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Review Article

Influencing Factors of High PTSD Among Medical Staff During COVID-19: Evidences From Both Meta-analysis and Subgroup Analysis

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ABSTRACT

Background: PTSD (Post-traumatic stress disorder, PTSD) had a great impact on health care workers during the COVID-19 (Corona Virus Disease 2019, COVID-19). Better knowledge of the prevalence of PTSD and its risk factors is a major public health problem. This study was conducted to assess the prevalence and important risk factors of PTSD among medical staff during the COVID-19.

Methods: The databases were searched for studies published during the COVID-19, and a PRISMA (preferred reporting items for systematic review and meta-analysis) compliant systematic review (PROSPERO-CRD 42021278970) was carried out to identify articles from multiple databases reporting the prevalence of PTSD outcomes among medical staff. Proportion random effect analysis, I^2 statistic, quality assessment, subgroup analysis, and sensitivity analysis were carried out.

Results: A total of 28 cross-sectional studies and the PTSD results of doctors and nurses were summarized from 14 and 27 studies: the prevalences were 31% (95% CI [confidence interval, CI]: 21%–40%) and 38% (95% CI: 30%–45%) in doctors and nurses, respectively. The results also showed seven risks ($p < 0.05$): long working hours, isolation wards, COVID-19 symptoms, nurses, women, fear of infection, and pre-existing mental illness. Two factors were of borderline significance: higher professional titles and married.

Conclusion: Health care workers have a higher prevalence of PTSD during COVID-19. Health departments should provide targeted preventive measures for medical staff away from PTSD.

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1. Introduction

With the pandemic of COVID-19 (Corona Virus Disease 2019, COVID-19), unprepared medical staff have to stick to the front line to fight against the disease epidemic. The extreme working environment and the large number of cases and death rates have resulted in a heavy burden on medical staff [1]; these will have a psychological impact on the medical staff, such as the lack of protective equipment, cooperation with new teams in a new environment, fear of being infected or infected patients or infecting their family members in the process of work, making difficult moral choices in priority care, and the sense of helplessness of losing social support in isolation space [2–6]. Some studies have confirmed that during COVID-19, the prevalence of anxiety and depression among medical-related personnel was relatively high [7–9], and there was an urgent need to prevent and treat common psychological problems in this population. Moreover, existing studies have shown that this outbreak can cause the occurrence of PTSD [10–12].

Post-traumatic stress disorder (PTSD) refers to the emotions and thoughts that result from traumatic events or negative events that cause individual mental and physical pain and anxiety [13]. After receiving such a trauma, the traumatized person will show symptoms such as traumatic repetitive experience, emotional numbness, typical avoidance behavior, and increased alertness, which seriously affects the social function of the patient [14]. Some patients

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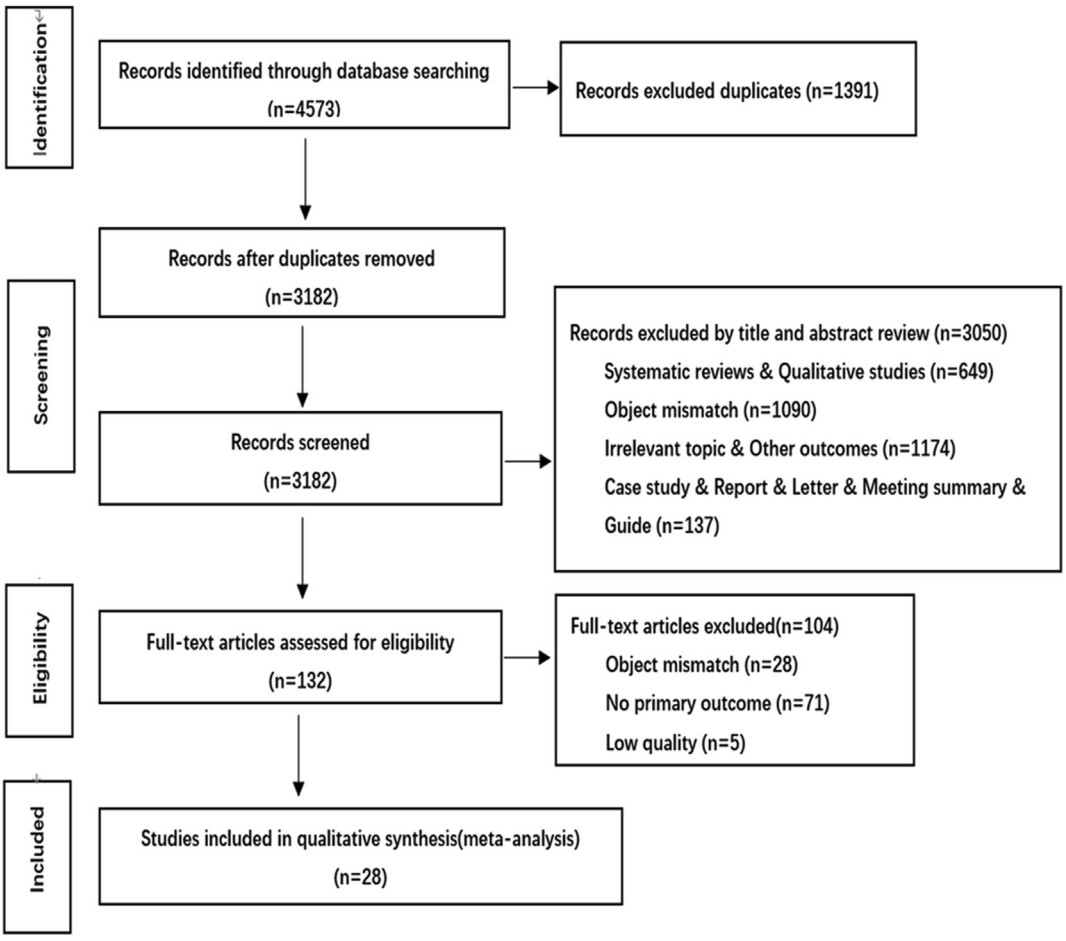

Fig. 1. PRISMA flowchart depicting the selection process of included studies.

also show abuse of addictive substances, aggressive behavior, self-harm, or suicidal behavior [15]. At the same time, depressive symptoms are also common accompanying symptoms in many PTSD patients.

Medical staff play an important role in the fight against the epidemic and face the virus, and medical and healthcare facilities are overwhelmed. Medical staff have exerted tremendous pressure to meet the needs of the people, which has caused adverse effects on mental health. The working environment and working conditions make them more susceptible to new coronary pneumonia and traumatic post-stress disorder [16–19]. Many factors can affect the psychological status of medical staff. Maintaining the mental state and medical conditions of medical staff who are responsible for the treatment of patients with coronavirus infection is essential to maintaining the quality of appropriate medical care services [20,21].

During the rapid transmission of COVID-19, scientific researchers have published a large number of relevant studies. Up to now, an urgent task is to obtain an overview of PTSD of medical workers around the world through the integration of these data and to understand and support the situation of PTSD of medical workers in a timely manner. The medical security service is very important, so the top priority is to solve the problem of PTSD prevalence among medical staff. In the previously published meta-analysis [22–25], the impact on the mental health of medical staff of different races during the COVID-19 pandemic was partly mentioned while not consistent. Some studies pointed out that the distribution areas were different; races were different, the mode of education and income were different, the fear of infection and the lack of confidence in the vaccine were related to the changes in the mental state [26,27].

During the COVID-19 pandemic, though most medical students were systematically trained and normatively managed to reduce the high-risk factors of contact with COVID-19 patients, they were asked to keep far away from the front-line of COVID-19 defense as they were inexperienced and needed protection. Therefore, medical students were not included in this study. As there are various diagnostic methods for PTSD, this meta-analysis is to present the prevalence of PTSD among medical staff and the differences in the prevalence of PTSD between doctors and nurses in different races, and to explore the prevalence of different assessment tools and the risk factors that cause PTSD in medical staff.

2. Method

The research protocol of this study has been registered with the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD420278970.

2.1. Search process

Original articles were searched from English-language paper-based databases such as PubMed, Cochran, Web of Science, Scopus, and the Chinese paper-based databases, including CNKI(China

Table 1
Characteristics of 28 included studies

Author & Year	Country	Design	Setting	Sample sizes		Assessment Instrument	Prevalence of PTSD		Risk factors	Quality Score
				Nurse	Doctor		Nurse	Doctor		
Amjed et al., 2021	Saudi Arabia	Cross-sectional study	Hospital	119	86	PCL-5	14.3%	17.4%	Hospital isolation, Current position necessitates contact with positive cases, Has a chronic disease	15
Asnakew et al., 2021	Ethiopia	Cross-sectional study	Eight Hospital	230	77	IES-R	59.1%	27.2%	Age, Sex, Marital status, Profession, Educational status, Having children, Personal protective equipment, Medical problems, Families with chronic illness, History of mental illness,t	16
Azoulay et al., 2021	France	Cross-sectional study	Hospital	412	175	IES-R	32.00%	21.70%	Resident or interns, fear of contracting COVID-19, considered a high-risk occupation, want to leave the intensive care unit	15
Bahadirli et al., 2021	Turkey	Cross-sectional study	Hospital	377	406	PCL-5	15.1%	22.9%	NA	16
Bai et al., 2021	China	Cross-sectional study	Three designated hospital for medical treatment in Wuhan	209	NA	IES-R	31.10%	NA	Age, current position and physical condition	15
Chen et al., 2020	China	Cross-sectional study	Bishan District, Chongqing	109	NA	PCL-C	21.10%	NA	Marital status, length of service, system support and humanistic care	15
Conti et al., 2021	Italy	Cross-sectional study	All Italian regions	395	224	IES-R	61.10%	50.50%	Mental status, work exhaustion, workload, work environment	17
Fan et al., 2020	China	Cross-sectional study	People's Hospital of Wuhan University	243	NA	PCL-C	13.99%	NA	Job position, number of children and coping style	16
Gu et al., 2020	China	Cross-sectional study	Fangcang shelter hospitals	410	112	IES-R	80.50%	57.20%	Nurses and participants with senior technical title	15
Guo et al., 2021	China	Cross-sectional study	Hospital in Hubei Province	554	202	PCL-C	11.00%	13.00%	educational level	19
Havaei et al., 2021	Canadian	Cross-sectional study	One Canadian province	3676	NA	PTSS-14	47.00%	NA	Work environment	15
Heesakkers et al., 2021	Netherlands	Cross-sectional study	Dutch association for ICU nurses	726	NA	IES-R	26.00%	NA	NA	15
Hu et al., 2020	China	Cross-sectional study	Third class hospital	749	NA	IES-R	44.86%	NA	Negative news, manager SARS	15

(*continued on next page*)

Table 1 (*continued*)

Author & Year	Country	Design	Setting	Sample sizes		Assessment Instrument	Prevalence of PTSD		Risk factors	Quality Score
				Nurse	Doctor		Nurse	Doctor		
Lasalvia et al., 2020	Italy	Cross-sectional study	Verona University Hospital	514	169	IES-R	64.80%	42.60%	Female, work more than 20 years, nurse, pre-existing psychological problems, fear of contracting COVID-19	15
Len et al., 2020	China	Cross-sectional study	Union Hospital Affiliated to Tongji Medical College of Huazhong University	72	NA	IES-R	73.61%	NA	Mental status, emergency work experience, having symptoms	16
Li et al., 2020	China	Cross-sectional study	First Affiliated Hospital of Bengbu Medical College	356	NA	PCL-5	61.80%	NA	Suspected ward, married	15
Li et al., 2020	China	Cross-sectional study	Wuhan ang foreign aid	205	NA	PCL-C	50.73%	NA	Working hours, external assistance, education	16
Li et al., 2021	China	Cross-sectional study	Liaoning Province Hospital	890	NA	IES-R	33.26%	NA	Mental status, emergency work experience, workload, work environment,	17
Liu et al., 2020	China	Cross-sectional study	Shanghai Pudong New Area People's Hospital	584	NA	IES-R	45.21%	NA	Age, professional title, whether there are children, whether protective materials are sufficient and whether relevant information can be obtained	15
Marco et al., 2020	US	Cross-sectional study	American College of Emergency Physicians	NA	1300	PCL-5	NA	22.30%	Exposed duration in the pandemic, obtain information, panic intensity, marital status	15
Marcomini et al., 2021	Italy	Cross-sectional study	Crema hospital	173	NA	IES-R	39.88%	NA	Lack of professional training	15
Moon et al., 2021	Korea	Cross-sectional study	NDIU ward	300	NA	IES-R	63.30%	NA	Age, have kids, working period, Isolation ward, ICU, workload, knowing infectious diseases, suspected COVID-19 Symptoms	16
Robert et al., 2021	US	Cross-sectional study	hospitals	410	638	PCL-5	23%	18%	Female, Age, Race, Health care personnel category, Home cohabitants, Community COVID-19 cumulative incidence, COVID-19 infection	15

Wang et al., 2020	China	Cross-sectional study	Wuhan fever clinic	1334	563	IES-R	10.90%	6.90%	Female, married, nurse, intermediate title, front, lack of training, lack of confidence	15
Wang et al., 2021	China	Cross-sectional study	Many hospitals in Anhui Province	261	25	PCL-C	13.99%	0.35%	Age, position and health status	16
Wanigasooriya et al., 2020	UK	Cross-sectional study	all hospital HCW in the West Midlands	776	460	IES-R	29.20%	13.30%	Female, pre-existing psychological problems, having a physical illness, inpatient ward, increase working hours, COVID-19 hospitalization	16
Xia et al., 2021	China	Cross-sectional study	Nationwide	1728	NA	PCL-5	39.10%	NA	High panic, insomnia, married	15
Zhang et al., 2020	China	Cross-sectional study	Wuhan Central Hospital	468	174	PCL-C	13.20%	23.70%	COVID-19 negative test of family members, social support	19

national knowledge infrastructure), VIP(Weipu), and WanFang. Effective search terms were extracted from relevant articles and medical subject words (MeSH) and combined them to use with keywords. The search terms include: Medical staff, Health care worker, Nurse, Doctor, Novel coronavirus pneumonia, COVID-19, Post-traumatic stress disorder, Mental disorders, PTSD, and using full-text search methods perform a search.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Reported the prevalence and/or risk factors of PTSD among doctors and/or nurses in many countries; (2) Used validated tools to evaluate doctors or nurses; (3) Can obtain sample size and prevalence.

Exclusion criteria: (1) Provide comprehensive prevalence other than medical staff; (2) Duplicate literature; (3) Low-quality literature with a score below 14; (4) Qualitative research, systematic review, case analysis, news reports, letters et al.

2.3. Quality evaluation and data extraction

Two members independently conducted literature reading and data extraction according to the literature inclusion and exclusion criteria. If there were differences, they were resolved through consultation with a third researcher. A self-designed data extraction table was used to extract from the included studies: first author, publication year, country, design type, research location, survey tool, sample size and prevalence of doctors and (or) nurses, and risk factors. The quality of the included studies was evaluated using the JBI scale [28,29], which consists of 10 questions. If the score is greater than 70% of the total score of 20, it can be considered that the risk of bias is low.

2.4. Statistical analysis

This meta-analysis was performed using Stata 14.0 software, and Q test was used for heterogeneity test. If $p \geq 0.10$ and $I^2 \leq 50\%$, the fixed effects model was used. Otherwise, the random-effects model was used. This study also used sensitivity analysis and subgroup analysis to assess the source of heterogeneity. The Egger test was used to evaluate the publication bias, and the difference was statistically significant with $p < 0.05$.

3. Results

3.1. Research characteristics and quality evaluation

A total of 4,573 articles were retrieved from the English and Chinese databases. First, 1,391 duplicate articles were excluded. Then, 3,050 articles were excluded based on titles and abstracts. After screening the full text of the remaining 132 articles, the research subjects did not meet the requirements, the sample size of doctors or nurses and the prevalence of PTSD have not been obtained, and the low quality of the literature excluded 104 articles. Finally, a total of 28 full-text articles that met the inclusion and exclusion criteria were included (Fig. 1).

Table 1 shows the basic characteristics of the included studies. These articles published reports on the prevalence of doctors and nurses of different races (Asian, Caucasian). Fourteen studies could obtain doctors' PTSD prevalence and sample size, 27 items the prevalence and sample size of nurses' PTSD could be obtained in the research; five studies [30–34] used offline self-filled questionnaires to conduct surveys, and the remaining 23 studies [14,10–12,35–53] were investigated online through the Internet. All studies were cross-sectional studies. The total sample size was

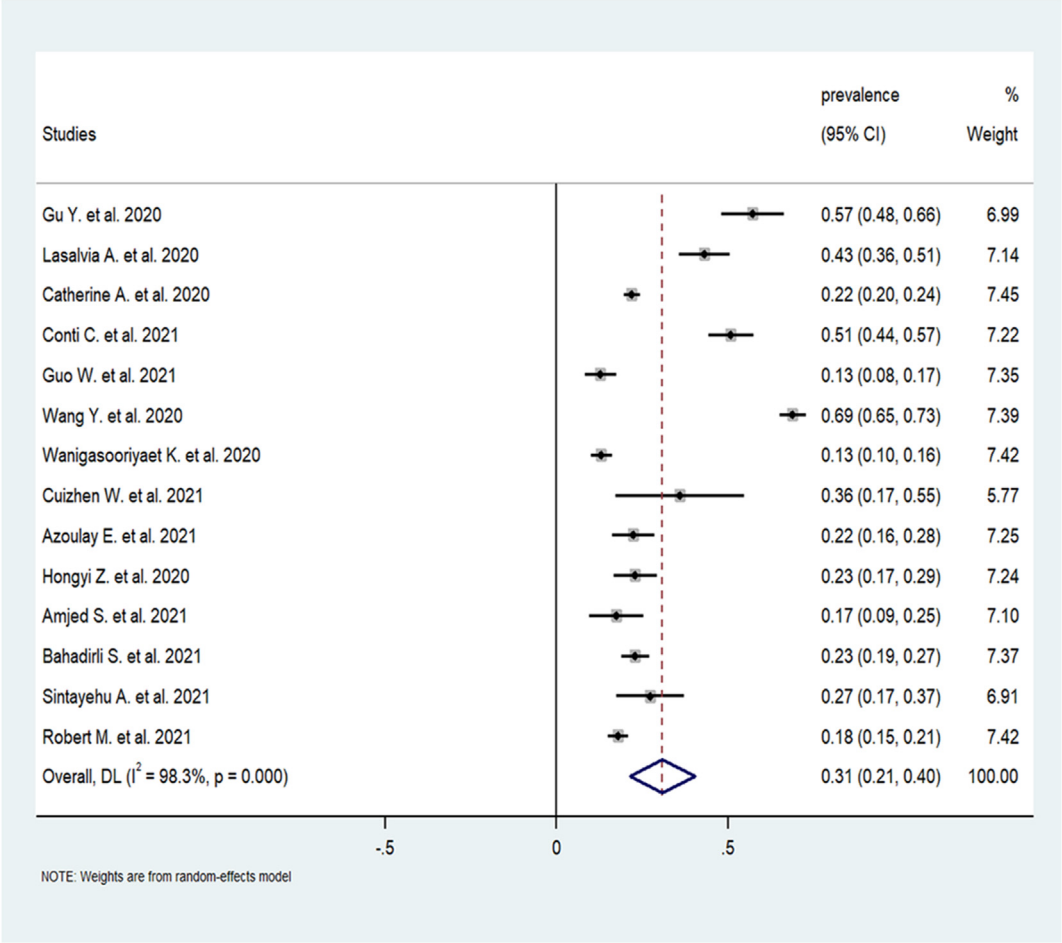

Fig. 2. Pooled prevalence of PTSD among doctors.

20,891 people. Doctors and nurses accounted for 22.07% and 77.93%, respectively, and there are 15 studies related to Asians and 13 studies related to Caucasians.

Moreover, all studies have used validated scales with specific cut-off values, such as the Event Impact Scale (IES-R), Post-traumatic Stress Disorder Screening Scale (PCL-C), list of post-traumatic stress symptoms (PTSS-14), 5th edition of the Post-traumatic Stress Disorder Screening Scale (PCL-5). The quality of each study was evaluated according to the JBI scale. After excluded lower-quality studies, the quality score ranged from 15 to 19, and 28 studies were finally included.

3.2. Meta-analysis of the prevalence of PTSD

This study used the random-effects model. Fourteen 14 studies evaluated the prevalence of PTSD among doctors, and the overall combined prevalence of PTSD was 31% (95% CI: 21%–40%), which was significantly heterogeneous ($Q = 753.01$, df = 13) (Fig. 2). Common study of 27 items evaluated the prevalence of PTSD among nurses, and the overall combined prevalence of PTSD was 38% (95% CI: 30%–45%), which was significantly heterogeneous ($Q = 3179.59$, df = 26) (Fig. 3).

3.3. Subgroup analysis

Doctors and nurses conducted subgroup analysis, respectively. Doctors (Asian: 44%, Caucasian: 26%) have different prevalence rates among different races, and nurses (Asian: 35%, Caucasian: 40%) also have different prevalence rates among different races. In the subgroup analysis of evaluation tools, the prevalence rates of the three evaluation tools were significantly different ($\chi^2 = 451.52$, $p < 0.01$). Studies involving prevalence in China include 15 studies (Table 2).

3.4. Risk factors for PTSD

The included studies involve a large number of relevant risk factors. If there were extra or equal to two studies involving the same risk factor and the odds ratio (OR) value and 95% confidence interval were provided, this factor would be extracted. The results mentioned nine factors: long working hours, isolation wards, COVID-19 symptoms, nurses, higher professional titles, married, women, fear of infection, and pre-existing mental illness (Table 3). After the summary of OR value, a total of seven factors were statistically significant and two factors approached significance. Among seven risk factors: long working hours (1.43, 95% CI: 1.23–1.67), isolation ward (1.56, 95% CI: 1.25–1.94), women (1.65, 95% CI: 1.40–1.94) and pre-existing mental illness (2.19, 95% CI: 1.83–2.62) adopted the fixed-effects model; COVID-19 symptoms (2.38, 95%: 1.09–5.22), nurses (1.74, 95% CI: 1.05–2.89), fear of infection (2.00, 95% CI: 1.15–3.48) adopted the random-effects model. Two factors: higher professional titles (2.24, 95% CI: 0.90–5.56, $p = 0.08$) and married (3.35, 95% CI: 0.87–12.79, $p = 0.08$) were of borderline significance, which adopted the random-effects model. Suffering

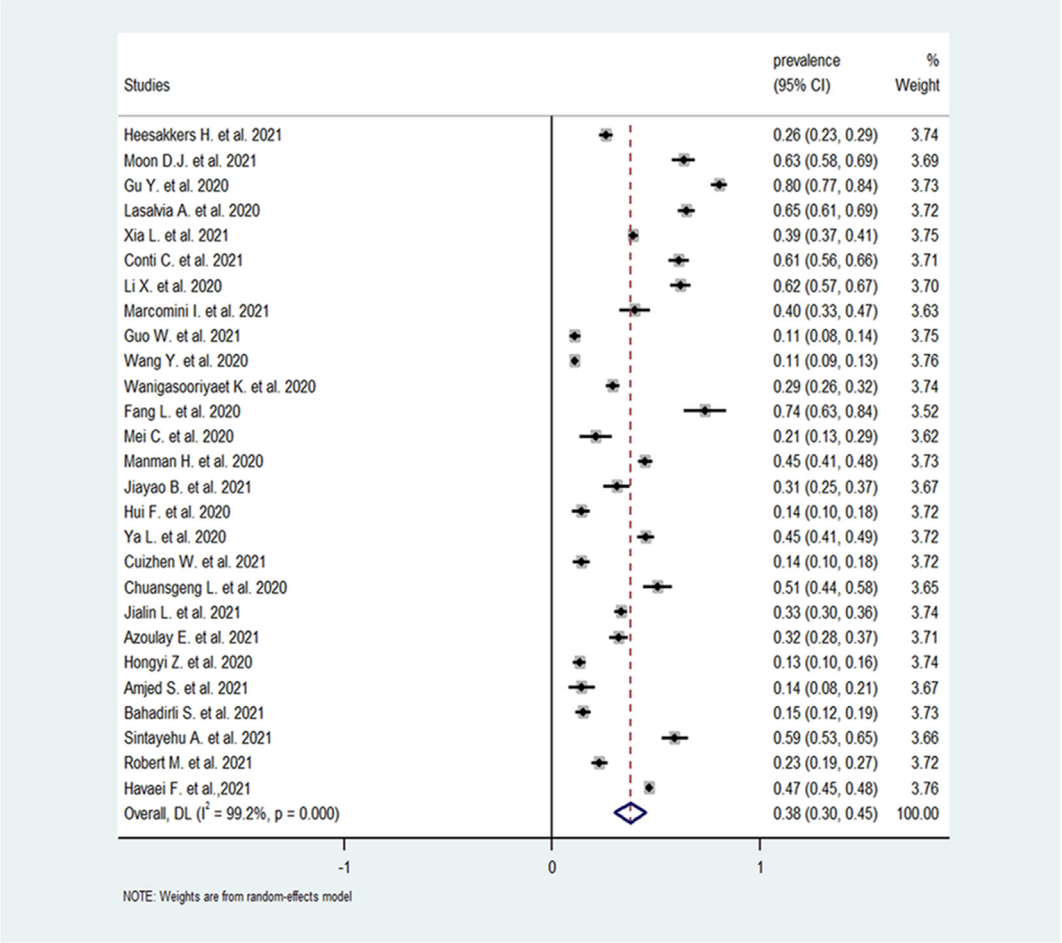

Fig. 3. Pooled prevalence of PTSD among nurses.

from COVID-19 symptoms was ranked the top risk factor, and working long hours was the weakest risk factor among the significant factors.

3.5. Publication bias and sensitivity analysis

An Egger's publication bias plots [54]were carried out to detect the presence of publication bias. Egger's results showed that publication bias was nonsignificant for doctors and nurses' PTSD: doctors ($t = 1.00$, $p = 0.339$), nurses ($t = 1.34$, $p = 0.194$), indicating that there was nonsignificant publication bias. According to the results of sensitivity analysis, none of the studies of doctors and nurses had a significant impact on the combined overall prevalence of doctors and nurses.

4. Discussion

4.1. The reason for the high prevalence of PTSD

This meta-analysis separately assessed the prevalence of PTSD among doctors and nurses during the pandemic period of COVID-19. Compared with the general population, the symptoms of

Table 2
Pooled prevalence of various subgroup categories of PTSD among medical staff

Variable	Doctor		Nurse		IES-R	PCL-5	PCL-C
	Asian	Caucasian	Asian	Caucasian			
No. of studies	4	10	15	12	15	6	6
No. of participants	3,055	4,611	9,862	12,604	9,554	5,420	2,241
No. of positive cases	1,020	1,343	3,704	4,391	3,765	1,573	396
$X^2(P)$	15.65 (<0.01)		17.76 (<0.01)		451.52 (<0.01)		
Prevalence (95%CI)	0.44 (0.10,0.78)	0.26 (0.20,0.31)	0.37 (0.30,0.45)	0.34 (0.24,0.45)	0.46 (0.35,0.58)	0.31 (0.16,0.46)	0.20 (0.12,0.28)
Heterogeneity							
I^2(%)	99.1	93.9	99.3	98.7	99.3	98.7	95.8
P	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Q	342.06	142.27	2070.40	741.81	1966.97	303.47	117.75

Table 3
Meta-analysis of risk factors for PTSD among medical staff

Risk factors	Mentioned articles	OR (95% CI)	Model	*p*	Heterogeneity	
					p	I^2 (%)
Long working hours	3	1.43 (1.23–1.67)	fixed	<0.01	0.17	43
Isolation wards	3	1.56 (1.25–1.94)	fixed	<0.01	0.256	26
COVID-19 symptoms	2	2.38 (1.09–5.22)	random	0.03	0.04	77.6
Nurses	3	1.74 (1.05–2.89)	random	<0.01	<0.01	85.6
Higher professional titles	2	2.24 (0.90–5.56)	random	0.08	<0.01	85.8
Women	3	1.65 (1.40–1.94)	fixed	<0.01	<0.01	0.95
Fear of infection	4	2.00 (1.15–3.48)	random	0.01	<0.01	97.5
Pre-existing mental illness	2	2.19 (1.83–2.62)	fixed	<0.01	0.22	34.1
Married	3	3.35 (0.87–12.79)	random	0.08	<0.01	95.3

PTSD in medical staff are similar to them, but there is a higher prevalence [55,56]. We must point out that the inclusion criteria of this study are different from those of published studies. This study was included in the COVID-19, published in Chinese and English, and contains the prevalence of PTSD among doctors or nurses. The date, demographic characteristics, and countries of the study can overlap. The researchers are not limited to front-line personnel or nonisolation ward staff [55,56].

Medical staff have a higher educational background and have mastered a lot of medical knowledge. They are more able to self-regulate their psychological impact and avoid the occurrence of PTSD. Therefore, it may underestimate the prevalence in this study. Medical staff have always been on the front line of the fight against the epidemic and are close to patients. Since the outbreak of COVID-19, the high mortality and sequelae have had a huge impact on the psychology of medical staff [1]. In the studies of Ali Sahebi and Beatriz Olaya et al, the prevalence of anxiety, depression, and insomnia was higher among medical staff [8,9,57,58], and these diseases might be affected by psychological factors, which corresponds to the higher prevalence of PTSD in this study.

4.2. Both races and diagnostic criteria affect PTSD prevalence

In the subgroup analysis, we found that there were significant differences in the prevalence of PTSD among medical staff of different races. Just like a study in the Middle East, the weakness of primary health care, inadequate social safety nets, inadequate institutions and governance systems, and economic depression would all have an impact on the psychology of medical staff [59]. According to COVID-19, there were differences in the time spent on mental health between different races [27]. The severity of COVID-19 in one region was different from that in another, which led to the difference in psychological pressure caused by the number of cases and deaths. In the vaccine era, there were differences in vaccine hesitation and doctor-patient communication among different people when patients chose to be vaccinated [26]. The direct contact between medical staff and patients also caused varying degrees of psychological pressure on the medical staff.

In another subgroup analysis, the diagnostic criteria of PCL-C, PCL-5, and IES-R were different, and there were significant differences in the reported prevalence of PTSD using different evaluation tools. The prevalence of PTSD among doctors and nurses in China was 26% (95% CI: 12%–40%), 36% (95%: 25%–47%). The prevalence of PTSD of Chinese medical staff was slightly lower than the total prevalence rate, which might be due to different prevention and control policies. Strict prevention and control measures had brought the epidemic under control and alleviated the pressure on medical staff facing the epidemic.

4.3. The risk factors of PTSD among medical staff

Medical staff spend a longer time in the ward, wear protective equipment for a long time, and more times a day. Studies have shown that wearing protective equipment for a long time might lead to increased mental stress on medical staff [60,61]. Long working hours, high work pressure, and irregular diets gradually broke down the health of medical staff, which increased the risk of post-traumatic stress disorder. The study found that the work department was related to the risk of PTSD, and the medical staff working in the isolated departments were at higher risk of PTSD [30,39,42]. In the isolation unit, the medical staff directly contacted the patient and wore protective clothing for a long time, and the risk of infection and psychological burden were relatively high.

Nurses have closer contact with patients than other medical staff, and the risk of infection is high. Providing patients with direct care made them more susceptible to emotions related to pain and fear of death [62,63]. The head nurse is expected to have a relatively poor experience in participating in the decision-making process in the ward, and it might also cause the nurse to revert a passive role, reduce self-efficacy, and increase the sense of worry [64]. Women were more sensitive and had a weaker psychological endurance in the face of emergencies. Previous studies have shown that women are more likely to suffer from PTSD [65]. Generally, women account for a larger proportion of nursing staff. The more patients nurses care for, the greater the pressure on nurses.

Since the outbreak of COVID-19, some medical staff have even died from this epidemic. The high-risk working environment had greatly stimulated the psychology of medical staff, which made medical staff afraid of contracting the new coronavirus [14,37,43]. When the corresponding symptoms of new coronary pneumonia appear, medical staff will suspect whether they are infected with the new coronavirus [42,43]. Moreover, medical staff with previous psychological problems were particularly vulnerable to the adverse psychological effects of the COVID-19 [37,42].

With the pandemic of the COVID-19, medical staff with higher professional titles need to take on more responsibilities, not only to actively deploy work, but also to ensure the safety of medical staff. They must take the lead and go to the front line, and the risk of exposure of front-line personnel is high. Working in a high-pressure environment for a long time, lacking sleep, and facing a higher infection rate and death risk of COVID-19, made medical staff with higher professional titles more likely to develop PTSD [11,41]. In this study, marriage was also a potential risk factor for PTSD [41,43]. Compared with medical staff who are single, they are more worried about their own infection and their families getting infected, and they have more burden of taking care of family members.

The high-risk working environment causes great psychological stimulation to medical staff [17–19], which could easily induce PTSD. Thus, a high pooled prevalence was obtained in this study. Studies had shown that the psychological problems of medical workers had an impact on work efficiency [6,20,21]. At present, many institutions have taken measures to address the mental health of medical personnel in this epidemic, such as telephone and online consultation, psychological support programs, activities, and assistance of mental health professionals [66,67].

4.4. Limitation

This study also has certain limitations. The heterogeneity was high, and this may be the reason that disproportionate spread of COVID-19, differences between diagnostic scales and characteristics of the research objects in many studies are inconsistent. The specific departments of doctors and nurses (even the administrative staff and technical staff) were not distinguished and analyzed. The influence of family factors of medical staff (such as whether they are the only child, the number of their children, etc.) on PTSD was also not analyzed. Moreover, this study only extracted and discussed the risk factors, not the protective factors.

5. Conclusion

During COVID-19, medical staff had a higher prevalence of PTSD. Thus, we should advocate the health care sector to fully consider the needs of medical staff, provide sufficient rest time for medical staff, improve the working environment, regularly screen mental health problems, and pay attention to physical symptoms. Give more care to nurses and ensure the safety of family members of medical staff, so that medical staff can reduce their worries and concentrate on their work.

Conflicts of interest

The authors disclose there are no conflicts of interest in this work.

Author contributions

Conceived and designed the study: G.Q. and X.S. Data collection and data clean-up: P.Y., M.Q., X.H. Analyzed the data: G.Q. Wrote the first draft: G.Q. Made revisions: S.S., X.S.

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