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Clinical characteristics of 3062 COVID-19 patients: A meta-analysis

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Abstract

We aimed to systematically review the clinical characteristics of coronavirus disease 2019 (COVID-19). Seven databases were searched to collect studies about the clinical characteristics of COVID-19 from January 1, 2020 to February 28, 2020. Then, meta-analysis was performed by using Stata12.0 software. A total of 38 studies involving 3062 COVID-19 patients were included. Meta-analysis showed that a higher proportion of infected patients was male (56.9%). The incidence rate of respiratory failure or acute respiratory distress syndrome was 19.5% and the fatality rate was 5.5%. Fever (80.4%), fatigue (46%), cough (63.1%), and expectoration (41.8%) were the most common clinical manifestations. Other common symptoms included muscle soreness (33%), anorexia (38.8%), chest tightness (35.7%), shortness of breath (35%), dyspnea (33.9%). Minor symptoms included nausea and vomiting (10.2%), diarrhea (12.9%), headache (15.4%), pharyngalgia (13.1%), shivering (10.9%), and abdominal pain (4.4%). The proportion of patients that was asymptomatic was 11.9%. Normal leukocyte counts (69.7%), lymphopenia (56.5%), elevated C-reactive protein levels (73.6%), elevated ESR (65.6%), and oxygenation index decreased (63.6%) were observed in most patients. About 37.2% of patients were found with elevated D-dimer, 25.9% of patients with leukopenia, along with abnormal levels of liver function (29%), and renal function (25.5%). Other findings included leukocytosis (12.6%) and elevated procalcitonin (17.5%). Only 25.8% of patients had lesions involving a single lung and 75.7% of patients had lesions involving bilateral lungs. The most commonly experienced symptoms of COVID-19 patients were fever, fatigue, cough, and expectoration. A relatively small percentage of patients were asymptomatic. Most patients showed normal leucocytes counts, lymphopenia, elevated levels of C-reactive protein and ESR. Bilateral lung involvement was common.

KEYWORDS
clinical characteristics, coronavirus disease 2019, meta-analysis, pneumonia, systematical review

1 | INTRODUCTION

Since December 2019, a number of cases of unexplained pneumonia have been reported in Wuhan, Hubei Province, China. On January 7, 2020, the Chinese Center for Disease Control and Prevention (CCDC) detected a novel coronavirus from a patient's throat swab,[1] which the World Health Organization (WHO) named as 2019-nCoV on January 12, 2020.[2] Subsequently, novel coronavirus-infected pneumonia (NCIP) spread to the whole world within a short time, and WHO declared NCIP as a Public Health Emergency of International Concern on January 30, 2020.[3] Then they renamed it coronavirus disease 2019 (COVID-19) on February 11, 2020.[4] In the past 2 months, the COVID-19 pandemic had spread to the whole world. As the COVID-19 pandemic accelerates, Director-General of WHO said on March 11 that COVID-19 can be characterized as a pandemic.[5] According to data released by WHO, as of 08:00 on April 7, the COVID-19 epidemic has affected 211 countries, areas or territories with a total of 1 214 466 confirmed cases and 67 767 deaths worldwide.[6] The confirmed cases in America, Italy, and Spain have surpassed 100 000 and the cases continue to climb rapidly over the whole world.[6]

As a new infectious disease, it is particularly important to find out its clinical characteristics, especially in the early stage, which is helping to detect and isolate patients earlier and to minimize its spread.[7] Although many clinical studies of this disease, have been published, most of them were single-centre, and in the same hospital. Due to the different designs and insufficient sample sizes, the clinical symptoms, the laboratory, and imaging results of the studies were different. In terms of systematic review, a recent meta-analysis by Sun et al,[8] showed that the incidence of fever was 89.1% while the incidence of cough was 72.2% in COVID-19 patients. Another study by Li et al,[9] indicated that the main clinical symptoms of COVID-19 patients were fever (88.5%), cough (68.6%) and myalgia or fatigue (35.8%). However, only 10 studies were included in these studies. Moreover, there have been many large-scale clinical research studies published,[10,11] and the reported results were not all the same. Therefore, we collected the latest studies about the clinical characteristics of COVID-19 and conducted this up-dated meta-analysis to provide references for further clinical practice.

2 | MATERIALS AND METHODS

2.1 | Search databases and search strategies

PubMed, Foreign Medical Literature Retrieval Service (FMRS), The Cochrane Library, EMBASE, Wanfang, VIP and CNKI database were electronically searched to collect clinical studies on the clinical characteristics of COVID-19 from January 1, 2020 to February 28, 2020. We also performed a manual search of the reference lists of included studies to avoid omitting any eligible study. When duplicate studies described the same population, the most informative or recent study was included. There was no language restriction placed

in the literature search, but only literature published online were included. The following terms were used in search alone or in combination: "Coronavirus" OR "2019-nCoV" OR "COVID-19" OR "SARS-CoV-2".

2.2 | Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) cohort studies, case-control studies, and case series studies; (2) the study population included individuals diagnosed with COVID-19; (3) the primary outcomes were: clinical symptoms, signs, laboratory, and imaging results; the secondary outcomes were the incidence of respiratory failure (RF) or acute respiratory distress syndrome (ARDS), fatality rate, etc.

The exclusion criteria were as follows: (1) overlapping or duplicate studies; (2) Tthe epidemiological analysis with only secondary outcomes such as fatality rate, without the primary outcomes; (3) had no clinical indicators or lacking necessary data; (4) case reports and studies with a sample size less than 10.

2.3 | Data extraction and quality assessment

Two reviewers according to the inclusion and exclusion criteria independently selected the literature, and extracted data to an Excel database. And any disagreement was resolved by consensus. Data extraction includes the first author's surname and the date of publication of the article, study region/country, study design, sample size, age, outcome measurement data such as clinical symptoms; relevant elements of bias risk assessment.

The included studies of this meta-analyses were observational case series studies, so the British National Institute for Clinical Excellence (NICE)[12] was used to evaluate the study quality by two independent reviewers. The evaluation included 8 items and the total score was 8. Studies with a score greater than 4 were seen as high-quality.

2.4 | Statistical analyses

All the meta-analyses were performed by using STATA 12 (StataCorp, Texas). In this study, incidence rates r of the included studies were first transformed by the double arcsine method to make them conform to normal distribution and then we carried out the single-arm meta-analyses with the transformed rate tr. The heterogeneity between studies was analyzed by the chi-square test with significance set at $P < 0.10$ and the heterogeneity was quantified using the I^2 statistic. The fixed-effects model was utilized when there was no statistical heterogeneity between the results of each study; if there was statistical heterogeneity, the subgroup analysis, sensitivity analysis were employed to explore the source of heterogeneity. After eliminating the influence of clinical heterogeneity, the random effect model was used for meta-analysis. Pooled incidence rates R were back-calculated from

transformed rates tr using the $R = [\sin(tr/2)]^2$. Funnel plot together with Egger's regression asymmetry test and Begg's test were used to evaluate publication bias. A two-tailed $P < .05$ was considered statistically significant.

3 | RESULTS

3.1 | Literature retrieval

Altogether, 2387 records were identified during the initial retrieval. After a detailed assessment based on the inclusion criteria, 38 studies[13-50] involving 3 062 COVID-19 patients were included in this meta-analysis (Figure 1).

3.2 | Characteristics of articles

All studies included in the meta-analysis were conducted in China and the publication time of the included studies was between February 4, 2020 to February 28, 2020. These retrospective studies examined Chinese patients distributed across 31 provinces.

The quality scores of the included studies were 5 to 8, all of them were high-quality studies (≥ 4 scores). Most of the studies were single-center and the criteria for inclusion and exclusion were not clearly explained (Table 1).

3.3 | Results of meta-analysis

3.3.1 | Gender distribution

A total of 38 studies[13-50] involving 3 062 COVID-19 patients were included. There was no significant heterogeneity across enrolled studies ($I^2 = 39.7\%$). The fix-effects model was used in the meta-analysis, which showed that the proportion of male was 56.9% (95% CI, 54.96%-58.42%) (Figure 2).

3.3.2 | Clinical symptoms

The incidence of most commonly experienced symptoms were as follows: Fever (80.4%; 95% CI, 73.0%-86.9%), fatigue (46%; 95% CI, 38.2%-54%), cough (63.1%; 95% CI, 57.9%-68.2%),
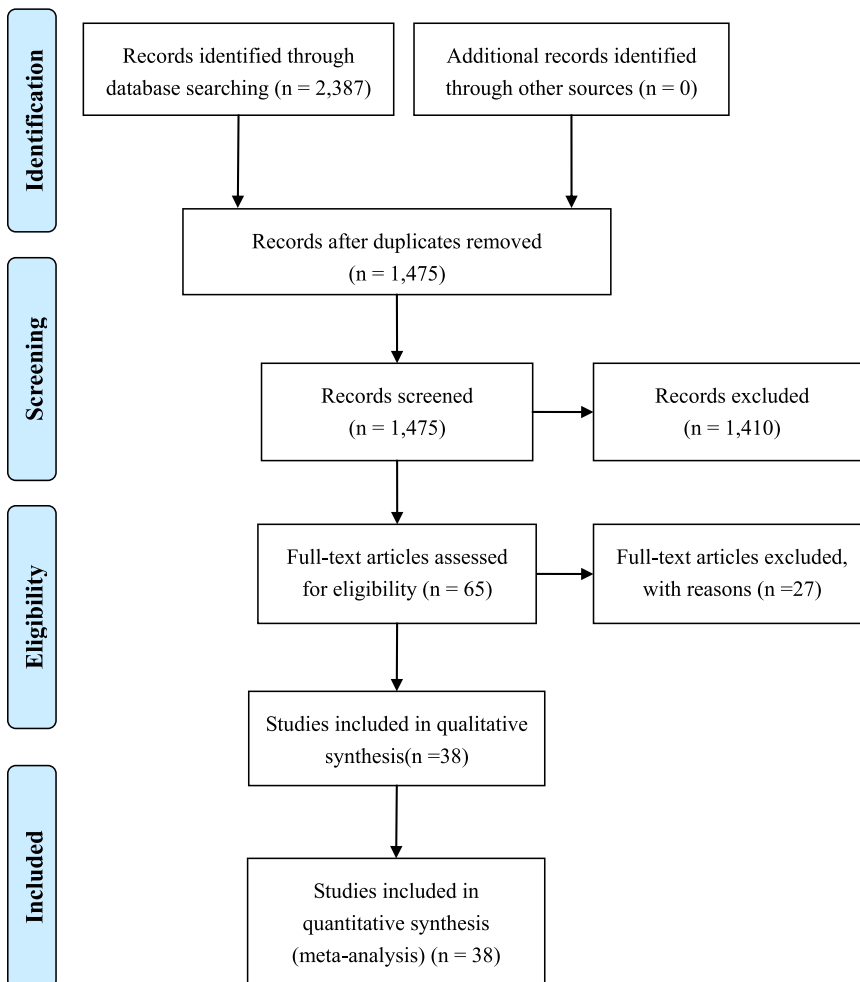

FIGURE 1 Flow chart of literature screening

TABLE 1 Basic characteristics of included studies

Region	No. patients	Study population	Age,[a] y	Male, %	Outcomes	Quality score	Study	Publication date
Jilin	50	Jan 28 to Feb 21, four hospitals in Jilin Province	44.52 ± 16.12	60	①	8	Wang et al[49]	Feb 28
Wuhan	29	Jan 14 to Jan 29, Tongji Hospital Affiliated to Huazhong University of Science and Technology	56 (26-79)	72.4	①②⑤	7	Chen et al[50]	Feb 07
Shenzhen	12	Jan 11 to Feb 2, The Third People's Hospital of Shenzhen	63 (46-73)	66.7	①②③④	6	Chen et al[13]	Feb 26
Anhui	79	Jan 22 to Feb 18, Anhui Provincial Hospital	45.1 ± 16.6	57	①②③④	5	Fang et al[14]	Feb 25
Beijing	40	Jan 21 to Feb, Chinese People's Liberation Army General Hospital	39.9 ± 18.2	65	①②③	6	Yu et al[15]	Feb 17
Nanjing	42	Jan 19 to Feb, Nanjing Hospital Affiliated to Nanjing University of Traditional Chinese Medicine	43 ± 16.8	55	①②	5	Zhang et al[16]	Feb 19
Wuhan	30	Jan 10 to Jan 31, Jianghan University Affiliated Hospital	35 ± 8	33.3	①②③④	6	Liu et al[17]	Feb 17
Wuhan	54	Jan to Feb, Wuhan Fourth Hospital	51.5	69	①②③	7	Li et al[18]	Feb 23
Chongqing	143	Jan 23 to Feb 8, Chongqing Three Gorges Central Hospital	45.13 ± 1.04	51	①②⑤	6	Xiao et al[19]	Feb 27
Tianjin	88	Jan 21 to Feb 8, Tianjin Haihe Hospital	48.52 ± 15.67	56	①	7	Sun et al[20]	Feb 24
Hubei	46	Jan 22 to Feb 5, HUbei Provincial Hospital of Integrated Chinese and Western Medicine	54.58 ± 17	56	①	7	Xu B[21]	Feb 25
Beijing	26	Jan, Chinese People's Liberation Army General Hospital	39.77 ± 15.55	69	①	6	Zhuang et al[22]	Feb 19
Shanghai	50	NR	50.4 ± 16.8	56	①②③	6	Lu et al[23]	Feb 10
Zhejiang	62	Jan 10 to Jan 26, Seven hospitals in Zhejiang Province	41	55.4	①②③④	6	Xu et al[24]	Feb 19
Wuhan	140	Jan 16 to Feb 3, No. 7 hospital of Wuhan	57.0	50.7	①②③	6	Zhang et al[25]	Feb 23
Wuhan	138	Jan 1 to Jan 28, Zhongnan Hospital of Wuhan University	56 (42-68)	54.3	①②③④⑤	6	Wang et al[26]	Feb 08
Hubei	137	Dec 30 to Jan 24, nine tertiary hospitals in Hubei Province	55 ± 16	44.5	①②③④	6	Kui et al[27]	Feb 18
Wuhan	41	Before Jan 2, Hospitals in Hubei Province	49 (41-58)	70.5	①②③④	6	Huang et al[28]	Feb 15
Wuhan	99	Jan 1 to Jan 20, Wuhan Jinyintan Hospital	55.5 ± 13.1	67.7	①②③④	6	Chen et al[29]	Feb 15
31 Provinces	1099	552 hospitals in 31 provinces	47.0	58	①②③④	8	Guan et al[30]	Feb 06
Sichuan	17	Jan 22 to Feb 10, Dazhou Central Hospital	45 (22-65)	52.9	①③④	6	Li et al[31]	Feb 11
Beijing	13	Jan 1 to Feb 4, three hospitals in Beijing	34	77	①③④	8	Chang et al[32]	Feb 07
4 Provinces	121	Jan 18 to Feb 2, four hospitals in four Chinese provinces	45.3 (18-80)	50	①③	8	Bernheim et al[33]	Feb 20
Zhuhai, Shanghai, Nanchang	21	Jan 18 to Jan 27, three hospitals in Nanchang, Shanghai, Zhuhai	51 ± 14.5	62	①③	6	Chung et al[34]	Feb 04
Shenzhen	15	Jan 16 to Feb 6, Shenzhen Third People's Hospital	4-14	33.3	①③	6	Feng et al[35]	Feb 16

(Continues)

TABLE 1 (Continued)

Region	No. patients	Study population	Age,[a] y	Male, %	Outcomes	Quality score	Study	Publication date
Zhejiang	52	Jan 9 to Feb 3, The First Affiliated Hospital of Zhejiang University	44 ± 14	56	①	6	Wang et al[36]	Feb 25
Chongqing	80	Jan to Feb, three hospitals in Chongqing	44 ± 11	80	①②③	7	Wu et al[37]	Feb 21
Guangdong	35	Dec 23 to Feb 14, Guangdong Second People's Hospital	44.0 ± 15.2	80	①②③	6	Huang et al[38]	Feb 28
Wuhan	36	Jan to Feb, Zhongnan Hospital of Wuhan University	72.45 ± 6.82	56	①②③	6	Cao et al[39]	Feb 28
Wuhan	42	Jan 16 to Feb 18, Zhongnan Hospital of Wuhan University	51.6	69	②③	6	Liao et al[40]	Feb 26
Zhejiang	40	Jan 17 to Jan 28, Wenzhou Sixth People's Hospital	45.9	55	①③	6	Yu et al[41]	Feb 26
Anhui	12	Jan 26 to Feb 6, The First Affiliated Hospital of Anhui Medical University	37	57	①②③	6	Li et al[42]	Feb 24
Hubei	41	Xiaochang First People's Hospital	48.45	78	②③	6	Liu et al[43]	Feb 18
Wuhan	32	Before Jan 25, Affiliated Xiaogan Hospital of Wuhan University of Science and Technology	NR	50	①②③	6	Wang et al[44]	Feb 19
Wuhan	54	Jan 1 to Jan 31, The Affiliated Puren Hospital of Wuhan University of Science and Technology	60.1 ± 17	54	①②	7	Cheng et al[45]	Feb 19
Shenzhen	12	Jan 11 to Jan 20, Shenzhen Third People's Hospital	10-72	67	①②	5	Liu et al[46]	Feb 12
Wuhan	30	Affiliated Hospital of Wuhan University	50.17 ± 17.6	60	①③	5	Zhong et al[47]	Feb 13
Xian	10	Jan, The First Affiliated Hospital of Xi'an Jiaotong University	41.8 ± 13.6	60	①②③	5	Gao et al[48]	Feb 13

Note: ①, symptoms; ②, laboratory findings; ③, imaging; ④, the incidence rate of RF or ARDS; ⑤, fatality rate; NR, not reported.
[a]Reported variously as range or mean ± SD or median, and interquartile range (IQR) values.

expectoration (41.8%; 95% CI, 33.9%-50%). Muscle soreness (33%), anorexia (38.8%), chest tightness (35.7%), shortness of breath (35%), dyspnea (33.9%) also occurred frequently. Less frequent symptoms were nausea and vomiting (10.2%), diarrhea (12.9%), headache (15.4%), pharyngalgia (13.1%), shivering (10.9%), and abdominal pain (4.4%). Patients who were asymptomatic was 11.9% (Table 2, Figures 3 and 4).

3.3.3 | Laboratory indicators

Most patients showed normal leucocytes counts (69.7%; 95% CI, 62.8%-76.2%), lymphopenia (56.5%; 95% CI, 46.5%-66.4%), elevated C-reactive protein (73.6%; 95% CI, 66.1%-80.4%) and Erythrocyte Sedimentation Rate (ESR) (65.6%; 95% CI, 36.8%-89.3%), and the oxygenation index decreased (63.6%; 95% CI, 32.4%-89.5%).
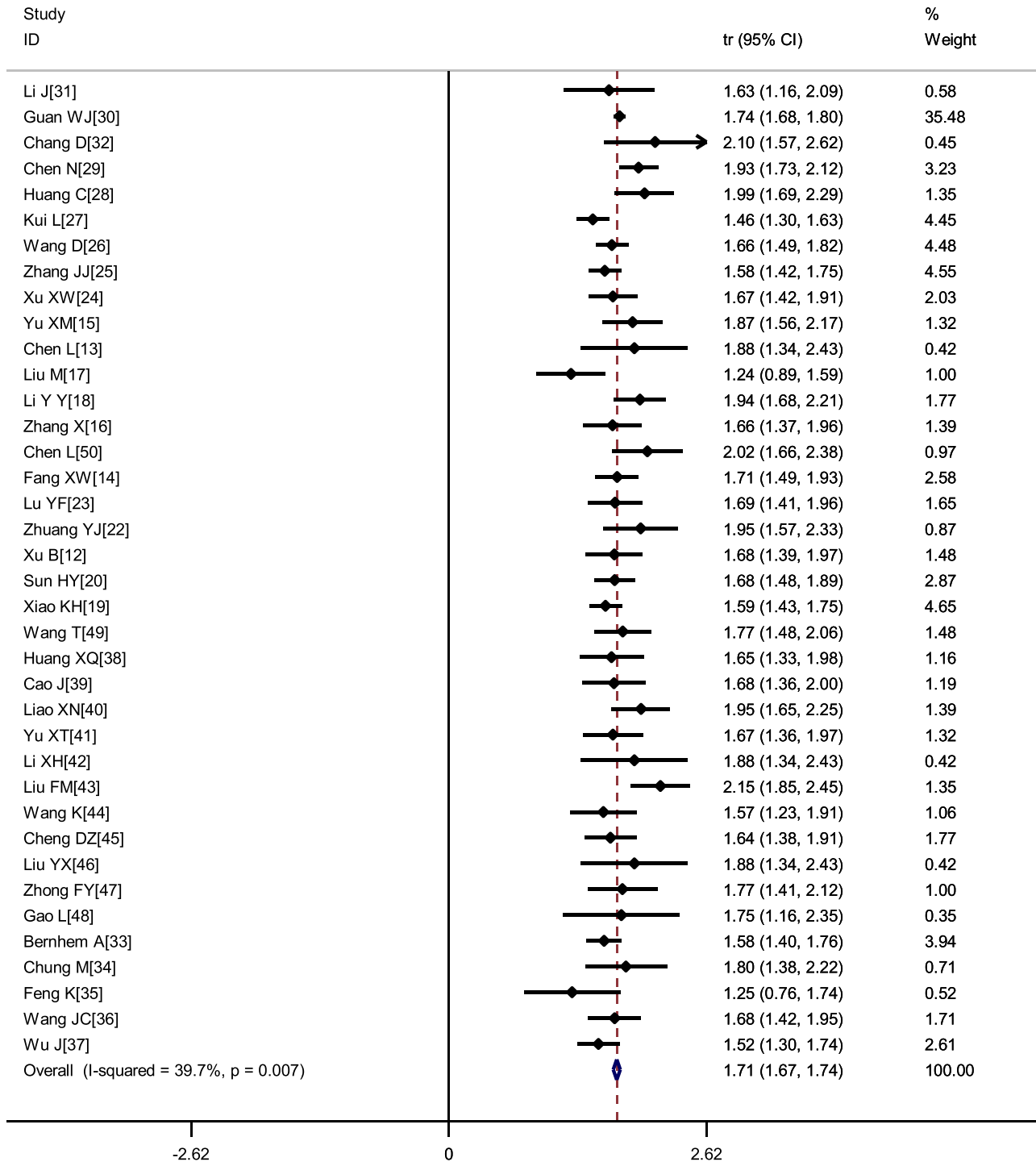
Study ID	tr (95% CI)	% Weight
Li J[31]	1.63 (1.16, 2.09)	0.58
Guan WJ[30]	1.74 (1.68, 1.80)	35.48
Chang D[32]	2.10 (1.57, 2.62)	0.45
Chen N[29]	1.93 (1.73, 2.12)	3.23
Huang C[28]	1.99 (1.69, 2.29)	1.35
Kui L[27]	1.46 (1.30, 1.63)	4.45
Wang D[26]	1.66 (1.49, 1.82)	4.48
Zhang JJ[25]	1.58 (1.42, 1.75)	4.55
Xu XW[24]	1.67 (1.42, 1.91)	2.03
Yu XM[15]	1.87 (1.56, 2.17)	1.32
Chen L[13]	1.88 (1.34, 2.43)	0.42
Liu M[17]	1.24 (0.89, 1.59)	1.00
Li Y Y[18]	1.94 (1.68, 2.21)	1.77
Zhang X[16]	1.66 (1.37, 1.96)	1.39
Chen L[50]	2.02 (1.66, 2.38)	0.97
Fang XW[14]	1.71 (1.49, 1.93)	2.58
Lu YF[23]	1.69 (1.41, 1.96)	1.65
Zhuang YJ[22]	1.95 (1.57, 2.33)	0.87
Xu B[12]	1.68 (1.39, 1.97)	1.48
Sun HY[20]	1.68 (1.48, 1.89)	2.87
Xiao KH[19]	1.59 (1.43, 1.75)	4.65
Wang T[49]	1.77 (1.48, 2.06)	1.48
Huang XQ[38]	1.65 (1.33, 1.98)	1.16
Cao J[39]	1.68 (1.36, 2.00)	1.19
Liao XN[40]	1.95 (1.65, 2.25)	1.39
Yu XT[41]	1.67 (1.36, 1.97)	1.32
Li XH[42]	1.88 (1.34, 2.43)	0.42
Liu FM[43]	2.15 (1.85, 2.45)	1.35
Wang K[44]	1.57 (1.23, 1.91)	1.06
Cheng DZ[45]	1.64 (1.38, 1.91)	1.77
Liu YX[46]	1.88 (1.34, 2.43)	0.42
Zhong FY[47]	1.77 (1.41, 2.12)	1.00
Gao L[48]	1.75 (1.16, 2.35)	0.35
Bernhem A[33]	1.58 (1.40, 1.76)	3.94
Chung M[34]	1.80 (1.38, 2.22)	0.71
Feng K[35]	1.25 (0.76, 1.74)	0.52
Wang JC[36]	1.68 (1.42, 1.95)	1.71
Wu J[37]	1.52 (1.30, 1.74)	2.61
Overall (I-squared = 39.7%, p = 0.007)	1.71 (1.67, 1.74)	100.00

-2.62   0   2.62

FIGURE 2 Transformed proportion of males in COVID-19 patients

TABLE 2 Meta-analysis of different clinical symptoms in COVID-19 patients

Symptoms	No. studies	No. patients	Heterogeneity		Model	Meta analysis	
			P	I^2		R (95% CI)	P
Fever	35	2966	<.001	95%	Random	0.804 (0.730, 0.869)	<.001
Cough	36	2979	<.001	85.5%	Random	0.631 (0.579, 0.682)	<.001
Fatigue	26	2595	<.001	92.6%	Random	0.460 (0.382, 0.540)	<.001
Muscle soreness	25	2444	<.001	91.3%	Random	0.330 (0.260,0.405)	<.001
Headache	24	2452	<.001	82.1%	Random	0.154 (0.116,0.196)	<.001
Diarrhea	24	2378	<.001	85.5%	Random	0.129 (0.899,0.174)	<.001
Expectoration	17	1908	<.001	88.2%	Random	0.418 (0.339,0.500)	<.001
Dyspnea	14	955	<.001	90.7%	Random	0.339 (0.242,0.443)	<.001
Chest tightness	14	660	<.001	92.0%	Random	0.357 (0.232,0.493)	<.001
Nausea and vomiting	10	1638	<.001	86.5%	Random	0.102 (0.054,0.163)	<.001
Pharyngalgia	10	751	<.001	85.5%	Random	0.131 (0.074,0.203)	<.001
Shortness of breath	8	1379	<.001	91.8%	Random	0.350 (0.217,0.498)	<.001
Anorexia	6	467	<.001	97.3%	Random	0.388 (0.141,0.671)	<.001
Abdominal pain	5	545	.161	39.1%	Random	0.044 (0.025,0.069)	<.001
Shivering	5	314	.057	56.4%	Random	0.110 (0.058,0.174)	<.001
Chest pain	2	87	<.001	94.8%	Random	0.283 (0.010,0.729)	.017
Asymptomatic	5	158	<.001	80.7%	Random	0.119 (0.029,0.258)	<.001

Also observed were elevated levels of liver function (29%), renal function (25.5%) and D-dimer (25.9%). Only a few patients had leukocytosis (12.6%) and elevated procalcitonin (17.5%) (Table 3).

3.3.4 | Imaging

There were 28 studies reported the imaging in COVID-19 patients. The results of the meta-analysis showed that 25.8% (95% CI, 15.6%-37.4%) of patients had lesions involving the single lung and 75.7% (95% CI, 65.7%-84.5%) involving bilateral lungs (Table 3).

3.3.5 | Incidence of RF or ARDS

There were 8 studies reporting the incidence of RF or ARDS in COVID-19 patients. The random-effects model was used in the meta-analysis, which showed that the incidence of RF or ARDS was 19.5% (95% CI, 5%-40.3%) (Table 3).

3.3.6 | Fatality rate

A total of 8 studies including 1 765 patients with COVID-19 were included. The meta-analysis result of the random effects model showed that the fatality rate in COVID-19 was 5.5% (95% CI, 2.3%-10.0%) (Table 3).

3.3.7 | Subgroup analysis

There was significant heterogeneity across enrolled studies. To explore the sources of heterogeneity, we performed a subgroup analysis by sample size (< 50, 50-100, and ≥100) and study region (Hubei Province and outside Hubei Province). As shown in Table 4, the results of subgroup analysis were consistent with the integrated results. In addition, the subgroup analysis to some extent decreased the heterogeneity between the studies. But when the study population was outside Hubei Province, a drop was observed in the incidence of fever and fatigue.

3.3.8 | Sensitivity analysis

To determine the sensitivity, we removed each study one by one and the pooled results did not change substantially, indicating the reliability and stability of our meta-analysis (eg, Figure 5).

3.4 | Publication bias

According to the funnel plot regarding the proportion of men in COVID-19 patients, together with Egger's regression asymmetry test and Begg's test, this indicated there was no notable evidence of publication bias, the P values were .531 and .269, respectively (Figure 6).
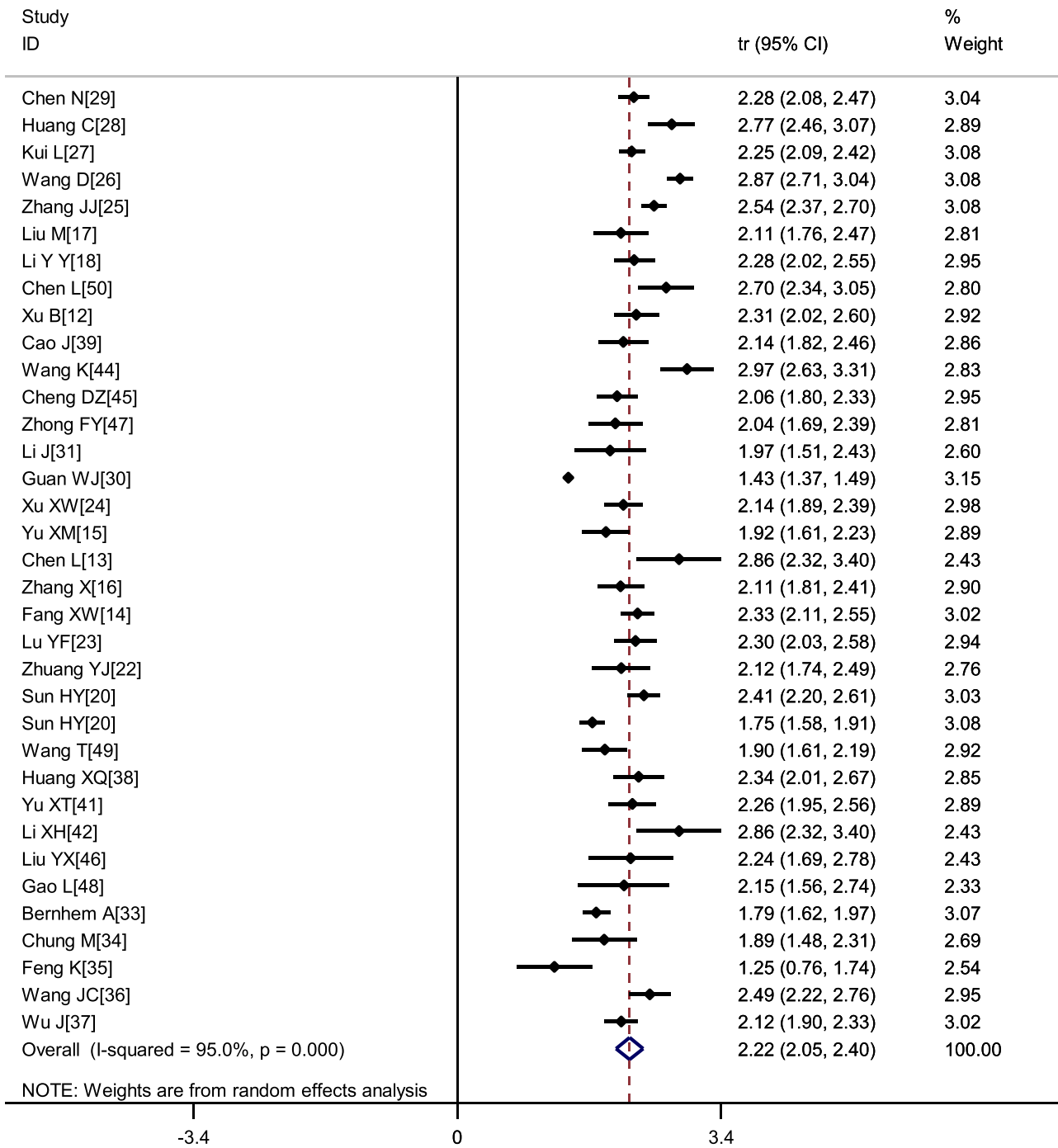
Study ID		tr (95% CI)	% Weight
Chen N[29]		2.28 (2.08, 2.47)	3.04
Huang C[28]		2.77 (2.46, 3.07)	2.89
Kui L[27]		2.25 (2.09, 2.42)	3.08
Wang D[26]		2.87 (2.71, 3.04)	3.08
Zhang JJ[25]		2.54 (2.37, 2.70)	3.08
Liu M[17]		2.11 (1.76, 2.47)	2.81
Li Y Y[18]		2.28 (2.02, 2.55)	2.95
Chen L[50]		2.70 (2.34, 3.05)	2.80
Xu B[12]		2.31 (2.02, 2.60)	2.92
Cao J[39]		2.14 (1.82, 2.46)	2.86
Wang K[44]		2.97 (2.63, 3.31)	2.83
Cheng DZ[45]		2.06 (1.80, 2.33)	2.95
Zhong FY[47]		2.04 (1.69, 2.39)	2.81
Li J[31]		1.97 (1.51, 2.43)	2.60
Guan WJ[30]		1.43 (1.37, 1.49)	3.15
Xu XW[24]		2.14 (1.89, 2.39)	2.98
Yu XM[15]		1.92 (1.61, 2.23)	2.89
Chen L[13]		2.86 (2.32, 3.40)	2.43
Zhang X[16]		2.11 (1.81, 2.41)	2.90
Fang XW[14]		2.33 (2.11, 2.55)	3.02
Lu YF[23]		2.30 (2.03, 2.58)	2.94
Zhuang YJ[22]		2.12 (1.74, 2.49)	2.76
Sun HY[20]		2.41 (2.20, 2.61)	3.03
Sun HY[20]		1.75 (1.58, 1.91)	3.08
Wang T[49]		1.90 (1.61, 2.19)	2.92
Huang XQ[38]		2.34 (2.01, 2.67)	2.85
Yu XT[41]		2.26 (1.95, 2.56)	2.89
Li XH[42]		2.86 (2.32, 3.40)	2.43
Liu YX[46]		2.24 (1.69, 2.78)	2.43
Gao L[48]		2.15 (1.56, 2.74)	2.33
Bernhem A[33]		1.79 (1.62, 1.97)	3.07
Chung M[34]		1.89 (1.48, 2.31)	2.69
Feng K[35]		1.25 (0.76, 1.74)	2.54
Wang JC[36]		2.49 (2.22, 2.76)	2.95
Wu J[37]		2.12 (1.90, 2.33)	3.02
Overall (I-squared = 95.0%, p = 0.000)		2.22 (2.05, 2.40)	100.00

NOTE: Weights are from random effects analysis

-3.4   0   3.4

FIGURE 3 Transformed incidence rate of fever in COVID-19 patients

4 | DISCUSSION

2019-nCoV is a type of coronaviruses which belongs to the β-coronavirus cluster, a positive-stranded single-stranded RNA virus.[51] In the past two decades, humans have experienced three fatal coronavirus infections. They are the outbreak of Severe Acute Respiratory Syndrome (SARS) in 2002, Middle East Respiratory Syndrome (MERS) in 2012 and COVID-19 in 2019.[52] As a newly emerging infectious disease, it is critical to understand and identify the key clinical characteristics of COVID-19 patients to help in early detection and isolation of infected individuals, as well as minimize the spread of the disease.

In this study, we updated the evidence and conducted this meta-analysis to systematically review the clinical characteristics of COVID-19 patients. Our analysis consisted of 3 062 COVID-19 patients in 31 provincial-level regions in China. The results showed
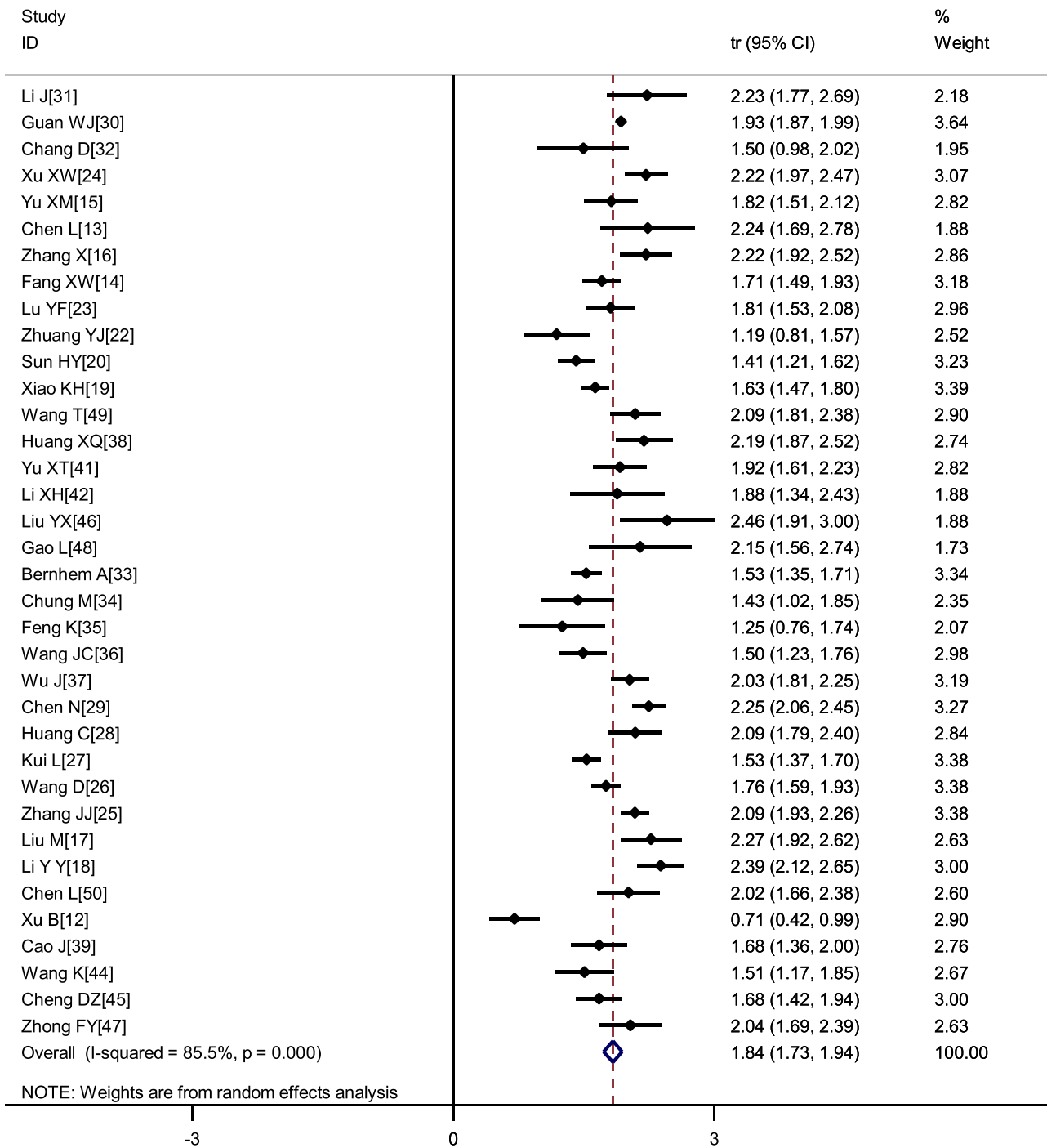
Study ID		tr (95% CI)	% Weight
Li J[31]		2.23 (1.77, 2.69)	2.18
Guan WJ[30]		1.93 (1.87, 1.99)	3.64
Chang D[32]		1.50 (0.98, 2.02)	1.95
Xu XW[24]		2.22 (1.97, 2.47)	3.07
Yu XM[15]		1.82 (1.51, 2.12)	2.82
Chen L[13]		2.24 (1.69, 2.78)	1.88
Zhang X[16]		2.22 (1.92, 2.52)	2.86
Fang XW[14]		1.71 (1.49, 1.93)	3.18
Lu YF[23]		1.81 (1.53, 2.08)	2.96
Zhuang YJ[22]		1.19 (0.81, 1.57)	2.52
Sun HY[20]		1.41 (1.21, 1.62)	3.23
Xiao KH[19]		1.63 (1.47, 1.80)	3.39
Wang T[49]		2.09 (1.81, 2.38)	2.90
Huang XQ[38]		2.19 (1.87, 2.52)	2.74
Yu XT[41]		1.92 (1.61, 2.23)	2.82
Li XH[42]		1.88 (1.34, 2.43)	1.88
Liu YX[46]		2.46 (1.91, 3.00)	1.88
Gao L[48]		2.15 (1.56, 2.74)	1.73
Bernhem A[33]		1.53 (1.35, 1.71)	3.34
Chung M[34]		1.43 (1.02, 1.85)	2.35
Feng K[35]		1.25 (0.76, 1.74)	2.07
Wang JC[36]		1.50 (1.23, 1.76)	2.98
Wu J[37]		2.03 (1.81, 2.25)	3.19
Chen N[29]		2.25 (2.06, 2.45)	3.27
Huang C[28]		2.09 (1.79, 2.40)	2.84
Kui L[27]		1.53 (1.37, 1.70)	3.38
Wang D[26]		1.76 (1.59, 1.93)	3.38
Zhang JJ[25]		2.09 (1.93, 2.26)	3.38
Liu M[17]		2.27 (1.92, 2.62)	2.63
Li Y Y[18]		2.39 (2.12, 2.65)	3.00
Chen L[50]		2.02 (1.66, 2.38)	2.60
Xu B[12]		0.71 (0.42, 0.99)	2.90
Cao J[39]		1.68 (1.36, 2.00)	2.76
Wang K[44]		1.51 (1.17, 1.85)	2.67
Cheng DZ[45]		1.68 (1.42, 1.94)	3.00
Zhong FY[47]		2.04 (1.69, 2.39)	2.63
Overall (I-squared = 85.5%, p = 0.000)		1.84 (1.73, 1.94)	100.00

NOTE: Weights are from random effects analysis

-3   0   3

FIGURE 4 Transformed incidence rate of cough in COVID-19 patients

that the most common symptoms of patients with COVID-19 were fever (80.4%), cough (63.1%), fatigue (46%), and muscle soreness (33%), which were basically consistent with the findings of Sun et al.[8] Some patients also experienced gastrointestinal symptoms, such as anorexia, nausea, vomiting diarrhea, etc. And some patients were asymptomatic. Therefore, for patients with a history of living in an epidemic area or having had contact with someone with suspected or confirmed COVID-19 infection in the 14 days before the onset of

symptoms, the fever clinic physicians should be alert to identify non-respiratory symptoms.

On blood biochemical examination, most patients showed normal leucocyte counts and lymphopenia. Only a few patients had leukocytosis and elevated procalcitonin, confirming that this disease is transmitted by a virus. Therefore, the clinician should pay attention to identify the presence of bacterial infection, and routine antibiotics should be avoided. Some patients presented with liver and renal

TABLE 3 Meta-analysis of different auxiliary examination results in COVID-19 patients

| Outcomes | No. studies | No. patients | Heterogeneity | | Model | Meta analysis | |
			P	I²		R (95% CI)	P
CT lesions involving single lung	12	600	<.001	89.3%	Random	0.258 (0.156, 0.374)	<.001
CT lesions involving bilateral lungs	22	2185	<.001	95.1%	Random	0.757 (0.657, 0.845)	<.001
Leukocytosis	15	1992	<.001	83.3%	Random	0.126 (0.084, 0.174)	<.001
Normal leukocytes	10	642	.001	68.5%	Random	0.697 (0.628, 0.762)	<.001
leukopenia	22	2258	<.001	89.3%	Random	0.259 (0.196, 0.327)	<.001
Lymphopenia	24	2507	<.001	95.3%	Random	0.565 (0.465, 0.664)	<.001
High C-reactive protein	21	2238	<.001	90.8%	Random	0.736 (0.661, 0.804)	<.001
High procalcitonin	9	1701	<.001	95.6%	Random	0.175 (0.078, 0.299)	<.001
High D-dimer	6	414	<.001	94.8%	Random	0.372 (0.177, 0.591)	<.001
Decreased oxygenation index	4	113	<.001	90.5%	Random	0.636 (0.324, 0.895)	<.001
High ESR	3	195	<.001	93.9%	Random	0.656 (0.368, 0.893)	<.001
Abnormal liver function	10	549	<.001	86.6%	Random	0.290 (0.175, 0.421)	<.001
Abnormal renal function	5	231	<.001	94.2%	Random	0.255 (0.056, 0.535)	<.001
RF or ARDS	8	1499	<.001	97.6%	Random	0.195 (0.050, 0.403)	<.001
Fatality rate	8	1765	<.001	87.9%	Random	0.055 (0.023, 0.100)	<.001

functions abnormalities, which manifested as an increase in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and creatinine. So intense monitoring and evaluation of the function of important organs in COVID-19 patients should be considered. In our study, the incidence of RF or ARDS in hospitalized patients was 19.5% and the case fatality rate was 5.5%, lower than those of the other two widely contagious coronavirus diseases, SARS (9.6%)[53] and MERS (35%).[54] However, the case fatality rate was higher than that

TABLE 4 Subgroup analysis of different clinical symptoms in COVID-19 patients

| Outcomes | No. studies | No. patients | Heterogeneity | | Model | Meta-analysis | |
			P	I²		R (95% CI)	P
Fever							
Hubei Province	13	865	<.001	93.4%	Random	0.87 (0.81, 0.92)	<.001
Outside Hubei Province	22	2101	<.001	83.3%	Random	0.76 (0.67, 0.84)	<.001
Sample size <50	21	570	<.001	75.5%	Random	0.81 (0.74, 0.87)	<.001
Sample size 50-100	9	618	<.001	18.4%	Random	0.82 (0.79, 0.85)	<.001
Sample size ≥100	6	1778	<.001	98.8%	Random	0.75 (0.52, 0.93)	<.001
Fatigue							
Hubei Province	10	704	<.001	90.9%	Random	0.62 (0.49, 0.73)	<.001
Outside Hubei Province	16	1891	<.001	85.1%	Random	0.36 (0.29, 0.43)	<.001
Sample size <50	14	419	<.001	82.9%	Random	0.49 (0.37, 0.60)	<.001
Sample size 50-100	8	519	<.001	92.3%	Random	0.42 (0.27, 0.57)	<.001
Sample size ≥100	5	1657	<.001	97.5%	Random	0.46 (0.28, 0.65)	<.001
Cough							
Hubei Province	13	865	<.001	90.9%	Random	0.64 (0.53, 0.74)	<.001
Outside Hubei Province	23	2114	<.001	80.0%	Random	0.63 (0.57, 0.68)	<.001
Sample size <50	21	583	<.001	83.5%	Random	0.64 (0.54, 0.73)	<.001
Sample size 50-100	9	618	<.001	88.4%	Random	0.66 (0.54, 0.76)	<.001
Sample size ≥100	6	1778	<.001	89.9%	Random	0.59 (0.50, 0.67)	<.001
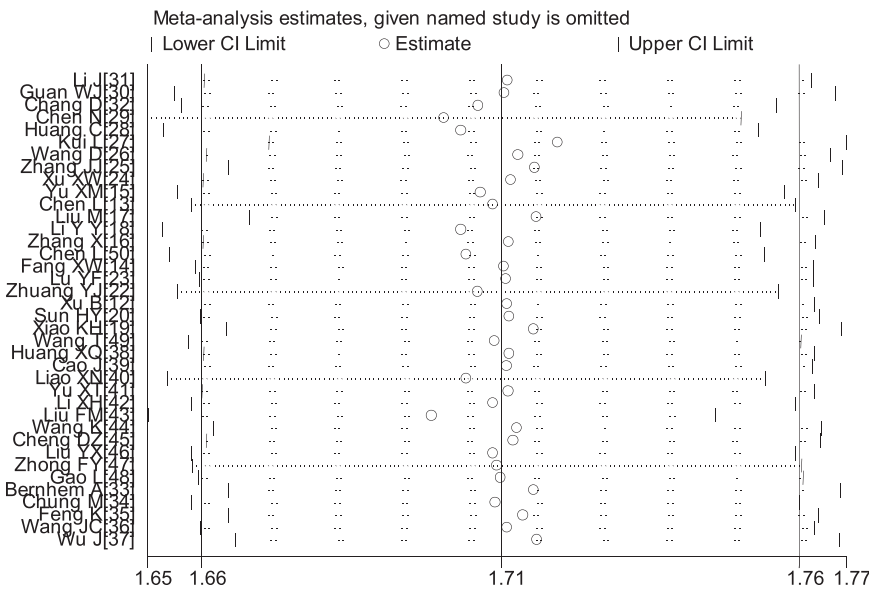
FIGURE 5 Sensitivity analysis of the proportion of males in COVID-19 patients

reported by CCDC (2.38%).[55] This may be explained by the fact that the patients included in our study were all hospitalized. In most of them, the condition was serious or critical. For example, Chen et al[13] included 12 critically ill patients.

This study has several strengths, including its large sample size and the high quality of the included studies. We conducted subgroup analysis according to the studies' region and sample size and conducted a sensitivity analysis by excluding each study one by one. The results did not change significantly, indicating the reliability and stability of our results. However, the results of subgroup analysis also showed that patients outside the Hubei Province had a lower ratio of fever and fatigue than patients in Hubei Province. According to CCDC, the case-fatality in Hubei Province was also higher than that outside Hubei Province.[55] All the above results indicated that the patients outside the Hubei Province had relatively mild symptoms.

Nevertheless, some limitations should be noted in our meta-analysis. First, most of our included studies are single-center, which may have admission bias and selection bias. Second, all of the included studies were retrospective studies, so we cannot rule out the influence of other confounding factors. The sample size in each studies is small, so the test efficiency may be insufficient. Third, most of our included studies did not clarify the inclusion criteria, course of disease, and severity of disease. Finally, this meta-analysis indicated a significant heterogeneity between the studies. Due to too many outcomes, there was no subgroup analysis and sensitivity analysis for each outcome indicator. So the subgroup analysis fails to eliminate all sources of heterogeneity, which will affect the accuracy of the results of the meta-analysis.

5 | CONCLUSION

In summary, current evidence shows that the most commonly experienced symptoms of COVID-19 patients were fever, fatigue, cough, and expectoration. A relatively small percentage of patients were asymptomatic. Most patients showed normal leucocytes, lymphopenia, elevated levels of C-reactive protein and ESR. Bilateral lung involvement was common. Due to the limited quality and quantity of the included studies, more high-quality prospective studies are required to verify the above conclusions.
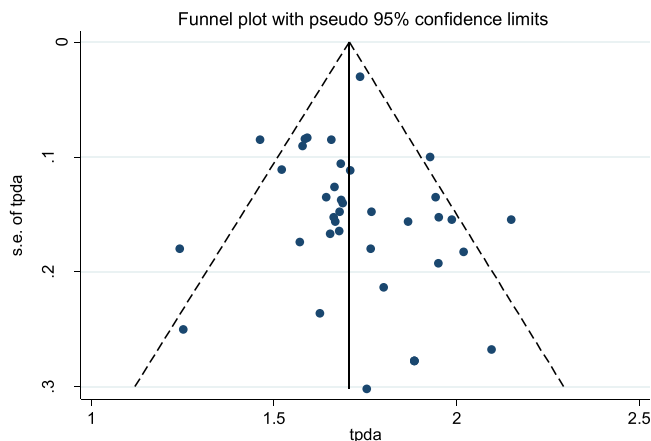
FIGURE 6 Evaluation of publication bias using a funnel plot based on the proportion of males

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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