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Healthcare Workers` Coronavirus (COVID-19) Infection during an Early Phase of the Pandemic: A Systematic Review and Meta-Analysis

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Abstract

Background: *Infection and death of health care workers (HCWs) with COVID-19 is an important health problem and will lead to inadequate care of patients, causes more damage and more spread of this pandemic. This study aimed to combine data on COVID-19 infection among HCWs through a systematic review and meta-analysis study.*
Methods: *We searched PubMed via MEDLINE, the SCOPUS, and Web of science (ISI) to identify the studies on the prevalence of HCWs infection among COVID-19 patients. We used an eight-item checklist critically appraised to assess the quality of publications on the COVID-19 infection among HCWs. Random-effect models and meta-regression were used for the meta-analysis of the results.*
Results: *Overall, 98 articles were retrieved from the databases, of which, seven met the eligibility criteria published between December 2019 to March 2020. The total sample size of the included studies contained 72677 COVID-19 confirmed cases, of which 3131 were HCWs. The pooled COVID-19 infection prevalence among HCWs was 4% (95% CI: 3% to 5%).*
Conclusions: *According to the results, COVID-19 infection in HCWs was 4% of all cases in the early phase of the pandemic. So HCWs need special care including regular screening and appropriate, adequate, and standard personal protective equipment (PPE).*

Keywords: Novel Coronavirus, COVID-19, Health care workers, Medical staff.
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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or COVID-19 is the cause of an emerging infectious disease with significant pulmonary involvement.[1] The disease was first detected in Wuhan, China, in December 2019, and on the 11th of March 2020, it was declared to be a pandemic by the world health organization (WHO).[2] Similar to other infectious diseases, health care workers (HCWs) are at the frontline of the fight against COVID-19. Hazards such as exposure to pathogens, working long hours, psychological stress, fatigue, occupational burnout, stigma, and physical and psychological violence can increase HCWs' risk of infection.[3] Transmission of infectious diseases such as severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS), and Influenza within the healthcare workers was well documented.[4-8] In the case of COVID-19, as

of the 8th of April 2020, about 20,073 healthcare workers were infected in 52 countries.[9]

During the COVID-19 pandemic, HCWs are expected to work long hours under significant pressure with often inadequate resources, while accepting the dangers inherent in close interaction with patients. Moreover, HCWs, like everyone else, are exposed to the disease and to rumors and incorrect information that necessarily decrease their mental health levels.[10] So, health care workers and researchers across all disciplines must be aware of the potential impact this disease can have on their respective health fields and the medical community at large.[11] Furthermore, reliable data on the percentage of HCWs among COVID-19 cases can assist us to better understand the nature of disease transmission. Designing an effective infection prevention plan and controlling measures to maximize HCWs' safety in healthcare facilities should be our priority. This requires an estimate of the prevalence of COVID-19 cases among HCWs. To the best of our knowledge, no pooled estimate of COVID-19 infection in HCWs is published so far. This study aimed to estimate the proportion of patients with COVID-19 infection who were HCWs.

Materials and Methods

The present systematic review and meta-analysis were conducted following the preferred reporting items for Systematic reviews and meta-analyses (PRISMA) statement.[12] A comprehensive systematic search of the literature was performed to find studies on the COVID-19 infection among HCWs. We searched PubMed/MEDLINE, SCOPUS, and Web of Science (ISI) databases by combining sets of related MeSH and Non-MeSH terms of "COVID-19" or "New Coronavirus" and "Health/HealthCare/Medical Staff" or "Health/ HealthCare Worker/s" or "Health/HealthCare Professionals" or "Health/HealthCare Personnel" to find any relevant studies until March 28th, 2020, limited to the English language. We further searched Google scholar for additional information on the infected HCWs. Studies were eligible for our review if they met the following criteria: original studies with Observational design; studies on HCWs' infection among patients with COVID-19, and studies that diagnosed COVID-19 infection with standard tests. Two authors independently searched in relevant databases, two authors screened title/abstracts, then reviewed the full texts of the studies, and discrepancies were resolved by discussing with the third author. The references of

eligible articles were also manually reviewed for other possibly related articles that were not found in the electronic search.

An eight-item checklist for the critical appraisal,[13] was used to examine the quality of eligible studies by two independent investigators. This tool defines eight following criteria.1) whether a random sample or whole population was used; 2) if an unbiased sampling frame was used; 3) adequacy of the sample size; the use of standard measures; 4) whether outcome measurements were made by unbiased assessors; 5) adequacy of the response rate; 6) confidence intervals (CIs) and subgroup analyses; and 8) whether the study subjects were described. Each item was scored as one if a study met the criterion and zero otherwise, and the scores were summed up. The range of the total score was from 0 (lowest possible quality) to 8 (highest possible quality). The studies' quality is defined as high-quality (score≥7), medium-quality (score between 4 and 6), or low-quality (score<4). The quality assessment results were also confirmed by the third investigator. Two of the co-authors extracted the following data from included studies, independently: Author, study date, country, mean age of participants, gender, the total number of HCWs, total number of HCWs infected with COVID-19, the total number of deaths among HCWs infected with COVID-19, COVID-19 infection among HCWs and its correspondence 95% confidence interval. The extracted data were compared, and discrepancies were discussed to reach a consensus. The number of patients and the total number of HCWs infected with COVID-19 disease were used to calculate the proportion of HCWs' infection among patients with COVID-19 (in logic form) and its corresponding standard error (SE).

The summary pooled proportion with 95% CI was obtained using the random-effects model. Person-day in a paper refers to a unit of measurement, especially in accountancy, based on an ideal amount of work done by one person in one working day. Cochran's Q test was used to identify the heterogeneity of the results, and it was quantified using the I2 statistic, which was above 50% or Q statistics with Pvalue<0·10 were considered as a significant between-study heterogeneity. Moreover, the between-study variance was assessed using the tau-squared (Tau2 or T2) statistic.[14]

A jack-knife sensitivity analysis was conducted by removing the studies from meta-analyses one by one. We also evaluated the publication bias using Begg's funnel plots and the asymmetry tests (Egger's and Begg's test). All statistical analyses were performed using STATA software (STATA; version 14). Pvalues less than 0.05 were considered statistically significant.

Results

As described in figure1, according to the PRISMA flow chart, a total of 98 studies were extracted by electronic and manual searching. Of these, 13 were excluded because of duplication. From the remaining 85 articles, 56 were excluded after titles and abstracts were assessed. Therefore, 29 studies remained to be carefully checked by examining the full texts, of which 22 articles were excluded for the following reasons: no relevant data (n=11), did not report the outcome of interest (n=2), did not report the COVID on HCWs (n=27). Finally, seven studies were included in qualitative synthesis, out of which seven 15-21 met our eligibility criteria and were included in the systematic review and meta-analysis. The main characteristics of the included studies are described in table 1.

Table 1. The main characteristics of the studies included in the present systematic review and meta-analysis

| Ref.	Author (s)	Date of pub.	Country	Study design	Sample size	HCW infected (%)	Type of HCW	Outcomes	Ward/ Data source	Duration of the study
15	Guan W et al.	28.2.2020	China	Cross sectional	1099	38(3.5%)	Healthcare worker	No report	National Health Commission	11 Dec 2019 to 31 Jan 2020
17	The novel COV-19 pneumonia emergency response epidemiology team		China	Cross sectional	44,672	1716 (3.8%)	Health worker (not specified)	5 (0.3%) died	China CDC (all provincial records)	31 Dec 2019 to 11 Feb 2020
19	Wang, D. et al.	7.2.2020	China	Retrospective, single-center case series	138	40(29%)	Medical staff	No report	Zhongnan Hospital of Wuhan University	1 Jan 2020 to 3 Feb 2020
16	Qui Li et. al	29.1.2020	China	Cross sectional	425	15(3.6 %)	Healthcare Worker (not specified)	No report	China CDC (all provincial records	3 Jan 2020 to 20 Jan 2020
18	Wang C et al.	6.3.2020	China	Cross sectional	25961	1316(5.1%)	Healthcare workers (not specified)	No report	Municipal Notifiable disease Report system	11 Jan 2020 to 18 Feb 2020
21	Zhang J et al	19.2.2020	China	Cross sectional	140	3(2.1%)	Hospital staff	No report	Zhongnan Hospital of Wuhan University	16 Jan 2020 to 3 Feb 2020
20	Wang G et al	Preprinted by Lancet	China	Case series	242	3(1.2%)	Medical staff (not specified)	No report	Second xiangya Hospital of central South university	17 Jan 2020 to 20 Feb 2020
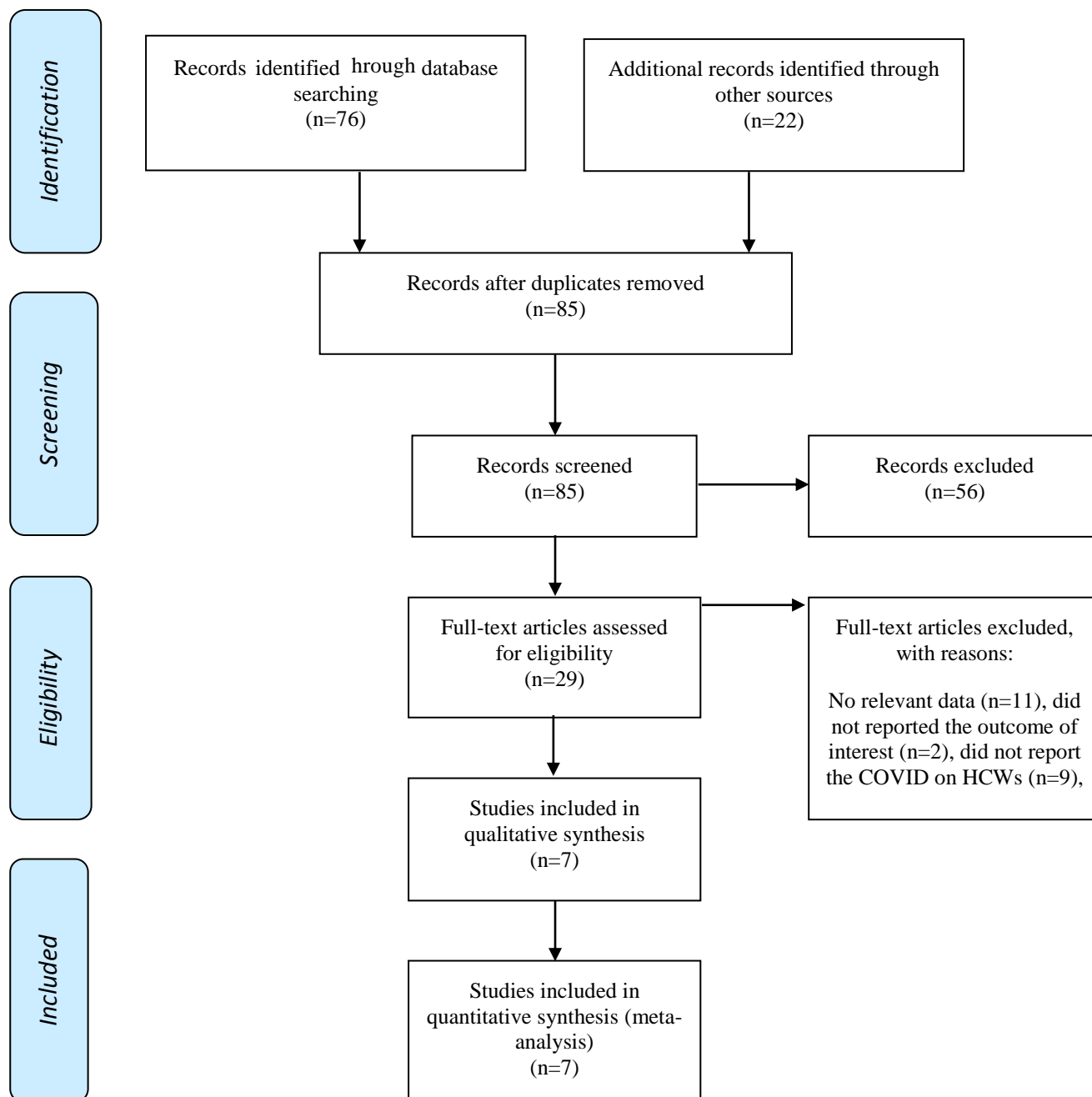
Figure 1. PRISMA flow diagram of studies included and excluded at each stage of screening

The seven relevant articles[15-21] were published from 11th Dec. 2019 to 28th Feb 2020 (the search was from 1st Dec 2019 till 28th March 2020). They consisted of 72677 patients, among which 3131 were HCWs with COVID-19. The lowest proportion of HCWs` infection with COVID-19 was reported by Wang G et al. (Prevalence=0.01, 95%CI: 0.00, 0.04)[20] and the highest rate was reported 29% by Wang D et al., (0.29, 95%CI: 0.22, 0.37).[19] Most studies were cross-sectional[15-18,21] in design except two case-series.[19,20]

According to critical appraisal, all studies were assigned as "high quality"[15,17-21] except one as "moderate quality".[16] The results

of methodological quality assessment are shown in table 2. Results of the random effect meta-analysis revealed that the pooled proportion of HCWs` infection with COVID-19 was 4% (prevalence=0.04, 95%CI: 0.03, 0.05) with a significant heterogeneity (I2=94.99%, Pvalue<0.001)(Figure 2).

We used the funnel plot and Egger test to assess publication bias. As presented in figure 3, no significant publication bias was found (t=25.31, Pvalue=0.08). Also, the results of sensitivity analysis suggest consistency with the result of pooled estimates of the prevalence after removing single studies.
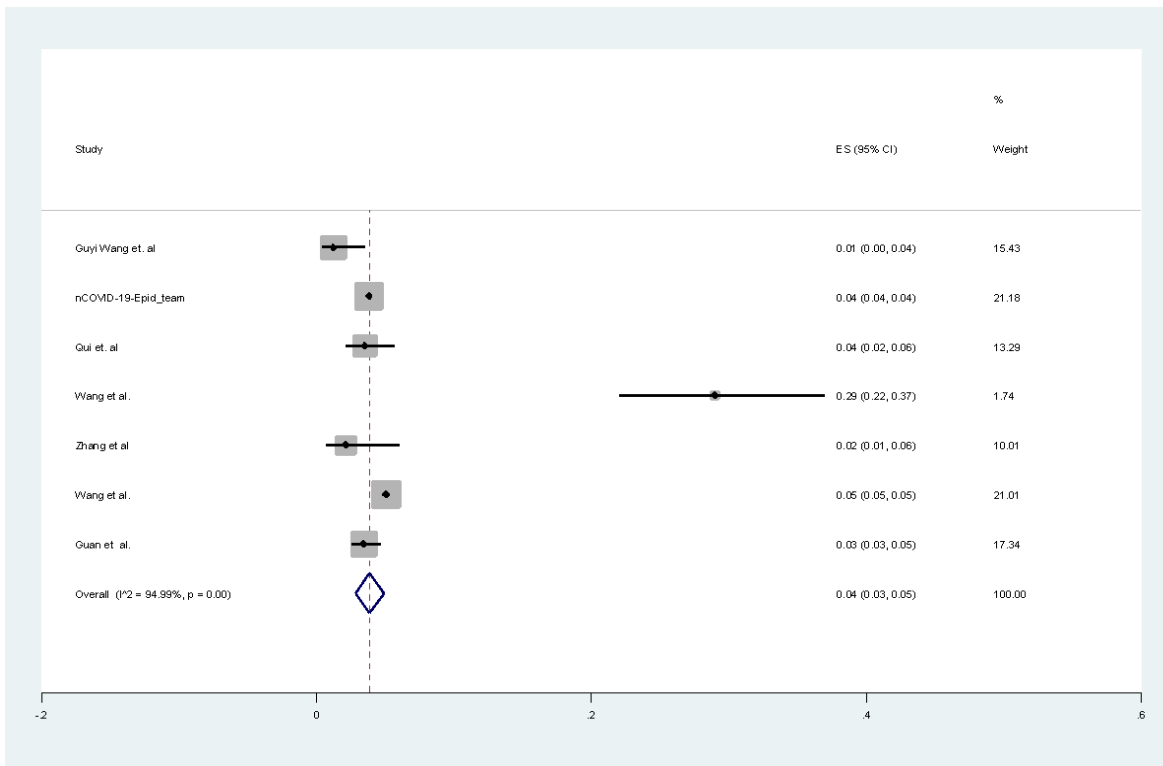
Figure 2. Number of studies and the pooled prevalence (95%CI) of COVID-19 infectiousness among HCWs
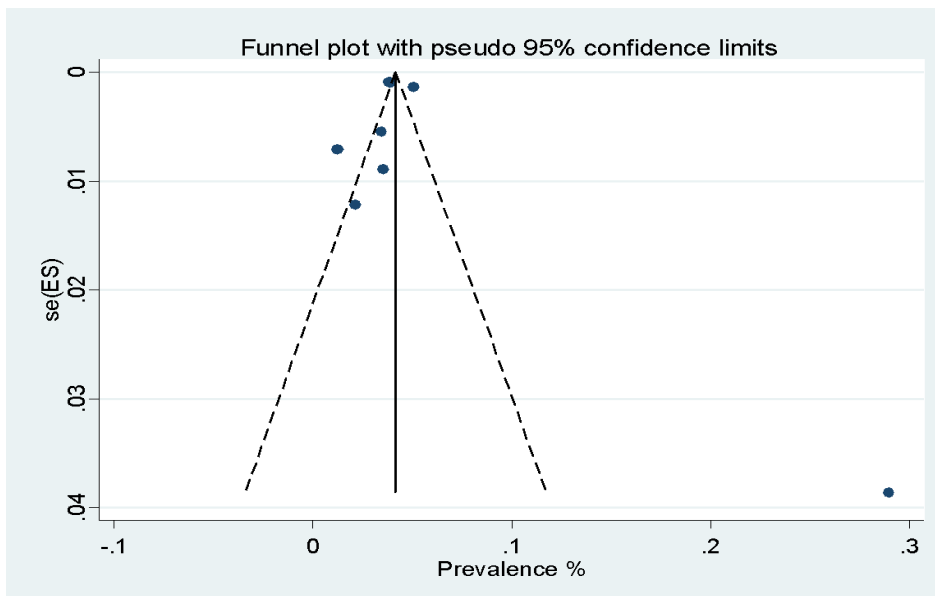

Figure3. Funnel plot of studies included in the meta-analysis

Table 2. Results of risk assessment bias using guidelines for critically appraising studies of prevalence or incidence of a health problem

Study	Are the study methods valid?						What is the interpretation of the results?	What is the applicability of the results?	Score
	a) re the study design and sampling methods appropriate for the research question?	b) Is the sampling frame appropriate?	c) Is the sample size adequate?	d) Are objective, suitable and standard criteria used for measurement of the health outcome?	e) Is the health outcome measured in an unbiased fashion?	f) Is the response rate adequate? Are the refusers described?	g) Are the estimates of prevalence or incidence given with confidence interval and in detail by subgroup, if appropriate?	h) Are the study subjects and the setting described in detail and similar to those of interest to you?	
Wang, D. et al.[19].	*	*	*	*	*	*	*	*	8
Zhang et al.[21]	*	*	*	*	*	*	*	*	8
Wang C et al.[18]	*	*	*	*	*	*	-	*	7
Wang G et al.[20]	*	*	-	*	*	*	-	*	6
Novel coronavirus Pneumonia emergency Response epidemiology Team[17]	*	*	*	*	*	*	-	*	7
Qui Li et.al[16]	*	*	*	*	*	*	-	*	7
Guan W et al.[15]	*	*	*	*	*	*	*	*	8

Discussion

Our hypothesis was to measures the prevalence of COVID-19 diseases in healthcare workers among patients via a systematic review and meta-analysis. Because they are on the front lines fighting COVID-19 every single day, hour by hour, minutes by minutes, and are at considerable risk. They would need tremendous support and care. Moreover, due to the nature of their work, they could be potential carriers, infecting others. Hence, the control of infection among HCWs is of great importance to control transmission in the community. Heterogeneity in the transmission is one of the characteristics of SARS and MERS epidemics, and especially the incidence of super-distribution events, particularly in hospitals.[22]

Our findings based on meta-analysis, on seven papers, indicated that the proportion of HCWs' infection among patients is 4% (95% CI: 3% to 5%). A study showed that while health care professionals are identified as high-risk groups, the frequency of Covid-19 infection has not been as great as cases identified among this group during the period of the SARS (33% in Meriland, China) and MERS epidemics.[23]

The first cases of COVID-19 disease were reported in China. The seven included studies during the first months of this pandemic (11 Dec.2019 to 28 Feb.2020) also were from this country.[15-21] Reporting the characteristics of the disease, including ways of transition, severity, trends, and proportion of HCWs' infection among patients, can help us strategize preventive measures and reduce the rate in this working group. Included papers in our systematic review have reported characteristics of the prevalence of COVID-19 in HCWs in four categories as follows:

1. Methods of transmission

The highest prevalence of COVID-19 among healthcare workers was 29% in Wuhan hospital in China. Among these groups of healthcare workers, no one worked in an isolated ward for COVID-19; they worked in the emergency department, intensive care unit (ICU), and general wards. A patient admitted to the surgery ward with abdominal pain was able to infect ten hospital staff and 4 patients.[16] This event occurred in the early stages of the pandemic disease and maybe abdominal pain was not recognized as a symptom of this disease.

Wang G. et al. indicated that three healthcare workers were infected among patients; one medical practitioner worked in a community health center and was responsible for monitoring the temperature of people from Wuhan. One was infected during this period, whereas another one was infected through her family. There was no confirmed case of infection among health care workers in the isolation ward of the public health treatment, center of Changsha, by Feb 20th.[20] At present, with a recognition of more than ten symptoms for COVID-19 and early detection of the patients with PCR laboratory test, we expected to prevent the transmission from late-diagnosed patients and in the other wards of hospitals to healthcare workers.

2. The severity of COVID-19 among healthcare workers

Jin-jin Zhang from Jan 2019 to Feb 3rd, 2020 in no.7 hospital of Wuhan found that infected Hospital staff was %2.1 among total patients, %3.7 in no severe patients, zero in severe patients. Also Pvalue for approval severity compared to general people was not significant (0.267).[21]

Wang C et al., in another study reported that health workers were not at the upper risk of severity (OR, 1.12; 95%CI 0.96 to 1.31) that increased by age.[18] In the study by Wang D et al., among 138 Covid19 patients, 40 cases were healthcare workers, only one was hospitalized in ICU. The differences between ICU and non-ICU patients were statistically

significant (Pvalue<0.05).[19] A study among health workers with symptoms of COVID-19 in 2 Dutch hospitals also indicated that most HCWs had mild disease.[24] This may be related to their health knowledge, self-care, and access to appropriate medications.

3. The rate of disease in health workers compared to the general population

The average attack rate in local health workers (144.7 per 1000,000 people) was largely higher than that of the general population (41.7 per 1000,000 people). The prevalence was higher in the third phase of the study (507.4 per 1000,000 people). The highest rate among the health workers reported from Jan 11 - Feb 1.[18] CDC weekly of China reported that the observed person-days were 28,069. The mortality due to COVID-19 was 0.002 per 10 person-days was 0.002 from Dec 31 2019, to Feb 11 2020, among 44672 confirmed cases in 31 provinces of China.[17]

4. Trends of HCWs' infection among patients with COVID-19

Qun Li et al., in a study in Wuhan among confirmed cases of COVID-19, reported the proportion of HCWs' infection among patients increased across the three periods. Before Jan 1 in 2020, among 47 cases, there were not any HCWs. From Jan 1 -11 of 2020 among 248 patients, there was %3, and from Jan 12 - 22 among 122 patients, 7% had infections.[16] It seems the trend has been upward until Jan 22. Chen et al., in a descriptive- retrospective study among 99 patients with 2019nCoV during Jan 1- 20, 2020, at a specialized hospital (Jinyintan] in adults aged ≥14 years in Wuhan, indicated none of the patients were healthcare.[25] In a study by CDC weekly from Dec 2019 to Feb11 among 44672 confirmed cases, the epidemic curve increased during 23-26 Jan then declined to Feb11. Before Jan 11, 4.1% of patients, Jan 11-22 8.9%, Jan 23- Feb 1, 4.9 %, Feb 2-18, 3.1 % were healthcare.[17] Based on the literature in occupational health and medicine, it is quite clear that occupational and work-related biological factors such as viruses in normal conditions, not only in the pandemic conditions of the disease, is one of the most important harmful factors in the environment of hospitals, private clinics, etc. among the health workers, especially physicians, nurses, laboratory staff, cleaners, hospital waste transportation staff, laundry, and repair staff, who are in close contact with infectious patients.[24-26] So, outbreaks of coronavirus-19 in health care workers are not unexpected due to the nature of their work, exposure to the patients, pathogenic respiratory droplets, pathogenic clothing, tools and equipment, and waste. Also, psychological problems in the workplace such as high workload, exposure to transmissible diseases, insufficient personal protective equipment, and the death of patients far away from family and worry about children, long, and continuous shift work make working conditions more difficult for these employees. Therefore, make them susceptible to disease.[9,24,25]

Our systematic review study indicated the prevalence of COVID-19 in health care workers among patients has great differences. It seems differences in different studies may be related to the definition of healthcare workers in these seven papers. The exact job of a health worker was not identified in most of these studies. On the other hand, differences may be related to lower awareness of healthcare in some hospitals from preventive measurement, in the initial situation of disease, deficiency of medical resources, including designated wards and personal protective equipment in hospitals. Almost in the middle of Feb 2020, WHO recommended masks, gloves, goggles, gowns, hand sanitizer, soap, and water cleaning supplies in sufficient quantity to healthcare for suspected and confirmed patients, that is used by them. Because no effective treatment or vaccine has been developed for these patients, the best way to fight against this virus is to prevent the spread of infection and control the sources of infection. The main strategies based on the recommendation of WHO are timely diagnosis and reporting of the disease, continuous review of the epidemiological pattern of the disease, isolation and timely treatment of patients, and control measures such as personal protective equipment and social distance at the community level. Working should be reasonably implemented in the hospital among healthcare workers in the rotation shift.

Our study has some limitations, one of them is that most of the included studies are cross-sectional, and data cannot be used to infer causality. Others are a low number of studies, insufficient sample size, low accuracy of studies at the beginning of the epidemic, no specific study in health workers, restricted studies to China, and the overlap of some studies. The strengths of our study are comprehensive search, appropriate search strategy, and to the best of our knowledge, it is the first systematic review and meta-analysis study in this field. Further research is needed to identify the risk factors for the spread of viral infections in workplaces, which can be used to plan preventive interventions at the organizational and individual levels. In the cohort study, the features of cases should continue to be monitored to identify any modifications, to identify the risk factors for the spread of viral infections in workplaces.

Our systematic review study indicated the proportion of HCWs' infection among patients is from 1.2% to 29% lead to 4% in meta-analyses. This has been approved with high sensitivity. The rate was higher than the general population, severity was mild and lower than the general population, and the method of transmission during the study period was different in the early situation of this pandemic disease compared to the next phases. These studies were all accidentally performed in China. Further studies are needed to identify other characteristics of this disease among healthcare in other countries for the prevention and control of the disease.

Acknowledgement

Conflict of Interest

The authors declare that they have no conflict of interest.

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