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Original Article

Determinants of Severity of COVID-19 Infection Among Health Care Workers in a Tertiary Hospital in Alexandria, Egypt

Rania A. Hussein [1¥], Engy M. El-Ghitany [2], Ehab G. Elmongui [3], Dalia Ismail [4] , Hossam M. Hassan [5], Mohamed K. Gomaa [6]

1 Department of Internal Medicine, Gamal Abdel Nasser Hospital, Health Insurance Organization, Alexandria, Egypt
2 Department of Tropical Health, High Institute of Public Health, Alexandria University, Egypt
3 Department of Biostatistics, North-West Branch of Health Insurance Organization, Alexandria, Egypt
4 Department of Clinical Pharmacy, Gamal Abdel Nasser Hospital, Health Insurance Organization, Alexandria, Egypt
5 Department of Clinical Research, North-West Branch of Health Insurance Organization, Alexandria, Egypt
6 Department of Pulmonology, Gamal Abdel Nasser Hospital, Health Insurance Organization, Alexandria, Egypt

Abstract

Background: Egypt joined several countries in immunizing her citizens with COVID19 vaccines; a priority was given to health care workers (HCWs), then to patients with chronic diseases. However, HCWs are exposed to a higher viral load; in addition, asymptomatic infection is commoner among them, thus potentially exposing them to a more severe illness.
Objective(s): To identify the determinants of the severity of COVID-19 infection among HCWs.
Methods: A case control study was conducted, where we recruited HCWs diagnosed as moderate or severe COVID-19 from isolation and critical care units; and compared their vaccination exposure with that among matched controls. A data collection sheet was filled by residents and included information about mask wearing, comorbidities, smoking, and COVID-19 manifestations.
Results: The predictors that significantly affected severity of infection were cardiovascular or cerebrovascular diseases, being a nurse, and mask compliance (OR 17.38 p=0.012 *, OR 5.86, p=0.002*, and OR=0.06, p=0.001 *****respectively). Most females, as well as nurses were not vaccinated (90% p= 0.009 *, and 83.3% p=0.016 *respectively). There was no significant difference in mean oxygen saturation between vaccinated and non-vaccinated cases.
Conclusion: Among HCWs, the most significantly protective factor against COVID-19 moderate and severe illness was mask compliance. Furthermore, being a nurse as well as having cardiovascular or cerebrovascular disease were significant positive predictors of getting a more severe disease. There was no significant effect of vaccination on severity of COVID19 illness.

Keywords: Health care workers, COVID-19, vaccination, severity of infection

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¥*Correspondence*:
Email: rahussein2002@yahoo.com

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INTRODUCTION

The COVID 19 pandemic evoked an unprecedented outbreak, with a sky rocketing incidence, despite global efforts to fight the disease. It has been three years since the virus attacked the world, causing more than three million deaths worldwide. To date, confirmed cases surpassed six hundred millions worldwide, including more than six million deaths.(1) . In addition, a suspected underreporting of cases and fatalities, is expected due to the subclinical presentation of the disease, relatively frequent in youth and children.(2) The disease commonest presenting symptoms are respiratory and gastrointestinal; elderly might present with fatigue and altered sensorium.(3)Fortunately, severe cases constituted a minority (nearly15%),(4)but not surprisingly, yielded higher mortality (10-30%). Predictors of severity were advanced age, and comorbidities, including cardiovascular disease, diabetes, chronic lung disease, and malignancies.(5)

As a consequence to the pandemic, countries embarked on the battle, by recommending different therapeutic guidelines, so far with no consensus, and poor benefit.(6) Vaccines therefore presented a key aspect of protection. In fact, Egypt joined several countries launching their immunization programs, starting (7) with Sinopharm, an inactivated vaccine , consisting of two doses, spaced 3 weeks apart , and offering 79% protection against severe COVID-19, two weeks after the second dose.(8)In addition, the viral vector based AstraZeneca vaccine was

introduced as well, with two shots spaced four to twelve weeks apart, and offering protection three weeks after the first dose.[9]

By far, HCWs represent the frontline fighters of the COVID pandemic; that is why governments are struggling to offer them protection, especially with an existing shortage in physicians.[10] However, being in close contact with COVID-19 victims at isolation wards, HCWs are exposed to a greater viral load, and hence may suffer from unfavorable disease outcomes ; in fact, research has recently shown that the prevalence of severe Covid-19 illness among HCW was 5%.[11] In addition, unprotected HCWs might be exposed accidentally to an asymptomatic COVID-19 patient in a general hospital ward. As more HCWs get infected, delivery of health care will be greatly hindered, and a nation's response to the pandemic would become paralyzed.[10]

Interestingly, in a study conducted in Wuhan, the authors argued that asymptomatic infection explains the discrepancy between actual COVID-19 reported number, and a higher seroconversion rate, clearly discovered among HCWs.[12] This raises questions about vaccine effectiveness in HCWs, especially that past exposure to the virus is expected to reduce it; owing to the partial immunity this population could have developed.[7]

There would therefore seem to be a definite need to explore the determinants of the severity of COVID-19 infection among HCWs, owing to its great impact on the health care sector.

METHODS

A case control study was conducted at a tertiary hospital in Alexandria, Egypt, receiving patients from and several governorates. Newly diagnosed, hospitalized COVID-19 HCWs (physicians, nurses, employees, and workers), 18 years and older were recruited from COVID-19 isolation units.

Diagnosis was based on WHO case definition,[3] classifying illness into three categories (besides mild picture):

- Moderate COVID-19: Defined by clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including $SpO_2 \geq 90\%$ on room air
- Severe Covid-19: Defined by any of:
  - Oxygen saturation < 90% on room air
  - Respiratory rate > 30 breaths/ min
  - Signs of severe respiratory distress (accessory muscle use, inability to complete full sentences).
- Critical COVID-19: Defined by "the criteria for acute respiratory distress syndrome (ARDS), sepsis, septic shock, acute thrombosis, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy ".[3]

Upon arrival to triage COVID-19 unit, internal medicine and pulmonology residents clinically assessed HCWs suspected of having COVID-19 infection. They measured Oxygen saturation by pulse oxymeter, and performed a CT chest.

Cases with CT COVID-19 confirmed pneumonia (moderate and severe COVID-19) were admitted to COVID-19 isolation unit, and critical care isolation unit respectively. The severity of illness was categorized according to WHO interim updated classification.[3] Internists explained the aim of the study to the HCWs diagnosed as having COVID-19. They discussed with them the study benefits from a public health perspective.

Then they were asked to fill a data collection sheet, including information about gender, age, comorbidities, smoking (past/ current), COVID-19 vaccination history and their dates if ever, history of a previous COVID infection and its date, as well as a detailed enquiry of the patient's current presenting manifestations. Contact was categorized into direct (for those directly delivering care to COVID-19 patients), or indirect for clerks.

All patients entering the units were potential cases till the sample size was completely collected. Enrollment started from 1st of April till 31st December 2021.

Health care workers with moderate Covid-19 who refused hospital admission were picked up at the office of Pulmonology Consultant and they followed the same criteria for recruitment as the admission cases.

Controls were recruited, through a notice hanged on the hospital advertisement board that explained the study objectives, and invited the HCWs who did not have a history of previous COVID-19 infection in the last 90 days, to participate. A list of volunteers was made and categorized by gender and age (young: 20-40y, middle aged: 40-65y, old: >65y). For each recruited case, three controls were randomly selected from the corresponding gender/ age, among the list of potential participants. All controls were free from any previous symptoms of COVID-19 infection in the last 90 days, as well as any symptoms suggestive of mild COVID-19 illness during their recruitment as controls.

Vaccines provided to HCWs at the hospital prior to the period of the study were Sinopharm, Astra Zeneca, and Pfizer. Enrollment started from 1st of April till 31st of December 2021.

Sample size calculation and statistical analysis: OpenEpi version 3.01 was used for calculating the sample size for a case control study using the Fleiss method with continuity correction, the proportions of exposure to vaccination was used among HCW cases

and controls as confirmed by the literature: 46% and 75% respectively.[13] Hence, while using a case to control ratio of 1 to 3, with a two-sided level of significance (0.05), (80%) power, and an additional 20% (accounting for incomplete dose administration, or difference in effectiveness among vaccines), the minimum required sample was estimated to be 153 (39 cases and 114 controls).

Before conduct of the study, we obtained an official approval from the hospital administration, as well as the approval of the Research Ethics Committee of the Egyptian Ministry of Health and Population, with reference number 14-2021/2020. Participants agreeing to share signed the consent of agreement before the start of data collection. This study complies with the international guidelines of Research Ethics. All participants have been assured about anonymity and confidentiality; and have been assured that they could withdraw from the study at any stage if they wished to do so. There is no conflict of interest.

Data were analyzed using R Software version 4.1.2. We used t-tests to compare the age (presented as mean ± standard deviation) of the participants between the relevant groups; while we used Mann Whitney U test for oxygen saturation which was not normally distributed (presented as median (min – max)). Chi-square test and odds ratio were used to assess the association between the different baseline characteristics and COVID-19 disease severity. We conducted Fisher exact for contingency tables with expected counts of less than five in more than 20% of the cells. Variables that showed significant association with the categories of COVID-19 severity in the bivariate analysis were included in the multiple logistic regression model, to assess the strength of association between COVID-19 vaccine administration and severity of infection, while adjusting for potential confounding variables. We used a significance level of 0.05.

RESULTS

The baseline characteristics of the cases and controls are presented in **Table** 1. We found that getting a moderate or severe COVID-19 infection had a positive significant association with being a nurse (OR: 7.5, p= 0.001*), cardiovascular or cerebrovascular disease (OR: 4.7, p=0.016*), liver disease (OR: 6.4, p=0.035*), or respiratory disease (OR: 4.5, p=0.003*). On the contrary, we found that always wearing the mask (mask compliance) had a significant protective effect against getting infected with Covid-19 (OR: 0.1, p=< 0.001*). Furthermore, the odds of cases vaccination with at least one dose or full vaccination were 0.9 times that among the controls (p= 0.857, 0.9 respectively).

Table 1: Characteristics of COVID-19 cases with moderate and severe infection, and controls

Characteristics	Total (n = 180)	Cases (n = 45)	Controls (n =135)	p value	OR [a] (95% CI)
Occupation (nurse)	65 (36.1%)	32 (71.1%)	33 (24.4%)	**<0.001***	**7.5 (3.6-16.4)**
Mask compliance	139 (77.2%)	17 (37.8%)	122 (90.4%)	**<0.001***	**0.1 (0.03-0.2)**
Smokers	14 (7.8%)	2 (4.4%)	12 (8.9%)	0.520	0.5 (0.07-2.0)
Pregnant	3 (1.7%)	0 (0%)	3 (2.2%)	0.737	0.0 (0.0-7.3)
Comorbidities					
Diabetes mellitus	19 (10.6%)	8 (17.8%)	11 (8.8%)	0.123	2.4 (0.9-6.6)
Hypertension	31 (17.2%)	3 (6.7%)	28 (20.7%)	**0.039***	**0.3 (0.06-0.9)**
Cardiovascular or cerebrovascular disease	12 (6.7%)	7 (15.6%)	5 (3.7%)	**0.016***	**4.7 (1.4-17.2)**
Renal disease	4 (2.2%)	2 (4.4%)	2 (1.5%)	0.559	3.1 (0.3-30.2)
Liver disease	6 (3.3%)	4 (8.9%)	2 (1.5%)	**0.035***	**6.4 (1.1-36.7)**
Respiratory disease	18 (10%)	10 (22.2%)	8 (5.9%)	**0.003***	**4.5 (1.6-12.7)**
Any comorbidity	70 (38.9%)	23 (51.1%)	47 (34.8%)	0.077	1.9 (0.9-4.1)
Immunosuppressive drugs	15 (8.3%)	6 (13.3%)	9 (6.7%)	0.276	2.2 (0.7-6.5)
Vaccination status [b]					
Vaccinated [c]	64 (35.6%)	15 (33.3%)	49 (36.3%)	0.857	0.9 (0.4-1.8)
Fully Vaccinated	47 (26.1%)	11 (24.4%)	36 (26.7%)	0.922	0.9 (0.4-1.9)

[a] Unadjusted odds ratio of getting a COVID-19 infection [b] the types of vaccines used were 8 Sinopharm, 6 AstraZeneica, and 1 Pfizer in cases, 40 Sinopharm and 9 AstraZeneica in the controls. [c] Vaccinated with at least one dose *=p <0.05

Multiple logistic regression analysis was done to control for significant predictors of COVID-19 severity of infection (Table 2). The model included vaccination, occupation as a nurse, mask compliance, and comorbidities (hypertension, cardiovascular or cerebrovascular disease, hepatic, respiratory diseases). Vaccination had a negative, still statistically insignificant effect (OR: 0.78, p=0.7), while the statistically significant positive predictors were being a nurse, mask compliance, and cardiovascular or cerebrovascular diseases; their regression coefficients, standard errors, and odds ratios are presented in Table 2.

Table 2: Logistic regression model of the significant predictors of severity of COVID-19 infection

	β	SE	p value	95 % CI		OR[a] (Exp(β))	OR 95 % CI	
				Lower	upper		Lower	upper
Vaccination	-0.25	0.65	0.701	-1.52	1.02	0.78	0.22	2.78
Occupation (nurse)	1.77	0.57	**0.002 ***	0.65	2.88	5.86	1.92	17.86
Mask compliance	-2.79	0.57	**0.001 ***	-3.91	-1.68	0.06	0.02	0.19
Hypertension	-1.07	0.82	0.193	-2.68	0.54	0.34	0.07	1.72
Cardiovascular or cerebrovascular disease	2.86	1.14	**0.012 ***	0.62	5.09	17.38	1.86	162.81
Liver disease	0.83	1.28	0.516	-1.67	3.33	2.29	0.19	27.90
Respiratory disease	-0.08	0.79	0.922	-1.63	1.48	0.93	0.20	4.39

[a] Odds ratio of getting infected *=p <0.05

Table 3 shows a comparison of the baseline characteristics and disease manifestations of COVID-19 cases according to their vaccination status: Most cases were females (77.8%). Most females, as well as nurses were not vaccinated (90% p= 0.009 *, and 83.3% p=0.016* respectively). There was no significant difference in mean oxygen saturation between vaccinated and non-vaccinated cases.

Table 3: Baseline characteristics and presenting manifestations of COVID-19 cases by vaccination status

Characteristics	Total cases (n = 45)	Vaccinated cases (n = 15)	Not vaccinated cases (n =30)	p value
Age	40.2 ± 10.7	41.4 ± 11.9	39.6 ± 10.2	0.614
Sex (female)	35 (77.8%)	8 (53.3%)	27 (90%)	0.009 *
Occupation (nurse)	32 (71.1%)	8 (53.3%)	25 (83.3%)	0.016 *
Mask compliance	17 (37.8%)	6 (40%)	11 (36.7%)	1.0
Smokers	2 (4.4%)	2 (13.3%)	0 (0%)	0.106
Comorbidities				
Diabetes mellitus	8 (17.8%)	2 (13.3%)	6 (20%)	0.699
Hypertension	3 (6.7%)	2 (13.3%)	1 (3.3%)	0.254
Cardiovascular or cerebrovascular disease	7 (15.6%)	3 (20%)	4 (13.3%)	0.670
Renal disease	2 (4.4%)	0 (0%)	2 (6.7%)	0.545
Liver disease	4 (8.9%)	0 (0%)	4 (13.3%)	0.285
Respiratory disease	10 (22.2%)	2 (13.3%)	8 (26.7%)	0.456
Any comorbidity	23 (51.1%)	7 (46.7%)	16 (53.3%)	0.916
Immunosuppressive drugs	6 (13.3%)	1 (6.7%)	5 (16.7%)	0.647
The setting of direct contact				
At hospital	33 (73.3%)	11 (73.3%)	22 (73.3%)	1.0
Outside hospital	6 (13.3%)	2 (13.3%)	4 (13.3%)	1.0
Presenting Manifestations				
Cough	11 (24.4%)	5 (33.3%)	6 (20%)	0.464
Dyspnea	29 (64.4%)	10 (66.7%)	19 (63.3%)	1.0
Diarrhea	26 (57.8%)	8 (53.3%)	18 (60%)	0.754
Myalgia	37 (82.2%)	11 (73.3%)	26 (86.7%)	0.410
Anosmia	32 (71.1%)	9 (60%)	23 (76.7%)	0.304
Loss of taste	30 (66.7%)	10 (66.7%)	20 (66.7%)	1.0
Altered Sensorium	6 (13.3%)	3 (20%)	3 (10%)	0.384
CT chest	37 (82.2%)	12 (80%)	25 (83.3%)	1.0
SaO2, median (min – max)	92 (70 – 98)	92 (84 – 98)	90 (70-98)	0.094
Death	2 (4.4%)	0 (0%)	2 (6.7%)	0.546

t-test was used to compare age Mann Whitney U test was used to compare oxygen saturation Chi-square test was used to compare categorical variables *=p <0.05

DISCUSSION

In the present study, the mean age of the cases was 40.2 ± 10.7 years, most cases were females (77.8%), and most of them were nurses(71.1%); this was parallel with a systemic review on HCWs, where the median age of HCWs cases was 47.3 years, and female prevalence was 71.6%[10] . In fact, the occupation of a nurse exposes those HCWs to a higher viral load, since they exhibit a longer duration of patient contact; this, in addition to the extended duty hours due to the COVID pandemic, has led to further mental and physical exhaustion, with a subsequent burden on their immune system, making them more prone to a moderate or severe infection than others.[14]

In the adjusted model (table 2), presence of cardiovascular and cerebrovascular comorbidities followed by being a nurse were the positive significant predictors of getting a moderate or severe infection with COVID-19 (OR 17.38, p=0.012 *, OR 5.86, p=0.002***** respectively), whereas mask compliance was the only significant negative predictor (OR=0.06, p=0.001*****). In fact, the association of COVID-19 infection with presence of comorbidities has been

highlighted, since the emergence of the virus pandemic.[15]Such chronic illnesses strongly alter the immune system of the host, by attenuating lymphocyte and macrophage response, thus predisposing to a severer disease.[16]

Interestingly, despite the availability of the vaccine at the hospital, a minority of the HCWs total sample had received it; and since most cases were females (77.8%), they showed the same feature. In fact, although HCWs perceived the morbidity of COVID-19 pandemic, they showed reluctance towards vaccination since actually, they constituted a part of the general community, and not all of them have gained proper information about immunization. This explains why previous studies have shown that a more advanced age and a higher socioeconomic level had a positive impact on HCWs acceptance to the vaccination [17]. Still vaccination did not predict a significant protective effect on severe infection with COVID-19 (table 2); and there was no significant difference in mean oxygen saturation between vaccinated and non-vaccinated cases (table 3) . In fact, despite diversity of researches on COVID-19, the latter remains an obscure disease, and scientists are still exploring its pathophysiology, and host immune response. In addition, mutations across this viral genome are frequent; and finally, we should remember that novel vaccines take decades to develop, and that their success rate is unfortunately poor (less than 10%). [18]

It is not surprising if an equal rate in mask-wearing and acceptance of vaccination exists among cases, since both reflect a stronger judgment about disease consequences, or a higher confidence in the scientific opinion.[19] This supports our result that among cases, only 37.8% were mask compliant, and only 33.3% and 24.4% were partially and fully vaccinated respectively (table 1).

Conversely, mask wearing correlated negatively with getting a moderate or severe infection ((90.4% among controls). This has been proven by two systematic reviews and 12 single studies (examining the impact of mask compliance on COVID 19 case rate). They have reported a decrease in COVID 19 case growth in response to mask mandates (Ontario, P. H., 2022), which is probably attributed to the reduction in the physical contact and exposure to infection provided by wearing the mask.[20]

While interpreting our findings, it is important to consider the potential limitations of the current study. The research was conducted at a single governmental hospital, and did not include participants from private health sector, in addition to the small sample size. However, this hospital represents the main Health Insurance tertiary hospital at North West Delta region in Egypt, receiving patients from Alexandria and a number of governorates, hence we argue that our sample was representative, and that the present study might provide evidence and guidance for future clinical researches.

CONCLUSION AND RECOMMENDATIONS

Our study detected that, among HCWs, the most significantly protective factor against COVID-19 moderate or severe infection was mask compliance. Furthermore, being a nurse as well as having cardiovascular or cerebrovascular disease were significant positive predictors. Vaccination offered no significant protective effect.

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