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Review Article

Risk Factors for COVID-19 Infection Among Healthcare Workers. A First Report From a Living Systematic Review and meta-Analysis

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ABSTRACT

Health care workers (HCWs) are more than ten times more likely to be infected with coronavirus infectious disease 2019 (COVID-19) than the general population, thus demonstrating the burden of COVID-19 among HCWs. Factors that expose HCWs to a differentially high-risk of COVID-19 acquisition are important to elucidate, enable appropriate public health interventions to mitigate against high risk and reduce adverse outcomes from the infection. We conducted a systematic review and meta-analysis to summarize and critically analyze the existing evidence on SARS-CoV-2 risk factors among HCWs. With no geographical limitation, we included studies, in any country, that reported (i) the PCR laboratory diagnosis of COVID-19 as an independent variable (ii) one or more COVID-19 risk factors among HCWs with risk estimates (relative risk, odds ratio, or hazard ratio) (iii) original, quantitative study design, and published in English or Mandarian. Our initial search resulted in 470 articles overall, however, only 10 studies met the inclusion criteria for this review. Out of the 10 studies included in the review, inadequate/lack of protective personal equipment, performing tracheal intubation, and gender were the most common risk factors of COVID-19. Based on the random effects adjusted pooled relative risk, HCWs who reported the use of protective personal equipment were 29% (95% CI: 16% to 41%) less likely to test positive for COVID-19. The study also revealed that HCWs who performed tracheal intubations were 34% (95% CI: 14% to 57%) more likely to test positive for COVID-19. Interestingly, this study showed that female HCWs are at 11% higher risk (RR 1.11 95% CI 1.01–1.21) of COVID-19 than their male counterparts. This article presents initial findings from a living systematic review and meta-analysis, therefore, did not yield many studies; however, it revealed a significant insight into better understanding COVID-19 risk

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factors among HCWs; insights important for devising preventive strategies that protect them from this infection.
PROSPERO registration number: CRD42020193508 available for public comments via the link below https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020193508).

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) emerged as the cause of coronavirus infectious disease 2019 (COVID-19) and a rapidly spreading pandemic [1]. Since its emergence in December 2019, there have been over 253 million confirmed cases worldwide as of 15th November 2021 [2]. The rapidly evolving situation required a quick action from policy makers, such as mandatory mask-wearing, social distancing, lockdowns, school and business shutdown, and cross-border restrictions, among others [3].

Public health systems in many countries were not adequately prepared to deal with the sudden surges in demand for personal protective equipment (PPE) and other consumables whose need became very high due to increases in COVID-19 case burden and the need to provide HCWs with additional layers of protection. Shortages of face masks and other pieces of PPE were reported across many countries due to an unexpected imposition of mandatory mask-wearing requirements in the general population to contain the spread of infection. The inadequate availability of PPE may have contributed significantly to the additional risk of COVID-19 infection among HCWs [4]. What is more, the severity and rapid transmission of COVID-19 overloaded the HCWs weakening the established infection prevention and control across many health settings [5]. Despite the high observed rate of the knowledge, attitude, and practices of HCWs toward COVID-19 containment compared to other communities, the overloaded working environment with the shortage of PPE made HCWs more vulnerable to COVID-19 infection [6–10].

Health care workers (HCWs) are more than ten times more likely to contract COVID-19 than the general population, thus demonstrating the burden of COVID-19 among HCWs [11]. Factors that expose HCWs to a differentially high-risk of COVID-19 acquisition are important to elucidate, enable appropriate public health interventions to mitigate against high risk and reduce adverse outcomes from the infection. In a previous systematic review, Gomez-Ochoa et al revealed the lack of PPE, patient contact, and suboptimal hand hygiene as risk factors for COVID-19 among HCWs [12]. However, no meta-analysis was conducted. Furthermore, Chou et al, living rapid review focused on a broad range of coronavirus infections. Of the 64 studies that met inclusion criteria, 43 studies addressed the burden of HCW infections (15 on SARS-CoV-2) and 34 studies addressed risk factors (3 on SARS-CoV-2) [13]. Only 3 studies included reported risk factors for SARS-CoV-2 infections among health workers.

Notably, from the onset of the COVID-19 pandemic, the frontline HCWs have played a significant role in saving lives of many regardless of their occupational exposure to COVID-19 [14]. Following a rapid review to understand the risk factors related to COVID-19 among HCWs, we demonstrated the need to establish sustainable measures to protect HCWs [5]. To better inform occupational health policy and map available evidence on the COVID-19 risk factors among HCWs, we conducted a systematic review and meta-analysis to summarize and critically analyze the existing evidence on SARS-CoV-2 risk factors among HCWs. Given the dynamic nature of the COVID-19 pandemic, there is an urgent need to continuously review the literature and update the aggregated evidence base to accurately and timely guide effective clinical and public health interventions. We present here the first report of a living systematic review and meta-analysis to inform evidence-based guideline recommendations for effective preventive measures to reduce the occupational transmission of SARS-CoV-2 infection among HCWs.

2. Materials and methods

2.1. Study design

The protocol was developed and published [15] and registered in PROSPERO (CRD42020193508). This review was reported in accordance with the reporting guideline provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement [16]. The systematic review and meta-analysis was conducted in line with the center for reviews and dissemination guidance for undertaking systematic reviews in healthcare [17], and the meta-analysis of observational studies in epidemiology guidelines for design and implementation [18].

2.1.1. Study selection

2.1.1.1. Search strategy. The search strategy used both medical subject heading and text word searches. Initial search terms in the published protocol [15] were adopted and used without changes. Two reviewers (MM and IC) searched EBSCOhost platform, specifically, Academic search complete, health source: nursing/academic edition, CINAHL with full text, Embase, PubMed, MEDLINE, ScienceDirect databases, Google Scholar and World Health Organization library databases for relevant studies. Two other reviewers (PG, JA) searched the China National Knowledge Infrastructure database.

2.1.2. Inclusion and exclusion criteria

Criteria were developed in an iterative process after preliminary searches during study protocol development [15]. Briefly, studies were eligible if they were (i) reporting PCR laboratory diagnosis of COVID-19 as an independent variable (ii) reporting one or more COVID-19 risk factors among HCWs with risk estimates (relative risk, odds ratio or hazard ratio) (iii) original, quantitative study design published in English or Mandarian.

2.1.2.1. Selecting studies. The titles and abstracts of all identified articles were assessed by two independent reviewers (IC and MM). If a study was deemed to potentially fulfil the inclusion criteria, full-text versions were retrieved and assessed. Reference lists of all retrieved articles were searched. To assess how reliably the study eligibility criteria were applied, a third reviewer (PGI) applied the inclusion criteria to all studies, given the small number of studies included, and agreement between the primary allocation and the third reviewer allocation had a Cohen's kappa score of 1 (denotes full agreement).

2.1.3. Data extraction

The data extraction table presented in the published protocol was piloted by MM and IC. The table was revised to exclude data on number of cases and controls for the initial extraction. This data was only collected from studies included in the meta-analysis for

COVID-19 risk factors stage. The final data extraction tool is available on Supplementary File 1.

2.1.4. Assessment of study quality and risk of bias

The NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies [19,20] was used to rate study quality. Two reviewers assessed methodological quality (MM and IC). Discrepancies were resolved by a third reviewer (TD). Meta-biases were assessed using funnel plots to detect potential reporting biases and small-study effects [21] and complemented with the Egger regression test [22].

2.1.5. Data synthesis

First, a narrative analysis of reported risk factors across studies was synthesized descriptively to understand the key risk factors for SARS-CoV-2 infection. Second, similar type of risk factors for SARS-CoV-2 infections reported in at least 2 studies were pooled from each study for overall estimates.

2.1.6. Statistical analysis

The outcome of interest was the incidence rates of and factors associated with COVID-19 across all studies estimated using the random-effects model. The Q and I2 were calculated in all the meta-analysis to assess heterogeneity. The I^2 statistic describes the percentage of variation across studies that are due to heterogeneity rather than chance. In this review, however, no meaningful conclusions could be drawn from these calculations because the number of studies included for meta-analysis was very small (i.e., less than 10). Egger's test and the funnel plot were not used for the evaluation of publication bias because the number of studies included for meta-analysis was very small (i.e., less than 10). All analyses were performed using Meta and Metasets statistical packages available in R version 4.2.1 software package. The summary measures calculated include a narrative report of all reported risk factors in the included studies, a pooled incidence of COVID-19 among health workers from included cohort studies and a pooled relative risk for risk factors reported by at least 2 included studies.

3. Results

Our initial search resulted in 470 articles overall (Supplementary File 2). After removing 8 duplicates, 462 articles proceeded to the title screening phase. Among these, 342 articles were excluded, and 120 articles proceeded to abstract review. Among these, 104 were excluded (Supplementary File 2). 16 full text articles were screened for eligibility [23–38], 6 were excluded [24, 28, 31–33, 36], and ultimately 10 eligible studies were included in this review and meta-analysis. Reasons for exclusion at full text review stage included lack of PCR confirmation of COVID-19 infection [24, 31–33, 36], and lack of evidence on risk estimates for COVID-19 risk factors [28]. Studies included were conducted in China [34, 35, 37], USA [26, 29], India [23, 27], Italy [25], Spain [30] and Colombia [38]. Of the studies included, 3 were retrospective cohorts [34, 35, 37], 2 were prospective cohorts [26, 29], 3 were case controls [23, 27, 38] and one was a cross sectional [30] and one case series [25]. More details on the included studies characteristics are available on Supplementary File 1.

Gender was reported as a risk factor for COVID-19 among HCWs [23,29,38]. In a study conducted in Colombia, male gender (AOR = 4.13 95% CI 1.70–10.05) was associated with the laboratory diagnosis of COVID-19 among HCWs [38]. In India, male HCWs had higher odds of COVID-19 infection than their female counterparts [23]. The lack/inadequate use of PPE was also reported in three studies; one conducted in Colombia [38], and in two studies from India [23,27]. HCWs performing tracheal intubation had higher odds of COVID-19 infection in two studies [23,37]. More details on reported risk factors are presented in Supplementary File 1.

Based on the available 5 cohort studies, the random effects adjusted pooled incidence of COVID-19 cases observed among HCWs was 12% [95% CI: 4% to 29%]. The forest plot for the meta-analysis of the cohort studies is presented in Fig. 1 for further details.

Out of the overall 10 studies included in the review, inadequate/lack of protective personal equipment (PPE), performing tracheal intubation, and gender were the most common risk factors of COVID-19. Out of the 10 studies, only 3 studies reported the use of PPE as a risk factor of COVID-19. Based on the random effects adjusted pooled relative risk, it is estimated that those who use PPE were 29% (95% CI: 16% to 41%) less likely to test positive for COVID-19. The forest plot for the meta-analysis of the effect of the use of PPE is presented in Fig. 2 for further details.

Out of the 10 studies, only 2 studies reported PTI as a risk factor of COVID-19. Based on the random effects adjusted pooled relative risk, it is estimated that those who PTI were 34% (95% CI: 14% to 57%) more likely to test positive for COVID-19. The forest plot for the meta-analysis of the effect of PTI is presented in Fig. 3 for further details.

Out of the 3 studies that reported gender as a risk factor, only 2 studies provided sufficient data and were included in the meta-analysis. Based on the random effects adjusted pooled relative risk, it is estimated that the female participants in these studies were 11% (95% CI: 1% to 21%) more likely to test positive for COVID-19. The forest plot for the meta-analysis of the effect of gender is presented in Fig. 4 for further details.

3.1. Quality assessment of included studies

Eight studies [21, 23, 27, 28, 32–35] had fair quality while 2 studies [25, 36] had good quality. More details are presented in Supplementary File 3.

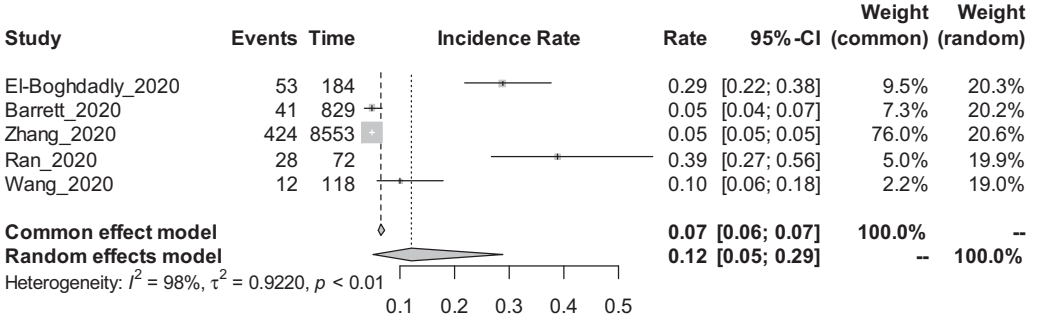

Fig. 1. Forest plot showing the meta-analysis for the incidence of COVID-19 among the cohort studies. COVID-19, coronavirus infectious disease-19.

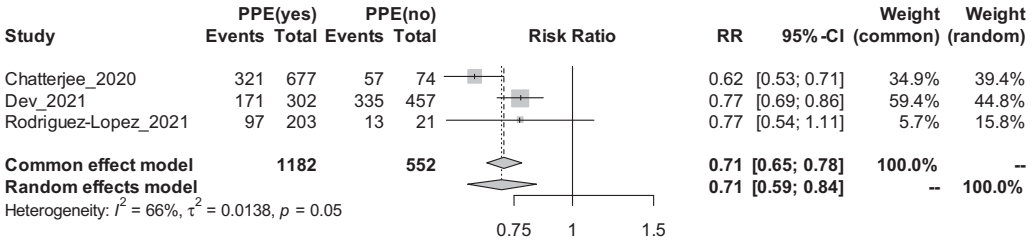

Fig. 2. Forest plot showing the meta-analysis for the effect of the use of PPE. PPE, personal protective equipment.

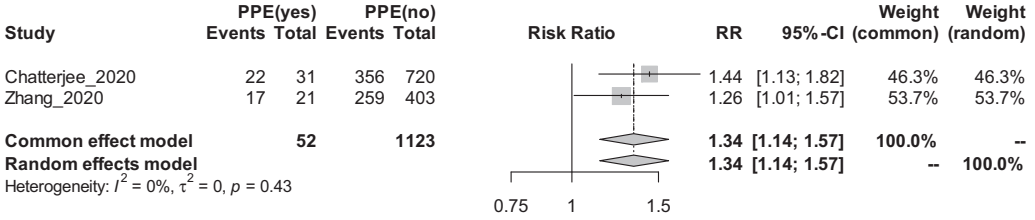

Fig. 3. Forest plot showing the meta-analysis for the effect of performing endotracheal intubations.

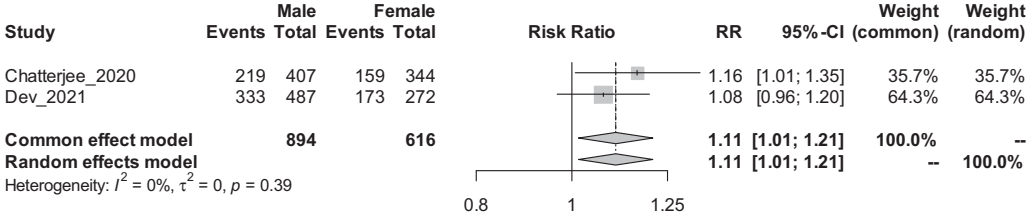

Fig. 4. Forest plot showing the meta-analysis for the effect of gender.

4. Discussion

Understanding COVID-19 risk factors among HCWs is critical to formulate the correct preventive strategies and policies, and make sure this critical population is protected from COVID-19 and its devastating health effects. This is more so as it becomes clearer that SARS-CoV-2 is likely to persist as a major respiratory pathogen in the future globally. The emergence of new variants of concern such as the beta variant and delta variant, and more recently, omicron, means effective preventive strategies over and above vaccination remain critical. In this systematic review with meta-analysis, we unveiled some of the risk factors for COVID-19 in this population, over and above other risk factors as pertains to the general population.

The study noted that the pooled incidence of COVID-19 from cohort studies was 12% (95% CI 5–26%), which is high, but highly unlikely representative of the global population of HCWs, as this meta-analysis only included 5 cohort studies which excluded some geographical regions such as Africa. These excluded settings may lack adequate PPE and other requisites for infection prevention and control such as good, controlled ventilation, and hence may have higher incidences of the infection among HCWs. Moreover, very high heterogeneity was noted among the included studies. However, this incidence is comparable to the 10% that has been reported elsewhere [39]. Accurate figures of incidence of infection among HCWs will be likely elusive because of different testing strategies in different countries, with some testing only symptomatic workers whilst some mandatorily test all their HCWs, and also similar to the general population, HCWs do not have uniform health seeking behaviors.

PPE remains a major component of infection prevention control; however, studies on this may be difficult as there are marked variations globally in what might be termed appropriate and adequate PPE for certain tasks. Depending on the level of exposure and aerosol generation, different tasks certainly require different levels of PPE, with anesthesiologists performing invasive airway procedures needing stronger protection than, for example, a HCW in an outpatients clinic seeing relatively stable patients. Thus, only 3 studies [23,27,38] were retrieved assessing the use of PPE and noted a 29% (RR 0.71, 95% CI 0.59–0.84) reduced risk in a random effects model. This did not vary in a fixed-effects model signifying less heterogeneity. PPE was also reported as a risk factor for COVID-19 infection among HCWs in an earlier review [12]. Chou et al also revealed the same results in their systematic review that included three studies reporting the SARS-CoV-2 risk factors among HCWs [13]. While the results of the present review and previous ones are consistent, more studies would be needed, with more uniformity and design to ascertain the effectiveness of PPE in reducing the risk of SARS-CoV-2 infection among HCWs. Meanwhile, resource limited countries must make use of WHO recommendations on rationalizing the use of this scarce commodity during pandemic times [40].

The availability, accessibility, and quality of PPE is an important modifiable risk factor for COVID-19 among HCWs. It is imperative therefore that administrators and policymakers must find effective ways of improving stocks and quality of this essential commodity, even including stocks in anticipation of further future waves. Local in-country production of PPE in resource-limited countries is cost-effective, and reduces the costs associated with importing from other countries. Ways of boosting local production include collaborating with local educational institutions such as Universities and Polytechnic colleges to test effectiveness of types of PPE and then produce en-masse. For example, in Zimbabwe, the government partnered with the University of Zimbabwe to boost the production of face-masks (and hand-sanitizers), which significantly improved the availability of these commodities. Additionally, encouraging foreign production companies to invest in resource-limited countries will boost the ability and capacity to produce PPE, especially in sub-Saharan Africa, whilst saving on the scarce foreign currency reserves, and improving local skills. This could be in the form of collaborations between local manufacturing companies or institutions of higher learning and foreign-based production companies.

Performing endotracheal intubation, not surprisingly, was noted as a significant risk factor for COVID-19 among HCWs, RR 1.34 95% CI 1.14−1.57. Endotracheal intubation is a highly aerosol-generating procedure, and in the absence of adequate PPE, significantly exposes the performing HCW to a significant concentration of SARS-CoV-2 particles hence COVID-19 infection; however, the level of PPE available for the HCW is a significant confounder for this analysis. Unfortunately, only 2 studies [23,37] were retrieved for this first report, limiting the analysis performed. Nevertheless, this result largely conforms to what is known/suspected and reinforces the need to provide any HCWs involved in performing this procedure with adequate prevention strategies [29,41].

This study showed that female HCWs are at 11% higher risk (RR 1.11 95% CI 1.01−1.21) of COVID-19 than their male counterparts. Unfortunately, only 2 studies were retrieved for the first report of the living systematic review, thus limiting the analysis that can be performed, and seem to deviate from the wider literature where males are at a significantly higher risk of COVID-19 and its associated adverse effects [42]. More well designed studies would be needed to answer this question but one key observation is that in general, the proportion of female HCWs is much higher than that of males [43].

A major strength of this review was the use of a comprehensive search strategy and searching multiple electronic databases. The included studies were all of acceptable quality grading, with seven being graded as fair and 3 as good. Seven cohort studies were assessed on 14 domains while the case control studies were assessed on 13 domains. The quality of evidence grades reflects the extent of confidence that our estimate of effect is correct, and this was generally acceptable for our review. However, a number of limitations are worth noting that include the limited number of studies in this area, and the lack of generalizability of findings. There is a paucity of studies looking at HCWs COVID-19 infections, and therefore some other risk factors may have been missed. Additionally, there is likely to be a higher level of interactions and confounding between the risk factors, including with the other risk factors that affect the general population such as obesity, smoking and the presence of comorbities, such as hypertension and diabetes [44, 45]. Unfortunately, with the dearth of studies, no advanced analyses such as meta regression could be performed in this study. Now that most countries initiated vaccination programs and prioritized frontline HCWs, it is important to understand how this is going to modify the risk factors among this population, hence ongoing studies are needed. Finally, no analysis was conducted to better understand the risk factors by profession. Analyses that distinguish between patient facing and non-patient facing HCWs may be informative as these two groups inherently have different incidence and risk factors.

5. Conclusion

Understanding COVID-19 risk factors among HCWs is important for devising preventive strategies that protect them from this infection, protecting the most vulnerable. This paper presents initial findings from a living systematic review and meta-analysis, therefore, did not yield many studies, however, it revealed a significant incidence of 12% of COVID-19 among HCWs, alongside lack of PPE, female gender, and performing endotracheal intubation as significant risk factors. More studies, especially among the low-resource settings of sub-Saharan Africa, which are not represented in this study, are needed to sufficiently inform policy and strategy and devise appropriate evidence-based preventive strategies to protect HCWs.

Conflicts of interest

All authors have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.shaw.2022.04.001.

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