-2 showed that countries with Bacillus Calmette-Guérin (BCG) immunization policies have a lower rate of SARS-CoV-2-related death than countries without such a strategy. [1, 13]. Several clinical trials are being done around the world to see if the BCG vaccine will protect healthcare personnel who work directly with SARS-CoV-2 patients from mortality. Clinical trials have shown that the BCG vaccine can reduce mortality from diseases caused by non-targeted microorganisms, most likely due to nonspecific effects (heterologous effects) [14]. By the end of May 2020, the available information on the SARS-CoV-2 pandemic indicated the great effect of the BCG vaccine in reducing the number of COVID-19 death cases [14-16]. However, other studies reported that BCG vaccine does not have any influence on the incidence of SARS-CoV-2 [17].

The BCG vaccine was first offered in Libya in the early 1950s. Libya was the first country in the region to implement BCG vaccination on a large basis, passing legislation in 1971 that made neonatal BCG immunization mandatory, resulting in 99.9% BCG vaccination coverage. [18]. In the Libyan situation, where the conflict is ongoing for years, with weakness of the health systems and limited access to even the most basic medical care services, ideally, SARS-CoV-2 was expected to hit the country as a disaster. However, what epidemiologists presented and anticipated for Libya using various modules does not reflect the true state of the disease in Libya. When comparing the disease pattern in Libya to that of other countries, there must be various aspects and reasons for these conclusions [19]. Therefore this study was aimed to find out impacts of influenza vaccination with the risk of SARS-CoV-2 infection and severe illness at the Al-Wafa House for the Care of the Infirm and the Elderly in Massa, Libya.

METHODOLOGY
Subjects Information and Data Collection
The Supreme Committee to Combat the Corona Epidemic of the Interim Government was tested for SARS-CoV-2, inmates and workers at the Al-Wafa House for the Care of the Infirm and the Elderly in the Massa region.

This study was collected information providing by the Center on the demographics, epidemiological information, clinical symptoms, and outcomes from all laboratory-confirmed cases of SARS-CoV-2 initially suspected/identified by symptoms between November 15th to December first, 2020. It was used the two weeks window to support the temporality between vaccination against influenza (VAXIGRIP Intramuscular Suspension (single dose) contains inactivated, split of Influenza virus) and SARS-CoV-2 infection, by excluding people who had received an influenza vaccination after November, 1, 2020, for a reason, that, it generally takes two weeks for the body to response and generates antibodies against influenza virus after vaccination, so the effect of the influenza vaccination would begin two weeks after the vaccination.

Forty two elderly and thirty seven workers were tested for evident clinical symptoms of SARS-CoV-2 and with a positive Nucleic Acid Amplification Test. The diagnosis of SARS-CoV-2 infection was based on the WHO interim guidance [20]. The clinical presentation of mild-to-moderate SARS-CoV-2 substantially varies according to the patients. Olfactory dysfunction seems to be an important underestimated symptom of mild-to-moderate SARS-CoV-2 that needs to be recognized as such by the WHO interim guidance [20].

Information about age, gender, receive/not receives influenza vaccine. All the elderly exposure (that is, influenza vaccination), presence of antibodies IgG/IgM (after fourteen days form PCR results) were used. Information regarding past and present BCG administration practices in every country was extracted from the BCG world atlas.

STATISTICAL ANALYSIS

The data were interconnected in Figures and Tables, with numerical data displayed as a number and a percentage. To find the significant difference between the observed and studied variables, the chi square was utilized in bivariate analysis to examine the relationship between categorical variables. The Paired T-test was used to find out the relationship between vaccination against influenza and asymptomatic, mild, moderate, and severe symptoms associated with the SARS-CoV-2. P value was taken as the level of significance at <0.05. Statistical analysis was carried out in Minitab software (version17).

RESULTS

This work resulted in a sample of 79 subjects, 42 of them were elderly persons and the rest 37 were staff working there. Elderly persons were 57.2% male and 42.8% female, and their age ranged from 51 years to < 80 years for all those who live at the Al-Wafa House for the Care of the Infirm and the Elderly in the Massa region. The highest prevalence of age was found among those aged 51-60 years (Figure 1). And staff working was 51.4 % male and 48.6 % female; their age ranged from 19 years to 60 years for all those who work at the Al-Wafa House for the Care of the Infirm and the Elderly in the Massa region. The highest prevalence of age was found in those aged 19-30 years (Figure 2). The job descriptions of the research sample of the employees working at the elderly home according to the age groups were described in Table 1. Figure 3 showed the number and percentage of 42 residents of the nursing home that were receiving BCG vaccination

according to age groups. Ten people had not received BCG vaccination, and all of them were over 60 years of age. Table 2 showed that on November 1st, all elderly people were immunized against influenza, and the PCR test results for inmates in the research sample were organized by age group, and all of them were positive for this test. Results of the presence of antibodies IgG, IgM against SARS-CoV-2 after fourteen days from PCR results are shown in Table 2. 83% of all subjects were positive for IgG and 16.7% were positive for both IgM and IgG at the same time. While 16.7% were negative for both antibodies (Table 2). Similar details were summarized for workers in Table 3. Only 17 workers were vaccinated against influenza on November 1st, all workers had received the BCG vaccination. In terms of PCR results, 51.4 % were negative and 48.6 % were positive for this test. Results of the presence of IgG and IgM against SARS-CoV-2 after fourteen days from PCR results are shown in the Table 3. 78.4% of all workers were positive for SARS-CoV-2 IgG and 16.2% were positive for both SARS-CoV-2 IgM and IgG. All previous parameters were not shown to have a significant difference between positive and negative for each observation. Table 4 illustrates the percentage and number of subjects who received or did not receive influenza vaccination with the four categories of symptoms associated with the SARS CoV-2 on the elderly and workers, which was found to be 2.604 upon Pearson Chi-Square analysis. The data in Table 5 indicates that there is a relationship between vaccination against influenza and asymptomatic, mild, and severe symptoms associated with the SARS-CoV-2 according to elderly and worker subjects based on the test (T). The significant relationship between influenza vaccination and asymptomatic, mild, moderate, and severe symptoms associated with SARS-CoV-2 was found to be 13.54, 25.64, and 20.14, respectively. However, the relationship between vaccination against influenza and moderate symptoms associated with SARS-CoV-2 was not significant.
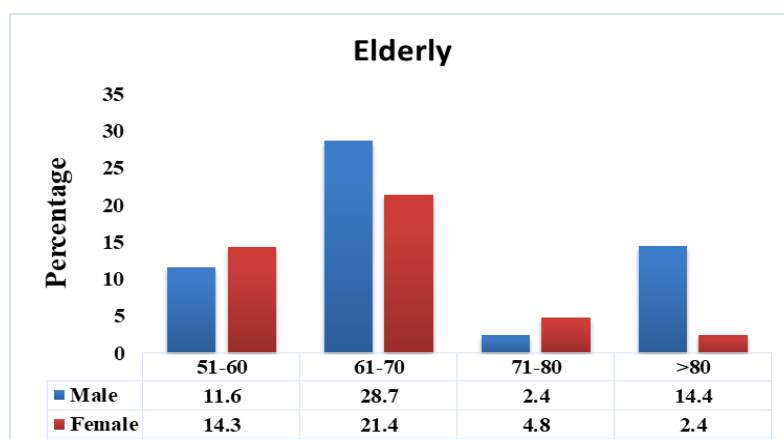

Figure 1: Distribution of age groups for inmates at the Al-Wafa House for the Care of the Infirm and the Elderly in the Massa region (%)
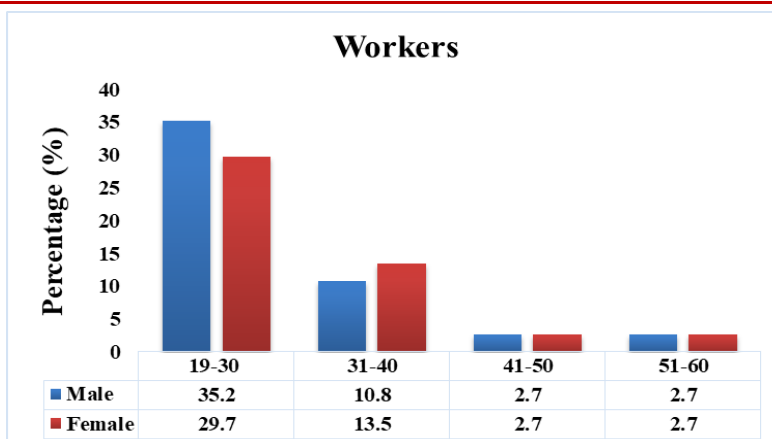
Figure 2: Distribution of age groups for workers at the Al-Wafa House for the Care of the Infirm and the Elderly in the Massa region (%)

Table 1: Job description of the research sample of the employees working at the elderly home according to the age groups (Number (%))

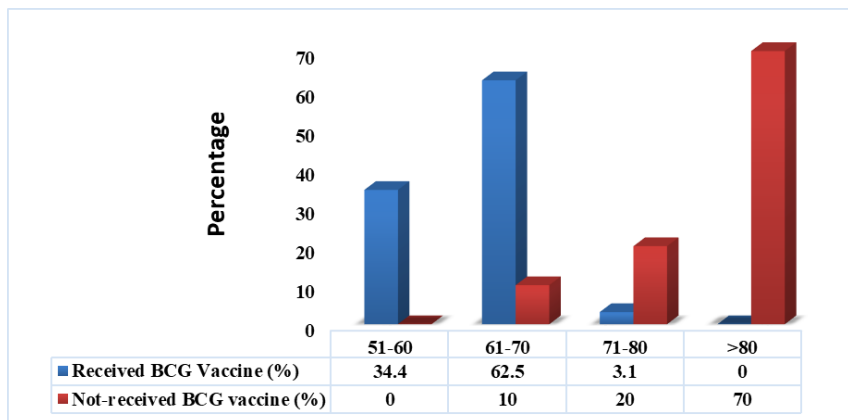|	Age group (Years)			
Job	**19-30**	**31-40**	**41-50**	**51-60**
Nurse	22 (59.5)	6 (16.2)	-	-
Employee	-	1 (2.7)	1 (2.7)	
Physical therapy	-	1 (2.7)	-	-
Driver	-	2 (5.4)	-	-
Washer		1 (2.7)	1 (2.7)	-
Chef	-	-	-	1 (2.7)
Director	-	-	-	1 (2.7)
Total	22 (59.5)	11 (29.7)	2 (5.4)	2 (5.4)

Figure 3: Inmates in the research sample who received BCG vaccination according to age groups

Table 2: An elderly at the Al-Wafa House in Massa region who were vaccinated against influenza, receive BCG vaccine, positive PCR, positive/ Negative IgM and IgG after 14 days from PCR results according to age groups (No. (%))

Age groups	Receive influenza vaccine. (%)	Receive BCG vaccine. (%)	Not-receive BCG vaccine. (%)	Positive PCR. (%)	Positive IgG (%)	Positive IgM. .(%)	Negative IgG or IgM.(%)
51-60	7 (16.7)	11 (26.2)	0	11 (26.2)	10 (23.8)	2 (4.8)	3 (7.1)
61-70	25 (59.5)	20 (47.6)	1 (2.4)	21 (50)	15 (38.1)	3 (7.1)	4 (9.5)
71-80	3 (7.1)	1 (2.4)	2 (4.8)	3 (7.2)	3 (7.1)	1 (2.4)	0
<80	7 (16.7)	0	7 (16.7)	7 (16.7)	7 (16.7)	1 (2.4)	0
P. Value					0.08		
Total. No. (%)	42(100)	32 (76.2)	10 (23.9)	42 (100)	35 (83.3)	7 (16.7)	7 (16.7)

Table 3: The employees working in the nursing home who were vaccinated against influenza, receive BCG vaccine, positive/negative PCR, positive/Negative IgM and IgG after 14 days from PCR results according to age groups (No. (%)

Age groups	Receive influenza vaccine. (%)	Not-receive influenza vaccine. (%)	Receive BCG. No. (%)	Positive PCR. No. (%)	Negative PCR. No. (%)	Positive IgG (%)	Positive IgM. .(%)	Negative IgG or IgM.(%)
19-30	6 (16.2)	18 (48.7)	24 (64.9)	14 (37.8)	10 (27)	16 (43.2)	4 (10.8)	6 (16.2)
31-40	7 (18.9)	1 (2.7)	9 (24.3)	4 (10.8)	5 (13.5)	10 (27)	1 (2.7)	0
41-50	2 (5.4)	1 (2.7)	2 (5.4)	0	2 (5.4)	1 (2.7)	1 (2.7)	0
51-60	2 (5.4)	0	2 (5.4)	0	2 (5.4)	2 (5.4)	0	0
P. Value	0.28			0.8		0.19		
Total. No. (%)	17 (45.9)	20 (54.1)	37 (100)	18 (48.6)	19 (51.4)	29(78.4)	6 (16.2)	6(16.2)

Table 4: Percentage and number of subjects who receive/not receive influenza vaccination with the four categories of symptoms associated with the SARS CoV-2. (No. (%))

Receive influenza vaccine No (%)	Asymptomatic. No (%)	Mild No (%)	Moderate No (%)	Severe No (%)	Pearson Chi-Square
Yes	59 (74.7)	52 (65.8)	4 (5.1)	1 (1.3)	2 (2.5)	2.604
No	20 (25.3)	20 (25.3)	0 (0)	0 (0)	0 (0)	
Total	79	72	4	1	2	

Table 5: The effect of influenza vaccination on the symptoms associated with the SARS CoV-2 on the elderly and workers using the (T) test

Paired Samples Test								
Receive influenza vaccine	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Asymptomatic	.8481	.55674	.06264	.72340	.97281	13.54	78	.000
Milled	1.658	.57481	.06467	1.5294	1.7869	25.64	78	.000
Moderate	.3544	1.79770	.20226	-.04823	.75709	1.752	78	.084
Severe	1.658	.73181	.08233	1.4943	1.8221	20.14	78	.000

DISCUSSION

In the current study, there were significant association between influenza vaccinations and asymptomatic, the mild, and severe symptoms associated with the SARS-CoV-2 infection. Several explanations could answer this association, including influenza vaccine's potential protective impact against SARS-CoV-2 disease [21-23]. This may happen if the vaccine generates enough innate immune memory that if a different respiratory infection similar to SARS-CoV-2 appeared, the resident lung immune system would be notified for a quick reaction, potentially affecting SARS-CoV-2 disease acquisition. However, with the attenuated influenza vaccine, which is more likely to induce local immunity than the inactivated vaccine, this condition is more likely to occur [24-26]. Immune system stimulation by influenza vaccines might happen through activation of the immune system by influenza vaccination which assists early recognition of SARS-CoV-2. Influenza vaccine maintains the immune system active through Toll-Like Receptor 7 (TLR7- R). TLR7- R plays an important role in binding of RNA respiratory viruses, like, SARS-CoV-2 [5]. Influenza A infection up-regulates pulmonaryACE2

receptors and thus leads to increased SARS-CoV-2 infection [7]. Vaccination against influenza can help reduce the severity of the disease and has been linked to a lower risk of death from SARS-CoV-2 infection in the elderly [27-29]. It's possible that the discovered link was discovered by chance, or that it's linked to seasonal diseases [4, 30].

Even if influenza vaccination was related to a significant reduction in the risk of SARS-CoV-2 infection compared to those who did not receive vaccination, this impact could be due to the healthy vaccine effect, as persons who were vaccinated may be healthier than those who were not [31]. Furthermore, people who have been vaccinated frequently engage in other healthy behaviour's that may help to prevent SARS-CoV-2 transmission or reduce SARS-CoV-2 severity [32]. And this could explain the findings of a recent research, which indicated that all workers were asymptomatic. This study results recommend that an influenza vaccine looks to have a protective effect against SARS-CoV-2 infection. This also, was consistent with previous data that proposed that an influenza vaccination may reduce the risk of a SARS-

CoV-2 infection or severe SARS-CoV-2 illness. Meanwhile, results from present study found that 87% of all subjects were had BCG vaccination and this might offer at least a partial protection against SARS-CoV-2. However, the increasing number of positive cases in Libya in following months from this study could support the reports claiming that BCG vaccine has no role in protection from SARS-CoV-2 [19, 33].

According to a recent study, influenza vaccination may be effective in protecting elderly adults against moderate and severe SARS-CoV-2 illness. Regardless of comorbidity, this protective effect remains. Natural killer cell activation has been suggested as a possible mechanism in the literature. Despite the fact that our findings may be limited in generalizability and our vaccination rate is low, it is extremely relevant given the forthcoming influenza season. Not only may boosting influenza vaccination reduce flu morbidity and death, but it could also help flatten the SARS-CoV-2 pandemic's curve.

CONCLUSION
The influenza vaccine may only provide a modest level of protection against SARS-CoV-2 infection. To lower the danger of co-infection with influenza and SARS-CoV-2, it is still necessary to have an influenza vaccination. Because influenza and SARS-CoV-2 have similar symptomatology and consume the same medical resources, the influenza vaccination is critical in reducing the number of severe influenza patients so that resources can be freed up to deal with another wave of SARS-CoV-2 patients.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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