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Efficacy of Influenza Vaccine on Prophylaxis of COVID-19 – a Prospective Cohort Study Done on 37 Patients in Armenia

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Abstract: There are currently no vaccines with hundred percent efficacy or no effective treatments for lessening hospitalizations brought about by Coronavirus disease 2019 (COVID-19). The influenza vaccination has proposed as a potential method to decrease the seriousness of COVID-19. A prospective cohort study of 37 individuals of Paediatric, Adult and Geriatric group was taken and they were vaccinated against the influenza virus for two consecutive years with the 'Influenza' vaccine. Antibody titers were then measured and PCR tests were done to confirm infections. The severity of infection was reflected by hospitalization and emergency unit admission. Examination was performed to analyze the connection between influenza vaccine status and hospitalization. As compared to those who had been vaccinated, COVID-19-positive patients who had not received influenza vaccine during the previous year had a higher risk of hospitalization and ICU admission. Some individuals who were vaccinated for influenza did not even develop any symptoms at all and the others were noticed to have very faint symptom onset. The findings from this study indicate that influenza vaccination can protect against COVID-19 infection in moderate and severe cases. Regardless of comorbidity, this calming influence remains. The literature indicates that RNA interference and natural killer cell activation could be involved.

Keywords: COVID-19, Influenza, Vaccine, Vaccination, Efficacy, Coronavirus

1. Introduction

An influenza vaccine is generally taken by all individuals living in endemic countries. It is a flu vaccine which is administered with the help of a needle which provides protection against four or five strains of influenza viruses that are prone to cause infection found out by researchers. These vaccines are developed twice a year and the versions are updated. Most of these provide protection in most of the cases and are proclaimed to be really effective.

The COVID-19 or the novel coronavirus is an on-going pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) which has created surge in infection rates all over the world. Different people have reported various symptoms to the COVID-19 but the most frequent presentation is pneumonia, manifested by fever, fatigue, dry cough, dyspnoea, and pulmonary infiltrations [4, 13]. This study was sought to find a possible area of correlation between the intensity of the symptoms of COVID 19 infected individuals who were vaccinated for influenza previously. Some major questions raised by this study are to find out if the previous administration of Influenza vaccine can cause a reduction in the disease severity of the

coronavirus. Since there is no powerful treatment or antibody accessible for COVID-19 to this date, different measures must be taken to diminish the bleakness and mortality of this infection. This sphere of research can also be taken as an opportunity to offer a good prophylaxis to people susceptible to severe infections by the Influenza vaccine.

2. Methods

A prospective cohort study of 37 individuals was undertaken for a time span of 23 months from February 2019 to January 2021 at Tairov Polyclinic, Armavir Province, Etchmiadzin, Armenia. These individuals are grouped into three categories for the purpose of classification of results. The first is the Paediatric group which included children aged 9-15 years, five males and four females. The second group including a total of 14 adults comprises five males and nine females. The third group includes 14 members of the geriatric population between the ages of 65-85, involving six males and eight females. One of the individuals in the geriatric group was on dialysis for numerous years. The members of the adult and geriatric groups have comorbidities like atherosclerosis, hypertension, type 2 diabetes, ischemic heart disease, atrial fibrillation and chronic renal failure, moderate or severe asthma, pre-existing COPD, pulmonary fibrosis and cystic fibrosis.

These individuals were vaccinated by the vaccine shot in February 2019, and then revaccinated in February 2020.

The influenza vaccination is an egg-derived vaccine which is inactivated. It is indicated for the prophylaxis of influenza for children and adults 6 months of age and above. It cannot treat an existing infection. Mild side effects can be caused by this vaccine which includes headache, weakness, tiredness, and pain or swelling at the vaccination site.

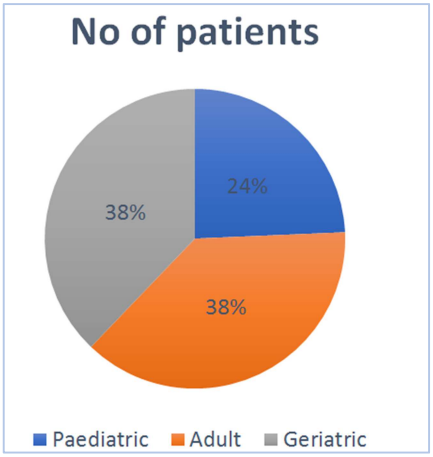

Figure 1. *Showing the percentage/number of patients in each group (out of 37).*

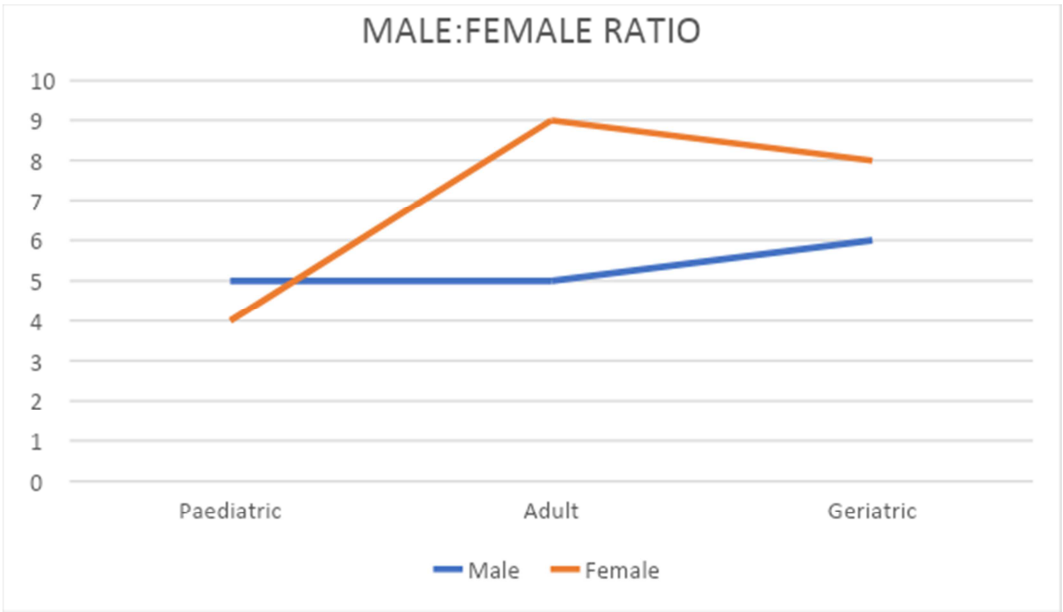

Figure 2. *Graph showing the ratio of Male/Female between each classified group.*

Mechanism of Action of Influenza Vaccine Used in Our Research

Influenza vaccine which comes in tetravalent form provides active immunisation against four influenza virus strains: An A/(H1N1) strain, an A/(H3N2) strain, a B/Victoria strain and a B/Yamagata strain, which was used in our research. Tetravalent form of vaccine is manufactured according to the same process as trivalent influenza vaccine which induces humoral antibodies against the hemagglutinins. These antibodies neutralise influenza viruses with matching antigens which has entered the body during infection. Specific levels of haemagglutination-inhibition (HI) antibody titre post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza illness but the HI antibody titres have been used as a measure of vaccine activity. Seroprotection is obtained within 2-3 weeks. The duration of post-vaccination immunity to homologous strains or to strains closely related to the vaccine strains varies but is usually between 6-12 months.

3. Result

A COVID ANTIBODY test was performed on all the subjects of this study in the first week of the month of January 2021 and the results have been illustrated below in the tabular column. Three members of the adult group (two males, one female) and five members of the geriatric group (two males, three females) upon anamnesis revealed that they have had mild symptoms of COVID 19 like body ache and malaise during the timeframe construct of the study but no RT-PCR test was done to confirm this information. They received symptomatic treatment for their complaints (PCM). Out of these eight individuals who experienced mild symptoms, five had high antibody titres (70-95) compared to the rest. None of the paediatric patients had high antibody titres or complained of any symptoms.

Group	No of patients who developed mild symptoms
Paediatric	0
Adult	3
Geriatric	5

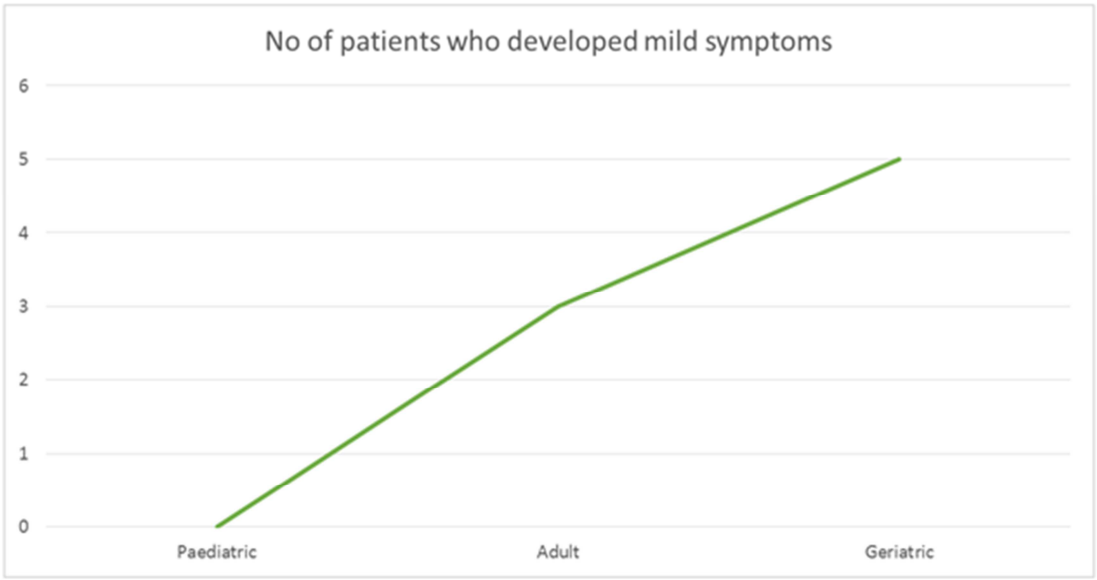

Figure 3. *Graphical representation of different patient groups which contracted COVID.*

Table 1. *Shows the number and description of patients who developed mild symptoms of COVID-19.*

S. N.	GROUP	SEX	AGE	CO-MORBIDITIES	Influvac 2019	Influvac 2020	Developed COVID-19	COVID Symptoms
1	PAEDIATRICS	M	14	NONE	Y	Y	NO	n.a
2	PAEDIATRICS	F	10	NONE	Y	Y	NO	n.a
3	PAEDIATRICS	F	9	NONE	Y	Y	NO	n.a
4	PAEDIATRICS	M	12	NONE	Y	Y	NO	n.a
5	PAEDIATRICS	M	14	NONE	Y	Y	NO	n.a
6	PAEDIATRICS	M	15	NONE	Y	Y	NO	n.a
7	PAEDIATRICS	M	11	NONE	Y	Y	NO	n.a
8	PAEDIATRICS	F	13	NONE	Y	Y	NO	n.a
9	PAEDIATRICS	F	10	NONE	Y	Y	NO	n.a
10	ADULT	M	25	NONE	Y	Y	NO	n.a
11	ADULT	F	36	Hypertension	Y	Y	YES	Loss of smell and taste, Fever
12	ADULT	M	45	NONE	Y	Y	NO	n.a
13	ADULT	F	18	NONE	Y	Y	NO	n.a
14	ADULT	F	27	COPD	Y	Y	NO	n.a
15	ADULT	F	49	NONE	Y	Y	NO	n.a
16	ADULT	M	53	Diabetes Mellitus	Y	Y	YES	Fever, Loss of smell
17	ADULT	F	41	NONE	Y	Y	NO	n.a
18	ADULT	M	20	Cholesterol	Y	Y	NO	n.a
19	ADULT	F	28	Cholesterol	Y	Y	YES	Fever, Dry cough, Fatigue
20	ADULT	F	34	COPD	Y	Y	NO	n.a
21	ADULT	M	38	Hypertension	Y	Y	NO	n.a
22	ADULT	F	57	NONE	Y	Y	NO	n.a
23	ADULT	F	43	NONE	Y	Y	NO	n.a
24	GERIATRIC	M	70	Hypertension, DM	Y	Y	NO	n.a

S. N.	GROUP	SEX	AGE	CO-MORBIDITIES	Influvac 2019	Influvac 2020	Developed COVID-19	COVID Symptoms
25	GERIATRIC	F	81	Atrial fibrillation	Y	Y	NO	n.a
26	GERIATRIC	F	67	Ischemic Heart Disease	Y	Y	YES	Fatigue, Fever, Dry cough
27	GERIATRIC	M	77	Chronic Renal Failure - on dialysis	Y	Y	YES	Fever, Loss of taste
28	GERIATRIC	M	84	COPD	Y	Y	NO	n.a
29	GERIATRIC	F	66	Asthma	Y	Y	YES	Loss of smell and taste, Dry cough
30	GERIATRIC	M	69	NONE	Y	Y	NO	n.a
31	GERIATRIC	F	83	Pulmonary Fibrosis	Y	Y	YES	Fever, Fatigue
32	GERIATRIC	M	72	Hypertension	Y	Y	NO	n.a
33	GERIATRIC	F	78	Cystic Fibrosis	Y	Y	YES	Body ache, Fever, Dry cough
34	GERIATRIC	F	75	Hypertension	Y	Y	NO	n.a
35	GERIATRIC	M	85	Diabetes Mellitus	Y	Y	NO	n.a
36	GERIATRIC	F	80	COPD	Y	Y	NO	n.a
37	GERIATRIC	F	73	NONE	Y	Y	NO	n.a

4. Discussion

Based on the interpretation of several published manuscripts and our study, some are of the proposal that Influenza vaccine is an absolute benefit for the elderly population. Another sphere where the vaccine can tend to have a very beneficial impact is the high-risk population for COVID 19. The vaccine was found to be successful at lessening the rate of hospitalization from pneumonia and furthermore the rate of death in older individuals with constant lung illnesses [18]. Other studies also claim the possibility of influenza vaccination leading to increased susceptibility to SARS-COV2 through immune mediated mechanisms like Antibody dependent enhancement (ADE) [11]. The sicknesses brought about by influenza infection and SARS-CoV-2 both offer a comparative course of transmission (respiratory droplets), some respiratory and some systemic manifestations, yet they firmly contrast regarding paces of serious and lethal cases, and peculiarly of the age groups predominantly affected [9]. Moreover, influenza specially influences kids and young grown-ups, but SARS-CoV-2 disease rate increases with age [15]. As neither a particular vaccine against SARS-CoV-2 nor anti-COVID-19 medications are accessible yet, studies propose a genuine danger of second, third and fourth waves of the COVID-19. It might be relevant to survey whether influenza vaccination could relieve another possible COVID-19 outbreak [1, 14].

A study based in Italy recognized limited cases of COVID 19 in the elderly population because they had been annually vaccinated against the seasonal Influenza A and B viruses [2]. Another study highlighted some more trends- In nations or territories with low influenza occurrence, influenza immunization will be defensive against COVID-19 severity. This system will be more effective in nations / areas with lesser populace density. Additionally, the option of pneumococcal immunizations or vaccinations would decrease COVID 19 severity in zones with a low frequency of influenza and lower respiratory tract infections. These can be devised as helpful interim measures before COVID-19 vaccines are distributed in the routine clinical practice around the world [3]. Furthermore, an interesting study based on healthcare workers in US found a positive correlation between the Influenza vaccinations COVID-19. In particular, physician and nurses were noted to have very high vaccine uptake rates and this showed a decrease in incidence of the SARS-COV-2 among them, coming to less than one percent of infection [8, 12]. Another feasible component by which influenza (H1N1) could decrease the SARS COV-2 seriousness is RNA interference. RNA interference need not be a synthesized phenomenon. It could be Nature's protection mechanism [19]. Likewise, rhinovirus can meddle with the influenza infection. Influenza vaccine can improve the trained immunity of the peripheral mononuclear cells in-vitro, and it can reduce the Covid19 incidence in a small cohort. The RNA interference can be a direct system without including memory cells [10, 16]. Lastly, some studies recommended to promote influenza vaccine as a global public health boon even if the evidence collected so far is limited, this would greatly benefit the management of the on-going pandemic by helping out in differential diagnosis and avoiding nosocomial influenza infections [8]. A study developed and validated a COVID-19 infection prediction model, in which influenza vaccines had a reduced COVID-19 infection risk [6]. A search of the literature produced two more hypotheses that could explain our findings. The first is that an adjuvant in the influenza vaccine causes an increase in immune response, which could ensure protection against COVID-19 [17]. Another fascinating hypothesis would be that the influenza vaccine can influence the cytotoxicity of natural killer cells (NK cells). Despite the fact that the precise role of NK cells in fighting viral infections is still uncertain, there have been a growing number of studies showing that NK cells do play a role in fighting virally infected cells. SARS-CoV-2 has been shown to reduce NK cell activity in patients with mild to serious disease [5, 7].

5. Conclusion

The trends observed in the case study above help us conclude that the annual dose of vaccine for Influenza has helped in the prophylaxis of Sars-COV2 by preventing severe symptoms or even the manifestation of the virus itself. The mechanism by which this happens is unclear. It is believed

that influenza vaccination provides protection against the SARS-COV-2 by unknown mechanisms. In conclusion, this article promotes the trend of vaccinating large populations with the influenza vaccine to provide herd immunity against COVID-19.

Limitations and Delimitations

These study results cannot be generalized and the trend was observed only for Armenian ethnicities.

Biosystems 7300 were used for conducting the PCR tests. This study was conducted assuming the machines have given an accurate result with minimal regard for false positives and false negatives.

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