Clinical Medicine 158 (2022) 603-607

MEDICINA CLINICA

www.elsevier.co.uk/medicinaclinica

Original short

Influence of influenza vaccination and comorbidity on the evolution of patients hospitalised for COVID-19

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ARTICLE INFORMATION

History of the article:
Received 25 February 2021
Accepted 2 June 2021 *On-line* 16 June 2021

Keywords:
Influenza vaccine
COVID-19
Inpatients Age
Comorbidity
Mortality

RESUMMEN

Background and objective: The outbreak of COVID-19 disease is evolving worldwide. The aim of the study is to assess the association between influenza vaccination and the risk of mortality in hospitalised COVID-19 patients, as well as other risk factors.
Materials and methods: Retrospective observational study. It was conducted among hospitalised patients with COVID-19 at Hospital La Mancha Centro between 5 and 25 March 2020. We used multivariate logistic regression to explore the association between influenza vaccination and mortality due to COVID and other risk factors.
Results: 410 patients were included. Influenza vaccination had no effect among patients hospitalised for COVID-19 (OR 1.55 [95% CI 0.96-2.48, p=0.071]). Increased in-hospital mortality was associated with older age (OR 1.05 [95% CI 1.02-1.07]), for each increase in age;
p < 0.001, Charlson ≥ 3 (OR: 1.84 [95% CI: 1.07-3.15, p = 0.027]) and heart failure on admission (OR: 6.00 [95% CI: 1.07-3.15, p = 0.027]).
[95% CI; 1.6-21.7; p = 0.007]).
Conclusions: Influenza vaccination had no effect on the outcome of patients hospitalised with COVID-19. Risk factors identified were older age, higher comorbidity and heart failure on admission.

Influence of influenza vaccine and comorbidity on the evolution of hospitalised COVID-19 patients

Keywords:
Influenza vaccine
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Hospitalized patients
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ABSTRACT

Background and objective: The COVID-19 coronavirus disease outbreak is evolving around the world. The aim of this study is to evaluate the association between influenza vaccination and the risk of mortality in hospitalized COVID-19 patients, as well as other risk factors.
Materials and methods: Retrospective observational study. This study was conducted among hospitalized patients with COVID-19 at Hospital La Mancha Centro between March 5 and 25, 2020. Information on influenza vaccination was extracted from electronic medical records. We used a multivariate logistic regression to explore the association between influenza vaccination and mortality from COVID and other risk factors.
Results: 410 patients were included. Influenza vaccine had no effect among COVID-19 hospitalized patients [OR: 1.55 (95%CI: 0.96 - 2.48; p=0.071)]. Increasing hospital mortality was associated with older age [OR: 1.05 (95% CI 1.02-1.07), per year increase; p<0.001)], Charlson ≥3 [OR: 1.84 (95%CI: 1.07-3.15, p=0.027)] and heart failure on admission [OR: 6 (95%CI: 1.6 - 21.7; p=0.007)].

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https://doi.org/10.1016/j.medcli.2021.06.003
0025-7753/

Conclusions: Influenza vaccine had no effect among COVID-19 hospitalized patients. The risk factors identified were older age, higher comorbidity and heart failure on admission.

Introduction

COVID-19 is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has resulted in a pandemic that started in Wuhan, China, in December 2019. As of February 2021, the number of cases worldwide has exceeded 103 million with more than 2.2 million deaths1.

There is currently no treatment with a sufficient level of evidence. Most countries have resorted to public health measures such as isolation, quarantine and social distancing to prevent the spread of the disease.

Until vaccination for SARS-CoV-2 becomes universally available, several authors suggest that influenza vaccination may offer cross-protection against respiratory viruses other than influenza and minimise the severity of COVID-192 disease.

Other authors propose increasing anti-influenza vaccination rates to prevent co-infection of influenza with SARS-CoV-23. However, others suggest that vaccination may increase susceptibility to SARS-CoV-24 infection.

In this article we analyse the influence of anti-influenza vaccination and other prognostic factors on mortality in COVID-19 patients admitted to Mancha Centro hospital during the first wave of the pandemic.

Material and methods

Design and participants

Retrospective observational cohort study. We consecutively included 410 patients admitted with a diagnosis of COVID-19 at Hospital Mancha Centro from 5 to 25 March 2020. Information on influenza vaccination in autumn 2019 was obtained from Primary Care records.

The diagnosis of COVID-19 was confirmed by polymerase chain reaction (PCR) test. Patients with negative PCR, indeterminate PCR or no PCR but with high clinical suspicion of disease were also included.

Variables studied

The main outcome variable was mortality. Influenza vaccination was the main independent variable. Control covariates were age, sex, residence (community or institution), functionality (Barthel scale), comorbidity (Charlson index) and underlying comorbidities at admission: obesity, chronic respiratory diseases, ischaemic heart disease and/or heart failure, renal failure, chronic liver disease, haematological malignancies, other malignancies, following immunosuppressive treatment, diabetes, arterial hypertension (AHT),

Table 1
Main characteristics of the patients included in the study and differences between vaccinated and unvaccinated patients

	Global (n = 410)	Unvaccinated (n = 201)	Vaccinated (n = 209)	p
Mean age in years (SD; range)	70,7 (13,9; 28 - 100)	65,6 (14,3)	75,6 (11,6)	< 0,001
Age groups				
Under 65 years of age	132 (32,2%)	103 (51,2%)	29 (13,9%)	< 0,001
Between 65 and 75 years of age	103 (25,1%)	45 (22,4%)	58 (27,8%)	
Between 75 and 85 years of age	113 (27,6%)	30 (14,9%)	83 (39,7%)	
Over 85 years old	62 (15,1%)	23 (11,4%)	39 (18,7%)	
Sex				
Man	202 (49,3%)	101 (50,2%)	101 (48,3%)	0,697
Woman	208 (50,7%)	100 (49,8%)	108 (51,7%)	
Barthel				
> 60	319 (77,8%)	167 (89,8%)	152 (79,2%)	0,004
≤ 60	59 (14,4%)	19 (10,2%)	40 (20,8%)	
Not available	32 (7,8%)	-	-	
Charlson				
< 3	232 (78,8%)	176 (87,6%)	147 (70,3%)	< 0,001
> =3	87 (21,2%)	25 (12,4%)	62 (29,7%)	
Comorbidities				
Obesity	88 (21,5%)	40 (19,9%)	48 (23%)	0,450
Chronic Respiratory Disease	145 (35,4%)	49 (24,4%)	96 (45,9%)	< 0,001
Ischaemic heart disease / heart failure	50 (12,2%)	14 (7%)	36 (17,2%)	0,002
Kidney failure	49 (12%)	20 (10%)	29 (13,9%)	0,221
Chronic liver disease	7 (1,7%)	4 (2%)	3 (1,4%)	0,719
Haematological neoplasia	9 (2,2%)	4 (2%)	5 (2,4%)	0,999
Other neoplasms	60 (7,3%)	12 (6%)	18 (8,6%)	0,304
Diabetes	109 (26,6%)	37 (18,4%)	72 (34,4%)	< 0,001
HTA	256 (62,4%)	106 (52,7%)	150 (71,8%)	< 0,001
Cognitive impairment	49 (12%)	16 (8%)	33 (15,8%)	0,015
Other neurological diseases	96 (23,4%)	41 (20,4%)	55 (26,3%)	0,157
Depressive syndrome	61 (14,9%)	27 (13,4%)	34 (16,3%)	0,420
Heart failure on admission	20 (4,9%)	6 (3%)	14 (6,7%)	0,081
Cardiovascular event during admission	6 (1,5%)	2 (1%)	4 (1,9%)	0,686
Immunosuppressive treatment	14 (3,4%)	6 (3%)	8 (3,8%)	0,639
Institutionalised	32 (7,8%)	10 (5%)	22 (10,5%)	0,036
ICU admission	24 (5,9%)	18 (9%)	6 (2,9%)	0,009
Hospital Exitus	142 (34,6%)	49 (24,4%)	93 (44,5%)	< 0,001

Table 2
Factors associated with in-hospital mortality according to bivariate analysis

	No exitus (n = 268)	Exitus (n =142)	p
Mean age in years (SD)	67,4 (13,8)	77 (12)	< 0,001
Age groups			
Under 65 years of age	113 (85,6%)	19 (14,4%)	< 0,001
Between 65 and 75 years of age	67 (65%)	36 (35%)	
Between 75 and 85 years of age	64 (56,6%)	49 (43,4%)	
Over 85 years old	24 (38,7%)	38 (61,3%)	
Sex			
Man	131 (64,9%)	71 (35,1%)	0,829
Woman	137 (65,9%)	71 (34,1%)	
Barthel			
> 60	225 (70,5%)	94 (29,5%)	< 0,001
≤ 60	27 (45,8%)	32 (54,2%)	
Not available	-	-	
Charlson			
< 3	230 (71,2%)	93 (28,8%)	< 0,001
= >3	38 (43,7%)	49 (56,3%)	
Obesity			
Yes	51 (58%)	37 (42%)	0,099
No	217 (67,4%)	105 (32,6%)	
Respiratory Disease Disease			
Yes	86 (59,3%)	59 (40,7%)	0,057
No	182 (68,7%)	83 (31,3%)	
Ischaemic Heart Disease / Heart Failure			
Yes	22 (44%)	28 (56%)	< 0,001
No	246 (68,3%)	114 (31,7%)	
Kidney failure			
Yes	23 (46,9%)	26 (53,1%)	0,004
No	245 (67,9%)	116 (32,1%)	
Chronic liver disease			
Yes	5 (71,4%)	2 (28,6%)	0,999
No	263 (65,3%)	140 (34,7%)	
Haematological neoplasia			
Yes	4 (44,4%)	5 (55,6%)	0,286
No	264 (65,8%)	137 (34,2%)	
Other neoplasms			
Yes	11 (36,7%)	189 (63,3%)	0,001
No	257 (67,6%)	123 (32,4%)	
Diabetes			
Yes	68 (62,4%)	41 (37,6%)	0,445
No	200 (66,4%)	101 (33,6%)	
HTA			
Yes	148 (57,8%)	108 (42,2%)	< 0,001
No	120 (77,9%)	34 (22,1%)	
Cognitive impairment			
Yes	29 (59,2%)	20 (40,8%)	0,332
No	239 (66,2%)	122 (33,8%)	
Other neurological diseases			
Yes	58 (60,4%)	38 (39,6%)	0,244
No	210 (66,9%)	104 (33,1%)	
Depressive syndrome			
Yes	35 (57,4%)	26 (42,6%)	0,155
No	233 (66,8%)	116 (33,2%)	
Heart failure during admission			
Yes	3 (15%)	17 (85%)	< 0,001
No	265 (67,9%)	125 (32,1%)	
Cardiovascular event during admission			
Yes	2 (33,3%)	4 (66,7%)	0,190
No	262 (65,5%)	138 (34,5%)	
Immunosuppressive treatment			
Yes	9 (64,3%)	5 (35,7%)	0,999
No	259 (65,4%)	137 (34,6%)	
Institutionalised			
Yes	15 (46,9%)	17 (53,1%)	0,022
No	253 (66,9%)	125 (33,1%)	
Flu vaccine			
Yes	116 (55,5%)	93 (44,5%)	< 0,001
No	152 (75,6%)	49 (24,4%)	
ICU admission			
Yes	14 (58,3%)	10 (41,7%)	0,456
No	254 (65,8%)	132 (34,2%)	

cognitive impairment and other neurological diseases and depression. Heart failure and cardiovascular events during admission were also included.

Statistical analysis

Quantitative variables were described by means of mean and standard deviation (SD) and qualitative variables by absolute and relative frequencies.

Bivariate analysis was used to identify the factors implicated in mortality, using Student's *t-test* for quantitative variables AND^2 (or Fisher's exact test) for qualitative variables.

A multivariate analysis (two-way logistic regression) was performed to independently identify possible risk factors and the role of influenza vaccination in the mortality of admitted COVID-19 patients.

All analyses were performed using the SPSS v18 statistical software and a p-value < 0.05 was taken as statistically significant.

Results

A total of 410 patients admitted for COVID-19 were included. The mean age was 70.7 years (SD: 13.9; range 28 - 100). Males were 49.3% and females 50.7%; 209 (51%) were vaccinated against influenza (101 males and 108 females) and 201 (49%) were not. The scale of
Barthel was > 60 in 84.4% of cases and ≤ 60 in 15.6%. The Charlson index was < 3 in 78.8% and ≥ 3 in 21.2% of cases. The most prevalent chronic diseases were hypertension (62.4% of cases) and hypertension (62.4% of cases).
patients), chronic respiratory diseases (35.4%), neurological diseases (35.4% including cognitive impairment), diabetes (26.6%) and obesity (21.5%). The PCR test was positive in 354 patients (86.3%), negative in 35 (8.5%), indeterminate in 6 (1.5%) and not performed in 15 (3.7%). Intensive care unit (ICU) admissions were 5.9% of patients (24) and in-hospital mortality was 34.6% (142) (table 1).

Vaccinated patients are more often older than 65 years (86.2%), more dependent (Barthel < 60 20.8 vs. 10.2%; p = 0.004 compared to non-vaccinated), with greater comorbidity (Charlson > 3 29.7 vs. 12.4%; p < 0.001), with a higher percentage of chronic respiratory diseases (45.9 vs. 24.4%; p < 0.001), ischaemic heart disease (17.2 vs. 7%; p = 0.002), diabetes (34.4 vs. 18.4%; p < 0.001),
HTN (71.8 vs. 52.7%; p < 0.001), cognitive impairment (15.8 vs. 8%; p = 0.001), cognitive impairment (15.8 vs. 8%; p
0.015) and are institutionalised patients (10.5 vs. 5%; p = 0.036). Vaccinated patients were admitted to the ICU less often (2.9 vs. 9%; p = 0.009) (table 1).

The factors associated with mortality were: age being more significant with increasing age (those over 85 years died 61.3%), Barthel scale (being more at risk of death than those over 85 ye, the Barthel scale (being more at risk of death than those over 85 yand the Barthel scale (being more at risk of death than those over 85 years of age).
those patients with Barthel ≤ 60 [54.2 vs. 29.5%; p < 0.001]),
Charlson index ≥ 3 (56.3 vs. 28.8%; p < 0.001), history
of ischaemic heart disease/heart failure (56 vs. 31.7%);
p < 0.001), having non-hematological malignancies (63.3 vs. 32.4%; p = 0.001), HTN (42.2 vs. 22.1%; p < 0.001), renal failure (53.1
vs. 32.1%; p = 0.004), being institutionalised (53.1 vs. 33.1%; p = 0.004), being in an institution (53.1 vs.
0.022) and influenza vaccination (44.5 vs. 24.4%; p < 0.001). Another risk factor for mortality was the presence of heart failure during admission (85 vs. 32.1%; p < 0.001) (table 2).

Multivariate analysis finally identified age (OR 1.05 [95% CI 1.02-1.07 per year increase; p < 0.001]), Charlson index > 3 (OR 1.84 [95% CI 1.07-3.15; p = 0.027]) and having heart failure during admission (OR 6 [95% CI 1.6-21.7; p = 0.007]) as independent risk factors for in-hospital mortality. Influenza vaccination was not associated with mortality (OR: 1.55 [0.96-2.48, p = 0.071]) (table 3).

Table 3
Multivariate analysis of factors associated with mortality

Variables	OR (95% CI)	P
Age	1,045 (1,024-1,066)	< 0,001
Charlson (=> 3 vs <3)	1,835 (1,07-3,148)	0,027
Heart failure on admission	5,993 (1,625-21,659)	0,007
Flu vaccine	1,545 (0,963-2,477)	0,071

Discussion

In this study we show that influenza vaccination has no effect on mortality in patients admitted for COVID-19, in agreement with other authors5,6.

Vaccinated patients are older and have higher comorbidity, which are the factors associated with higher mortality in COVID-19 patients without influencing influenza vaccination.

Age, a high number of pre-admission comorbidities and the presence of heart failure on admission were the risk factors independently associated with higher in-hospital mortality in COVID-19 patients.

The vast majority of studies find age as an independent risk factor for mortality in COVID-19 patients which could be explained in relation to immunosenescence7.

Consistent with other studies, our patients with high comorbidity have a significantly higher mortality than those with low comorbidity8 .

The presence of heart failure on admission was shown to be an important independent predictor of mortality in our study. According to some studies, left ventricular diastolic impairment appears to be common in acute SARS infection, even among those without underlying cardiac disease9.

Our study has some limitations. We did not include analytical data that may be associated with increased mortality in various studies8 , but our aim was to assess influenza vaccination and other comorbidities in the risk of in-hospital mortality. Nor have we taken into account the treatments administered during admission, due to their heterogeneity and low level of evidence in the published studies10. In addition, the epidemiological situation may have conditioned admission criteria and bed availability and may have influenced mortality outcomes.

The strengths of our study were that the vast majority of COVID-19 cases were laboratory confirmed and all patient data were systematically collected, so we believe that the sample is representative of COVID-19 cases treated in our area.

Conclusions

Influenza vaccination does not seem to have an effect on in-hospital mortality in COVID-19 patients admitted to our hospital. Age, high comorbidity and the presence of cardiac insufficiency on admission are independent prognostic factors for mortality, which could help physicians to identify patients with poor prognosis for management and treatment.

Funding

This work has not received any funding.

Conflict of interest

The authors declare that they have no conflicts of interest.

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