Demographic, Practice Characteristics, and Risk Factors of SARS-CoV-2 Infection among ICU Healthcare Workers: A Cross Sectional and Nested Case Control Study

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ABSTRACT

Objectives: To describe demographic and practice variables of SARS-CoV-2 infected healthcare workers in ICU, and variables significantly associated with infection.

Method: Cross sectional survey study method was used for the descriptive objective, and a nested case control method was used for significant association. The study was conducted in the ICU of a tertiary referral center in Saudi Arabia, including healthcare workers practicing during the study period between March 1st and June 31st, 2020.

Results: 462 responses were received, of which 78 were SARS-CoV-2 positive, two thirds were females, mainly bedside nurses. The positive group had a median experience of 6 years, and bronchial asthma as the most common comorbidity. All positive group members practiced universal masking and hand hygiene, however; only one third used appropriate N95 size, and they worked a mean shift duration of 12.3 ± 2.7 hours, two thirds cared for intubated patients, and were exposed to a mean of 6.74 ± 10.5 aerosol generating procedure, the most common of which was endotracheal intubation. In the nested case control study, only endotracheal intubation and applying nebulization were significantly associated with increased risk of infection, adjusted OR=3.4, 95% CI: 1.2-9.6; p = 0.015, and OR=3.5, 95% CI: 1.02-12.1; p = 0.03 respectively.

Conclusion: Main predisposing factors for COVID-19 infection amongst HCWs were lack of PPE, unavailability of fit tested size N95 respirators, caring for intubated COVID-19 patients, and performing aerosol generating procedures. Endotracheal intubation and applying nebulization were associated with increased odds of SARS-CoV-2 acquisition by HCWs.

Keywords: Demographic, practice characteristics, SARS-CoV-2, COVID-19, ICU healthcare workers

INTRODUCTION

The novel SARS-CoV-2 disease (COVID-19) emerged from China, in 2019, and spread worldwide ⁽¹⁾. COVID-19 was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 ⁽²⁾. To date, more than 68.000.000 infected cases were reported, whilst the death toll reached to 1.565.000 patients worldwide ⁽³⁾. The multifactorial blow of the COVID-19

pandemic on global health and economy remains to be fully evaluated (4). Although infected individuals most remain asymptomatic, COVID-19 patients can develop life-threatening features such as acute respiratory distress syndrome, sepsis, multi-system organ failure, neurological manifestations, cytokine storm, and thromboembolic disease, requiring thus intensive care unit (ICU) care $^{(1,2)}$.

The risk for cross-infection of healthcare workers (HCWs) and other front liners ⁽¹⁾, particularly those exposed to aerosol generating procedures (AGP) in the intensive care unit (ICU) and/or the emergency department (ED) cannot be underestimated^(5,6). Of note, early reports during the course of the pandemic outlined the increased risk of exposure of HCWs to COVID-19, and thus the necessity for implementation of strict protective measures to mitigate in-hospital viral spread ^(1,7,8). SARS-CoV-2 Although is highly transmissible, further exploration of other putative factors enabling the viral transmission to HCWs such as their demographics, and practice related variables (i.e., habits/norms) is a new area of ongoing research. Hence, we conducted this study to explore the demographics and practice related variables of HCWs in our ICU during the early stages of the pandemic.

Study objective

The primary end-point was to investigate the demographics and practice related variables of ICU HCWs who were infected by SARS-CoV-2 and designated, hereafter, as positive group. Secondary objective was to explore possible correlations in between the aforementioned parameters in the positive group of HCWs.

Study design

This cross-sectional study was performed by means of an electronic survey platform. With a nested case control design to identify risk factors significantly associated with infection.

METHODS

Study setting

This study was conducted at the level III ICU of King Saud Medical City (KSMC), which is the largest Ministry of Health (MOH) hospital in the Kingdom of Saudi Arabia, between March 1 and June 31, 2020. Our ICU expanded during the pandemic to include more than 300 beds, one third of which were negative pressure single rooms. Since we could not maintain single-patient occupancy, we have decided to cohort COVID-19 patients in multipleoccupancy glass rooms equipped with gas access, power circuits, monitors, and HEPA purifiers (pop-up COVID-19 units). The ICU HCWs initially included 750 staff (physicians, nurses, respiratory therapists, and administrative personnel); while our task force gradually increased to a total of 1.200 HCWs by deploying nurses and physicians from other hospital departments.

Inclusion criteria

We included all HCWs who were scheduled to work in the ICU during the study period (from March 1 to June 31, 2020).

Data collection and timeframe

This cross-sectional study was conducted by means of an electronic survey platform that was launched by the ICU research department and the infection control department of KSMC. The survey required participants to indicate whether or not they have tested positive for COVID-19. Questions included demographic variables such as age, gender, experience, and comorbidities. The survey also included questions such as use of face masks/respirators, role of HCW in the ICU, their involvement in AGPs, working hours, the airway status of cared patients, and possible exposure to COVID-19 positive HCWs. The survey was distributed to ICU personnel on July 1st, 2020 by e-mails and was followed up by two reminders at weekly intervals. We estimated that given a total of 1200 HCWs, and for a 95% confidence interval (CI) and a margin of error of 5%, an inflated sample size of 300 was required.

Consent and ethical considerations

The survey stated that responding will be considered as the participants' consent to be included in the study with complete anonymity. Furthermore, this study was approved by our institutional review board (IRB). Personal identifiers of

participants were only used to ascertain a valid positive real-time-polymerase-chain-reaction (RT-PCR) test for COVID-19 (if applicable).

Data management

Replies to the electronic survey by HCWs who were tested positive for COVID-19 (positive group) as well as those who were tested negative for the virus (negative group) were recorded on a spreadsheet, which automatically was generated by the pertinent website. Thereafter, data regarding the positive group were separated for the purpose of the primary objective. While for the secondary objective the complete set of data was used with an indicator variable of positive or negative COVID-19 result, and continuous variables were stratified into quartiles or above and below the median as appropriate (see below).

Statistical considerations

For the primary objective of describing demographic and practice related factors in the positive group, continuous variables were summarized as mean \pm standard deviation (SD) as well as median and interquartile range (IQR), to provide insight about the normality of distribution. Discrete variables were summarized as number and percentages. Each summary statistic was presented with a corresponding 95% confidence interval (CI).

For the nested case control study, continuous variables were stratified into quartiles when possible, one continuous variable (working hours) was stratified into above and below the median, since the majority of ICU personnel worked 12 hours shifts, yielding a median (IQR) of 12 (12-12).

We assured proper classification of cases and controls by comparing responses of the survey to the official registry system of COVID-19 swab results in Saudi Arabia (HESN). Cases (COVID-19 positive) were matched to controls (COVID-19 negative) in a 2:1 ratio on age category of 5 years intervals, gender, experience category of 5 years intervals, and role in the ICU (physician, bedside nurse, administrative nurse, and respiratory therapist). Accordingly, matching variables were not used again to explore confounding effect between exposure and outcome.

We presented the odds ratio (OR) of correlation between outcome (case or control) and different exposures (identified in the descriptive study). ORs of each exposure were presented as crude and adjusted values for potential confounders. ORs were adjusted for each potential confounder separately, and thereafter for all potential confounders integrated in one model, along with results of Mantel Haenszel combined OR and test of homogeneity. Additionally, chi square test of trend was performed for multi-categorical exposures to explore for dose dependent relationship.

We separately conducted a logistic regression model of the outcome (positive or negative) as the dependent variable, and the exposure and potential confounders as the independent variables to assess results sensitivity.

Statistical tests were two tailed and considered to be statistically significant when p values were<0.05. All resulting ORs were accompanied by their corresponding 95% CI. Commercially available statistical package was used in the analysis (StataCorp. 2015. *Stata*).

Statistical Software: Release 14. College Station, TX: StataCorp LP.)

RESULTS

A total of 462 responses (response rate of 38.5%) were received, of which 78 were from HCWs of the positive COVID-19 group. Data of positive cases was separately analyzed and accurate classification was checked via the HESN registry.

Description of positive group

The median (IQR) age was 33.5 (29-40) years and two thirds were females (opposed to the usually observed distribution of gender among COVID-19

patients). However, the latter sex distribution could have represented the actual distribution of ICU HCWs (not related to COVID-19 per se). The majority of responses (46.2%) were from bedside nurses, followed by physicians (20.5%), and respiratory therapists (19.2%). Of note, non-ICU personnel provided 55% of the total replies. The positive group of HCWs had a median experience of 6 (4-10) years, and a median number of comorbidities of 0 (0-1). The most common comorbidity identified was bronchial asthma (14.1%) followed by hypertension (11.5%), (Table 1). Additional information is presented in the supplementary file (figures S1-S4).

 Table 1: Demographics of COVID-19 positive health care workers.

Variable	Summary	95% CI
Age (years):		
$Mean \pm SD$	34.8 ± 7	33.2 - 36.4
Median (IQR)	33.5 (29 - 40)	32 - 35
ICU experience (years)		
Mean \pm SD	7.7 ± 5.8	6.4 - 9
Median (IQR)	6 (4 – 10),	5 - 8.1
Gender:		
Males (n, %)	52 (66.7%)	55.1% - 77%
ICU Role (n, %):		
Bedside Nurse	36 (46.2%)	34.8% - 57.9%
Physician	16 (20.5%)	12.2% - 31.1%
Respiratory therapist	15 (19.2%)	11.2% -29.7%
Administrative Nurse	11 (14.1%)	7.3% - 23.8%
Non –ICU HCWs (n, %)	43 (55%)	43.3% - 66.3%
Number of Comorbidities		
(n , %)		
No Comorbidities	51 (65.4%)	53.8% - 75.8%
One comorbidity	16 (20.5%)	12.2% - 31.1%
Two comorbidities	4 (5.1%)	1.4% - 12.6%
Three or more	7 (9%)	3.7% - 17.7%
Comorbidities (n, %)		
Bronchial Asthma	11 (14.1%)	7.3% - 23.8%
Hypertension	9 (11.5%)	5.4% - 20.7%
Sinusitis	7 (9%)	3.7% - 17.7%
Diabetes Mellitus	4 (5.1)	1.4% - 12.6%
Allergic Rhinitis	3 (3.8%)	0.8% - 10.8%
Cardiac Disease	1 (1.3%)	0.03% - 7%
Old CVA	1 (1.3%)	0.03% - 7%

Clinical practice related variables and correlations

All members of the positive group practiced universal masking and hand according hygiene to ICU recommendations. Also, 77 HCWs (98.7%) stated that hand hygiene facilities were available all the time, 72 persons (92.3%) acknowledged wearing full personal protective equipment (PPE) irrespective of patient category (intubated or non-intubated patients) and type of provided care: routine care in ICU and AGPs, and in-hospital patient transfer. Eye shield and face protection were used by 74 HCWs (94.9%), whilst 68 HCWs (87.2%) declared working in ICU areas were HEBA filters were available. Approximately two thirds of HCWs practiced extended use of N95 respirators (as opposed to reuse); however, only one third of HCWs used the appropriate size of N95 respirators for which they were fit tested during AGP. This was mainly due to the fact that the proper size was available all the time only for 18% of them (initial stage of the pandemic). Thirty four HCWs (43.6%) declared exposure to a COVID-19 positive colleague for more than 15 minutes or at distance less than 1.5 meters. HCWs of the positive group worked in ICU for a mean duration of 12.3 \pm 2.7 hours, two thirds of them cared for intubated patients (Figure 1), and they were involved in a mean number of 6.74 \pm 10.5 AGPs. Members of the positive group were involved in a total of 625 AGPs. The most common of AGPs was endotracheal intubation (20%),followed by cardiopulmonary resuscitation (CPR) (16%), and nasogastric tube (NGT) insertion (14%), (Figure 2). Forty four HCWs (56.4%) stated that they worked in single bed areas of the ICU, the remainder worked in pop-up cohort units. One third of HCWs believed that they were infected from continuous exposure to COVID-19 positive patients, 20% responded "I don't know", and 14% attributed their infection to the lack of PPE. This is further detailed in Table 2 and figures S5-S10 of the supplementary file.

variables Four (age, gender, experience, and role in ICU) were used to match cases to controls in a 2:1 ratio, and were not used in further analysis. We the following variables identified as potential exposures: presence of HEPA filters, re-use of N95 respirators (versus extended), wearing of proper size of N95 respirator, exposure to COVID-19 positive colleagues, ICU area (single rooms or open cohort areas), non-ICU HCWs, and all

categories of AGPs. In table 3 we present crude and adjusted ORs of the aforementioned exposures adjusted for: comorbidities, N95 respirator availability, intubated or non-intubated patients, working hours, and number of AGPs. Only two exposures had statistically significant adjusted ORs for increased risk of infection namely performing intubation [(adjusted OR (aOR) = 3.4, 95% CI: 1.2-9.6; p= 0.015), and applying nebulization to the patient (aOR=3.5, 95% CI: 1.02-12.1; p = 0.03)]. Re-use of N95 respirator, working in cohort performing areas. tracheostomy. and performing CPR had statistically a significant unadjusted OR but results were not significant when adjusted for cofounders. Both of significant the exposures (intubation and applying nebulization) had significant p values for M- H test of combined ORs across strata of variables for which they were adjusted; moreover both exposures showed evidence of homogeneity across the aforementioned strata (Table S1, supplementary file). However, only intubation showed evidence of trend for increased risk of infection with increasing working hours and number of AGPs, but interestingly not with age or experience. In contrast, applying nebulization showed no significant trends across strata (table S2, supplementary file). In a multivariable logistic regression model for each exposure as a sensitivity test, intubation was robust as a risk factor for infection (OR=1.97, 95% CI: 1.1-3.5; p= 0.025); while applying nebulization was not statistically significant (OR = 1.51, 95% CI: 0.99-2.8;p=0.051) (Table S3, supplementary file).

Table 2: Clinical practice characteristics		
Characteristic	Summary (n = 78)	95% CI
Universal Masking	78 (100%)	95.4% - 100%
Hand hygiene facilities:		
Available	77 (98.7%)	93% - 100%
Full PPE:		
All the time	72 (92.3%)	84% - 97%
Patient care	2 (2.6%)	0.3% - 9%
Patient transfer	2 (2.6%)	0.3% - 9%
During AGP	2 (2.6%)	0.3% - 9%
Face shield / Eye protection	74 (94.9%)	87.4% - 98.6%
HEBA filter available	68 (87.2%)	77.7% - 93.7%
N95 Respirator use:		
Extended	53 (68%)	56.5% - 78.1%
Re-use	25 (32%)	21.9% - 43.5%
Proper N95 size worn during AGP:		
All the time	26 (33.3%)	23% - 45%
Sometimes	29 (37.2%)	26.5% - 49%
Never	23 (29.5%)	19.7% - 41%
Proper N95 size available:		
All the time	14 (18%)	10.2% - 28.3%
Sometimes	23 (29.5%)	19.7% - 40.9%
Never	41 (52.5%)	40.9% - 60.9%
Exposure to positive HCW		
Yes	34 (43.6%)	32.4% - 55.3%
Working hours		
Mean \pm SD	12.3 ± 2.7	11.7 - 12.9
Median (IQR)	12 (12 – 12)	12 - 12
HCW cared for:		
Intubated patients	52 (66.7%)	55.1% - 77%
Non-intubated patients	26 (33.3%)	23.1% - 45%
Number of AGP:		
Mean \pm SD	6.74 ± 10.9	4.4 - 9.1
Median (IQR)	3 (1 – 8)	2 - 5
Frequency of AGP (n = 625):		
ET Intubation	125 (20%)	17% - 23.4%
CPR	100 (16%)	13.2% - 19.1%
NGT Insertion	88 (14%)	11.4% - 17%
BiPAP application	75 (12%)	9.6% - 14.8%
Nebulization	75 (12%)	9.6% - 14.8%
Sputum sampling	63 (10%)	7.8% - 12.6%
Dislodgment of ETT	44 (7%)	5.1% - 9.3%
Tracheostomy	31 (5%)	3.4% - 7%
Bronchoscopy	24 (4%)	2.6% - 5.9%

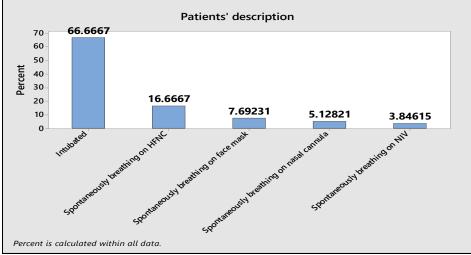
Table 2: Clinical practice characteristics of positive grou	n of health care workers
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Table no. 2 continued		
Working area in ICU (n, %)		
Single beds	44 (56.4%)	44.7% - 67.6%
Open cohorting area	34 (43.6%)	32.4% - 55.3%
HCWs' opinion on source of infection (n, %):		
COVID-19 positive patient	25 (32%)	21.9% - 43.5%
Don't know	16 (20%)	11.8% - 30.6%
Shortage of PPE	11 (14%)	7.2% - 23.7%
Community acquired	10(13%)	6.5% - 22.5%
Performing AGP	7 (9%)	3.7% - 17.7%
COVID-19 positive HCWs	5 (7%)	2.5% - 15.1%
Comorbidities	4 (5%)	1.4% - 12.4%

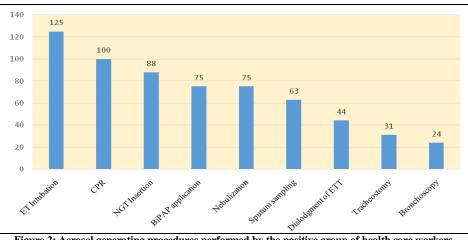
Table 3: Crude and adjusted odds ratio of risk factors for SARS-CoV-2 acquisition by health care workers.

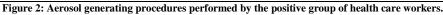
Exposure	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
HEBA filter	0.8 (0.4 - 1.9)	0.7	2.5 (0.2 - 26.3)	0.4
Re-use of N95	2.3 (1.3 – 4.1)	0.004	1.5(0.5-4.5)	0.4
Using proper N95 size	0.9 (0.7 – 1.2)	0.5	2(0.95-4.1)	0.07
Exposure to colleagues	0.9 (0.5 - 1.6)	0.8	0.7(0.2 - 2.5)	0.6
ICU Cohorting area	1.96 (1.1 – 3.4)	0.02	2.2(0.6-8.1)	0.2
Non-ICU HCW	1.2 (0.8 - 1.9)	0.4	1.1(0.7-2.1)	0.6
Intubation	1.9 (1.1 – 3.4)	0.02	3.4 (1.2 – 9.6)	0.015
Tracheostomy	1.05 (1.02 – 1.1)	0.04	1.01 (0.9 - 1.05)	0.06
CPR	1.8 (1.05 – 3.2)	0.03	3.01 (0.93 - 9.7)	0.053
BiPAP	0.9 (0.5 – 1.7)	0.9	3 (0.8 – 11.9)	0.1
NGT	0.8 (0.4 – 1.3)	0.3	0.5(0.2-1.4)	0.2
Sputum sampling	2.4 (1.2 – 4.5)	0.007	1.1 (0.2 – 1.7)	0.6
ETT Dislodgment	1.2(0.6-2.4)	0.6	0.8 (0.3 – 2.8)	0.8
Bronchoscopy	1.1 (0.3 – 1.8)	0.4	1.03 (0.1 – 5.7)	0.6
Nebulization	1.5 (1.2 – 1.8)	0.02	3.5 (1.02 – 12.1)	0.03

Adjusted OR for: comorbidities, N95 availability, patient airway, working hours, number of aerosol generating procedures.









DISCUSSION

In this cross-sectional study, 78 HCWs who responded to the designated electronic survey were positive for COVID-19. These HCWs were of relatively young age and were predominantly females. The unbalanced sex distribution is explained by the default gender distribution pattern of HCWs (mainly nurses and respiratory therapists) in our ICU as others also observed ^(8, 9); moreover, this should not be related to COVID-19 status per se. Also, the majority of HCWs were bedside nurses being the largest group of personnel in the ICU, which is in accordance with published data ⁽¹⁰⁾. The majority of HCWs had no comorbidities; while a minority of HCWs comorbidity a single of had nonincapacitating nature such as bronchial asthma or chronic sinusitis. Of note, HCWs had a reasonable experience practicing in ICU or in the general wards; hence we presumed that they exhibited strict adherence to hospital regulations and infection control measures during the outbreak. The professionalism of our HCWs was further reflected by the fact that the most of them reported use of universal masking and performed hand hygiene as per recommendations. Moreover, ICU an overwhelming majority used full PPE during all aspects of patients' care including face shields and eye protection.

We presume that risk factors for SARS-CoV-2 acquisition by HCWs were the availability of PPE per se rather than their proper application. In our positive group of HCWs only one third reported using N95 respirator every time when they performed an AGP, whilst another third never actually did. This might be partially explained by the fact that more than 50% of HCWs reported that the N95 respirator for which they were fit tested was not always available, especially during the early phase of the pandemic. This is an illustration of the burden that COVID-19 pandemic imposed on healthcare systems and available resources. Several other authors have identified lack of various types of PPEs as a risk factor for HCWs infection ^(11, 12). In our study, the lack of PPE, the reported exposure to a COVID-19 positive colleague by 43% of the positive group, and the median of 12 working hours were promptly presented to hospital administrators and policy makers as well as the ICU crisis management team, which in turn resulted to improved resources utilization, shifts duration, and staffing plans (late phase of the pandemic) ⁽¹³⁾.

Other risk factors for SARS-CoV-2 acquisition by HCWs were related to the nature of ICU procedures. In our study, two thirds of personnel cared for intubated critically ill patients. In the study by Chen WQ et al (10), these critically ill patients were termed as "super-spreaders" as the authors found significantly increased odds for COVID-19 acquisition by HCWs' involved in their care. In our study, HCWs of the positive group were involved in seven AGPs, of which the most common were endotracheal intubation, followed by CPR, and NGT insertion. Although there is no consensus, endotracheal intubation remains particularly hazardous ^(5,6), and was found to be directly associated with HCW infection during other infectious outbreaks ^(7,14). Although CPR was associated with the risk of SARS infection ⁽¹⁵⁾, it was reported to have an insignificant association to COVID-19 cross-infection in a recent study ⁽⁸⁾. The view of HCWs about the reasons for their COVID-19 status is important, although not formally evaluated in previous studies. In this study, the majority of HCWs believed that they became infected due to constant exposure to COVID-19 patients, lack of PPE, and their participation in numerous AGPs.

In this study, we further explored the association of all known predisposing factors for HCWs acquisition of COVID-19 after matching cases with controls (negative group). Adjusted ORs of two exposures were significantly associated with COVID-19 infection: endotracheal intubation and applying nebulization. Intubation remains a rational risk factor, which is consistent with

previous results ^(7,14), although the study by Ran et al.⁽⁸⁾ did not establish a significant association, in that study none of the HCWs participated actively in the intubation process; while in our study all HCWs were of the intubating ICU team. part Nebulization procedures emerged as another important risk factor, although the adjusted ORs were not significant. The application of nebulization does not only generate aerosols, but also stimulates patients' cough, which led to suggestions for reconsidering all nebulization plans early in the COVID-19 outbreak ⁽¹⁶⁾. Moreover, this notion was based on the significant relative risk of transmission of SARS infection among HCWs during nebulization procedures in a previous study by Loeb et al. ⁽¹⁷⁾. In our study, the risk of infection when performing endotracheal intubation showed a trend of increase with increasing working hours and/or number of AGPs. This was not observed in nebulization procedures, which may be partially attributed to the small number of applied nebulization in our study (75 out of 625). Endotracheal intubation was robust as a predisposing factor for infection in our sensitivity analysis, unlike nebulization, again possibly due to differences in numbers of each procedure. We detected a significant OR for intubation of 3.4 (95% CI: 1.2-9.6), which provides the study with a high power (about 90%) with the included sample size.

Our study has many limitations. First, our sample size calculation was for all responses. whereas. the presented demographics and practice variables were applied only on the positive group, which renders the results relatively underpowered. Second, the questionnaire could have been more detailed to probe further and detailed predisposing factors. For example, we did not require details of the duration of patient care, proximity between patient and HCW, or exposure to patients' body fluids, although the latter were managed as biohazardous material as per unit protocol ⁽¹⁸⁾.Third, cross-sectional study design carries inherent limitations such as recall bias. Fourth, this study reflects infrastructural details, hospitals practices, clinical notions, and HCWs norms during the early phase of the pandemic.

CONCLUSION

In this electronic survey, main predisposing factors for COVID-19 infection amongst HCWs were lack of PPE, unavailability of fit tested size N95 respirators, caring for intubated COVID-19 patients, and performing aerosol generating procedures. Endotracheal intubation was associated with increased odds of SARS-CoV-2 acquisition by HCWs.

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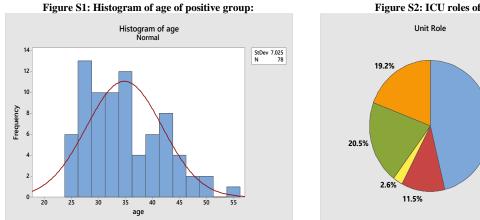
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***** **Supplementary Files**



Demographics of Positive Group:

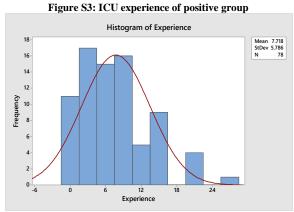
Reject normality (Shapiro-Wilk p = 0.003)

Figure S2: ICU roles of positive group:

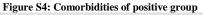
Category Bedside Nurse Charge Nurse Head Nurse Phjysician

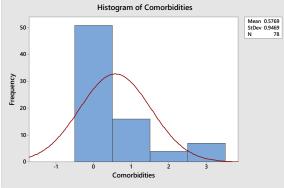
46.2%

iratory Therapist



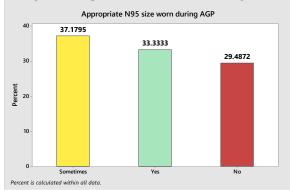
Reject normality (Shapiro-Wilk p < 0.001)





Reject normality (Shapiro-Wilk p < 0.001)

Clinical practice of positive group: Figure S5: Proper size of N95 mask worn during AGP



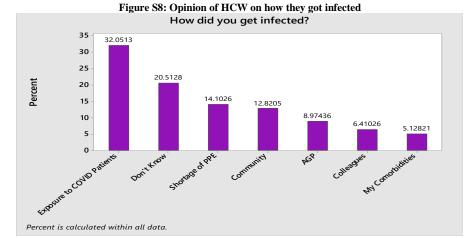


Figure S6: Proper size of N95 mask available in ICU

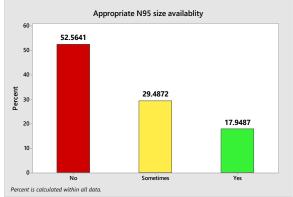
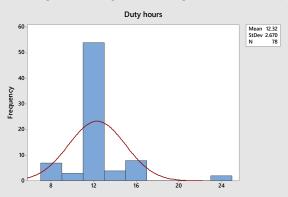


Figure S7: Histogram of working hours in ICU



Reject normality (Shapiro-Wilk p < 0.001)

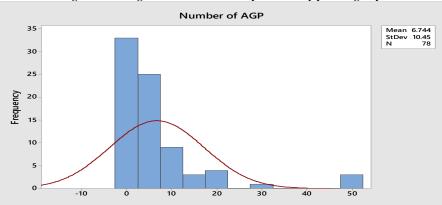
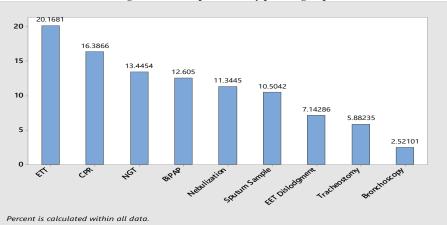


Figure S9: Histogram of number of AGP performed by positive group

Reject normality (Shapiro-Wilk p < 0.001)

Figure S10: AGP performed by positive group



Case Control Study:

Table S1: Mantel Haenszel homogeneity and combined OR test, for significant variables

	M-H Homogeneity	M-H Combined OR
Intubation:		
Comorbidities	0.4	0.017
N95 Availability	0.99	0.014
Patient airway	0.4	0.02
Working hours	0.2	0.03
Number of AGP	0.5	0.012
Nebulization:		
Comorbidities	0.97	0.02
N95 Availability	0.2	0.01
Patient airway	0.9	0.03
Working hours	0.4	0.03
Number of AGP	0.8	0.02

M-H test of homogeneity: $p > 0.05 \mbox{ indicates homogeneity across strata.} \label{eq:m-H}$

Table S2: Chi square test of trend for significant variables

	Chi ² test of trend p value
Intubation:	
Age	0.4
Experience	0.3
Working hours	0.03
Number of AGP	0.01
Nebulization:	
Age	0.2
Experience	0.2
Working hours	0.3
Number of AGP	0.2

 $P \ value < 0.05$ indicates significant trend with increased "dose" across strata.

	Adjusted OR	95% CI	Р
Intubation	1.97	1.1 - 3.5	0.025
Nebulization	1.51	0.99 - 2.8	0.051

Adjusted OR for: comorbidities, N95 availability, patient airway, working hours, number of aerosol generating procedures.