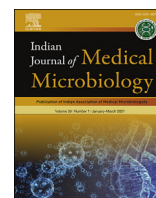




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Review Article

Clinical, epidemiological, laboratory, and radiological characteristics of novel Coronavirus (2019-nCoV) in retrospective studies: A systemic review and meta-analysis



Ebrahim Kouhsari^{a,b}, Khalil Azizian^c, Mohammad Sholeh^d, Mohammad Shayestehpour^{e,f}, Marzieh Hashemian^a, Somayeh Karamollahi^a, Sajad Yaghoubi^{g,**}, Nourkhoda Sadeghiifard^{a,*}

^a Clinical Microbiology Research Center, Ilam University of Medical Sciences, Ilam, Iran

^b Laboratory Sciences Research Center, Golestan University of Medical Sciences, Gorgan, Iran

^c Department of Lab Science, Sirjan School of Medical Sciences, Sirjan, Iran

^d Department of Microbiology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran

^e Department of Microbiology and Immunology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran

^f Autoimmune Diseases Research Center, Kashan University of Medical Sciences, Kashan, Iran

^g Department of Clinical Microbiology, Iranshahr University of Medical Sciences, Iranshahr, Iran

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ABSTRACT

Background: In December 2019, a novel pneumonia related to the 2019 coronavirus unexpectedly developed in Wuhan, China. We aimed to review data of the novel Coronavirus (2019-nCoV) by analyzing all the published retrospective studies on the clinical, epidemiological, laboratory, and radiological characteristics of patients with 2019-nCoV.

Methods: We searched in four bibliographic databases PubMed, Scopus, Embase, and Web of Science) for studies March 10, 2020 focused on the clinical, epidemiological, laboratory, and radiological characteristics of patients with 2019-nCoV for meta-analysis. The Newcastle-Ottawa Scale was used to quality assessment, and publication bias was analyzed by Egger's test. In the meta-analysis, a random-effects model with Stata/SE software, v.14.1 (StataCorp, College Station, TX) was used to obtain a pooled incidence rate.

Results: Fifty studies were included in this systematic review and meta-analysis with 8815 patients and the mean age was 46 years and 4647 (52.7%) were male. The pooled incidences rate of clinical symptoms were: fever (83%, 95% CI: 0.77, 0.89), cough (59%, 95% CI: 0.48, 0.69), myalgia or fatigue (31%, 95% CI: 0.23, 0.39), sputum production (29%, 95% CI: 0.21, 0.39), and dyspnea (19%, 95% CI: 0.12, 0.26). The pooled incidence rate of acute respiratory distress syndrome (ARDS) was (22%, 95% CI: 0.00, 0.60).

Conclusion: The results of this systemic review and meta-analysis present a quantitative pooled incidence rate of different characters of 2019-nCoV and has great potential to develop diagnosis and patient's stratification in 2019-nCoV. However, this conclusions of this study still requisite to be warranted by more careful design, larger sample size multivariate studies to corroborate the results of this meta-analysis.

1. Introduction

In December 8, 2019 a new coronavirus, which was called 2019 novel coronavirus (2019-nCoV), arise the pneumonia epidemic of the severe respiratory disease from Wuhan (Huanan seafood market) across China which now causes the main public health threats worldwide [1,2]. On January 30, 2020, WHO stated that the epidemic of the Severe Acute

Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) become as a public health emergency of international concern (PHEIC) [3]. Currently, the number of patients with 2019-nCoV is dramatically increasing to other countries around the world [4,5]. According to worldwide statistics, the death rate is ~4.6%. Main symptoms of 2019-nCoV include pneumonia, fever, myalgia or fatigue [4,5]. However, some characterizations and conclusions in the published relevant research were varied, limited and

* Corresponding author. Banganjab, Pazhouhesh Blvd, Ilam University of Medical Sciences, Ilam, Iran.

** Corresponding author. Noor St, Shahdai Anonymous Park, Iranshahr School of Medical Sciences, Iranshahr, Iran.

E-mail addresses: sajadyaghuby@gmail.com (S. Yaghoubi), Sadeghiifard@gmail.com (N. Sadeghiifard).

controversial. At present, there is no successful vaccine or antiviral drugs has been clinically approved for 2019-nCoV. Therefore, to acquire more exact conclusions on the clinical, epidemiological, *laboratory, and radiological* characteristics and also to propose significant help for current clinical studies of patients with 2019-nCoV, we performed a systemic review and meta-analysis of all these evidence-based medical epidemiological, clinical, laboratory, and radiological characters.

2. Methods

2.1. Search strategy and study selection

Four bibliographic databases, including international databases (PubMed, Scopus, Embase, and Web of Science) for relevant articles were searched (Until 10th/March/2020) by using the following keywords: ("2019 Novel coronavirus" OR "2019-nCoV" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "SARS-CoV-2" OR "COVID-19" OR "Wuhan Coronavirus" OR "Wuhan pneumonia") in the Title/Abstract/Keywords fields. No limitation regarding ethnicity, language, country, gender, patient age was used while searching databases, but inclusion of the study in our full analysis required at least the abstract to be available in English. The records found through database searching were merged

and the duplicates were removed using EndNote X7 (Thomson Reuters, New York, NY, USA).

2.2. Selection criteria and data extraction

One of the team researchers randomly evaluated the search results and reported that no relevant study was ignored. Three authors (Ebrahim Kouhsari, Mohammad Sholeh and Sajad Yaghoubi) independently done all these steps and reviewed the potentially relevant studies to clarify whether they met the predetermined eligibility criteria. Any discrepancies and inconsistencies with article selection were resolved through discussion, and a fourth author (Nourkhoda Sadeghifard) was available to resolve the disagreement. In the first phase, studies obtained from the literature search were precisely screened by titles and abstracts to exclude irrelevant studies. The full text of relevant studies was reviewed in depth conferring to definite criteria. References lists of all related studies were also reviewed for any other related publication.

Studies were excluded if they met the following conditions: reviews, theses, books, conference papers, repeat articles, letters, editorials, expert opinions, animal, *in vitro* studies, and overlapping, unusable data sets (Fig. 1). Information extracted from retrospective

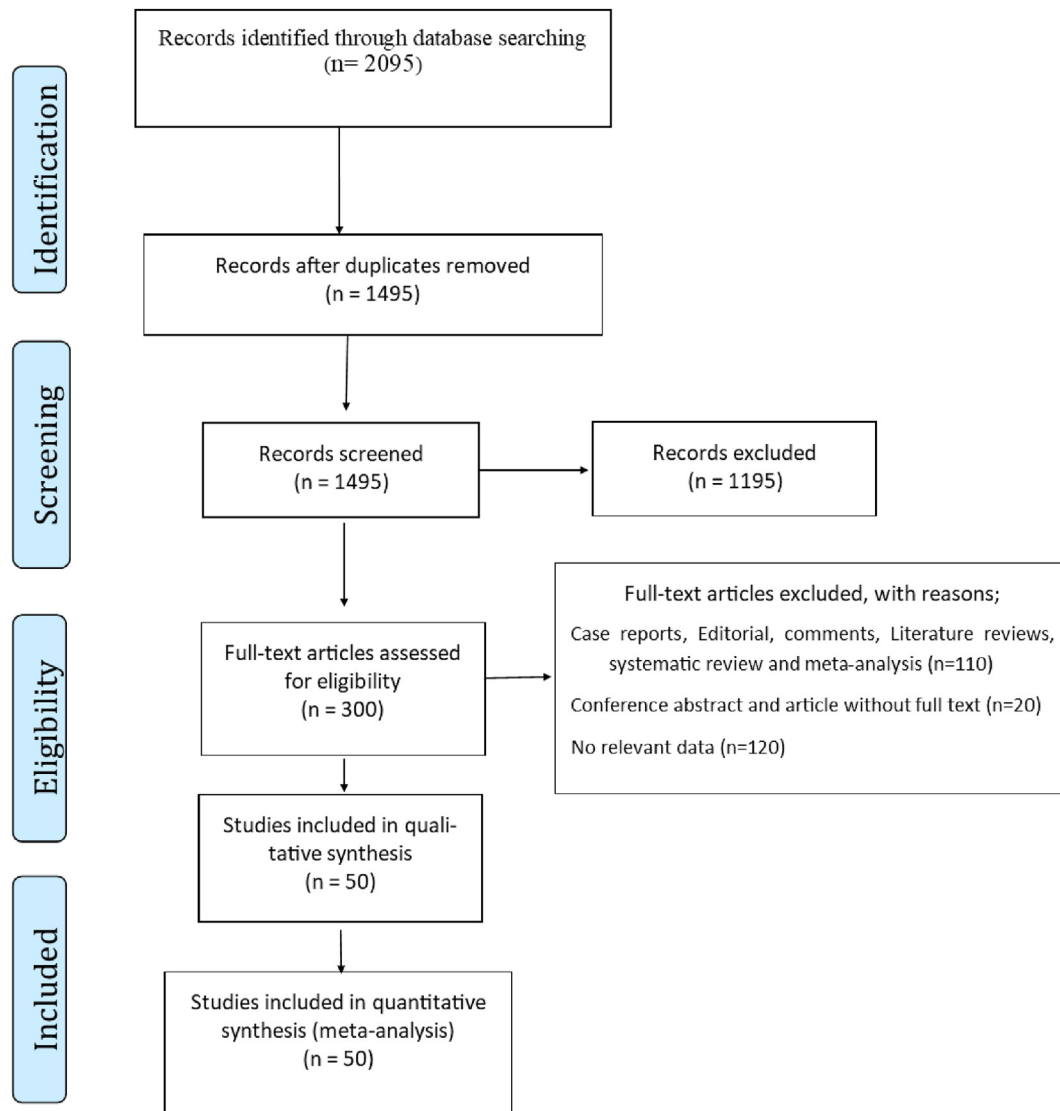


Fig. 1. Flow diagram showing the data selection process.

studies on the clinical, epidemiological, laboratory, and radiological characteristics of novel Coronavirus (2019-nCoV) infected patients (supplementary data 1).

2.3. Outcomes

The main outcome of interest was the clinical, epidemiological, laboratory, and radiological characteristics of 2019-nCoV infected patients.

2.4. Quality assessment

Quality evaluation of the included studies was performed using by two authors (Marzieh Hashemian, Somayeh Karamollahi) independently, using an adapted version of the tool proposed by the Newcastle-Ottawa assessment scale [6]. A score ranging from 0 to 9 points was attributed to each study (≥ 7 points: high quality, 4–6

points: Moderate quality, ≤ 3 points: low quality). Higher score indicates higher study quality. A third reviewer (Ebrahim Kouhsari) adjudicated in any case of disagreement. Need for arbitration and reason was reported in the data collection tool.

2.5. Publication bias

Publication bias was analyzed using Egger's linear regression test, which measures funnel plot asymmetry.

2.6. Statistical analysis

All statistical analyses were performed using a random-effects model with Stata/SE software, v.14.1 (StataCorp, College Station, TX). A chi-squared test and I^2 statistic were used to assess the inter-study heterogeneity. Hence, values above 75% are considered heterogeneity [7];

Table 1

Characteristics and Quality assessment of included studies.

ID	First Author, Year	Country	Study Design	Selection (4 points)	Comparability (2 points)	Outcome (3 points)	Total (9 points)
1	Guan W, 2020	China	retrospective	3	2	3	8
2	Huang Y, 2020	China	retrospective	3	2	2	7
3	Tang N, 2020	China	retrospective	1	2	2	5
4	Cai s, 2020	China	retrospective	3	2	2	7
5	Chen L, 2020	China	retrospective	3	2	2	7
6	Feng K, 2020	China	retrospective	3	2	2	7
7	Liu W, 2020	China	retrospective	3	2	2	7
8	Chen C, 2020	China	retrospective	2	2	2	6
9	Zhang L, 2020	China	retrospective	2	2	2	6
10	Tian S, 2020	China	retrospective	3	2	2	7
11	Bernheim S, 2020	China	retrospective	3	2	2	7
12	Wu J, 2020	China	retrospective	2	2	2	6
13	Peng YD 2020	China	retrospective	3	2	2	7
14	Wang D 2020	China	retrospective	3	2	3	8
15	Xu H-Y, 2020	China	retrospective	3	2	2	7
16	Xia W, 2020	China	retrospective	3	2	2	7
17	Yang W, 2020	China	retrospective	2	2	2	6
18	Xiong Y,2020	China	retrospective	3	2	2	7
19	Hu Z,2020	China	retrospective	3	2	2	7
20	Zhang JJ,2020	China	retrospective	2	2	2	6
21	Wang D,2020	China	retrospective	3	2	2	7
22	Walker,2020	Australia	retrospective	1	2	1	3
23	Liu K,2020	China	retrospective	3	2	2	7
24	Yang X,2020	China	retrospective	2	2	2	6
25	Wang X,2020	China	retrospective	3	2	2	7
26	Chung M,2020	China	retrospective	3	2	2	7
27	Li Q,2020	China	retrospective	3	2	3	8
28	Ki M,2020	Korea	retrospective	2	2	3	7
29	Chen N,2020	China	retrospective	2	2	3	7
30	Fan BE,2020	China	retrospective	3	2	3	8
31	Chang D,2020	China	retrospective	3	2	2	7
32	Yao Y,2020	China	retrospective	2	2	1	5
33	Cheng J,2020	China	retrospective	2	2	1	5
34	Song F,2020	China	retrospective	3	2	3	8
35	Zhou S,2020	China	retrospective	3	2	3	8
36	Yueying P,2020	China	retrospective	4	1	2	7
37	Liu C,2020	China	Retrospectively	3	2	2	7
38	Shi H,2020	China	retrospectively	3	2	2	7
39	Zhao W,2020	China	retrospectively	3	2	2	7
40	Pan F,2020	China	retrospectively	3	2	2	7
41	Huang C,2020	China	retrospectively	3	2	2	7
42	Li YY,2020	China	retrospectively	3	2	2	7
43	Yang HY,2020	China	retrospectively	2		1	3
44	Zhu ZW,2020	China	retrospectively	3	2	2	7
45	Ai T,2020	China	retrospectively	3	2	2	7
46	Ling Y,2020	China	retrospectively	3	2	2	7
47	Lan L,2020	China	retrospectively	3	2	2	7
48	Sun,2020	USA	retrospectively	2	2	1	5
49	Li J,2020	China	retrospectively	3	2	1	6
50	Xu,2020	China	retrospectively	3	2	1	6

Table 2 (continued)

Characteristic	Value	(-CL, +CL)	I ²	P	Positive	Number of patients
Albumin (Decrease)	0.54	(0.00, 1.00)	99.38	0.00	121	277
Albumin (Increase)	0.03	(0.01, 0.06)	*	*	7	181
Serum Creatinine (Normal)	1.00	(0.99, 1.00)	*	*	190	190
Serum Creatinine (Decrease)	0.17	(0.10, 0.26)	*	*	17	99
Serum Creatinine (Increase)	0.03	(0.01, 0.08)	*	*	5	128
D-Dimer (Normal)	0.94	(0.82, 1.00)	93.22	0.00	440	475
D-Dimer (Increase)	0.48	(0.04, 0.94)	99.24	0.00	254	479
Procalcitonin (Normal)	0.88	(0.67, 1.00)	95.57	0.00	313	368
Procalcitonin (Increase)	0.60	(0.15, 0.96)	99.00	0.00	276	461
Blood Urea nitrogen (Normal)	0.98	(0.88, 1.00)	94.23	0.00	382	399
Blood Urea nitrogen (Decrease)	0.14	(0.10, 0.18)	*	*	34	248
Blood Urea nitrogen (Increase)	0.08	(0.04, 0.13)	*	*	11	128
Thromboplastin time (Normal)	0.98	(0.87, 1.00)	96.48	0.00	559	599
Thromboplastin time (Decrease)	0.05	(0.02, 0.09)	*	*	16	99
Thromboplastin time (Increase)	0.20	(0.04, 0.45)	94.02	0.00	72	298
C-reactive protein (Normal)	0.48	(0.26, 0.69)	96.21	0.00	211	599
C-reactive protein (Increase)	0.72	(0.54, 0.87)	97.46	0.00	865	1159
Total Bilirubin (Normal)	0.95	(0.85, 1.00)	92.38	0.00	514	541
Total Bilirubin (Decrease)	0.05	(0.02, 0.09)	*	*	7	149
Total Bilirubin (Increase)	0.20	(0.04, 0.45)	94.02	0.00	38	297
Prothrombin time (Normal)	0.95	(0.83, 1.00)	95.40	0.00	532	571
Prothrombin time (Decrease)	0.10	(0.00, 0.33)	95.30	0.00	35	282
Prothrombin time (Increase)	0.44	(0.00, 0.97)	99.44	0.00	177	420
Creatinine (Normal)	0.98	(0.88, 1.00)	95.81	0.00	502	546
Creatinine (Decrease)	0.53	(0.47, 0.59)	*	*	151	299
Creatinine (Increase)	0.24	(0.18, 0.31)	*	*	47	190
Platelet count (Normal)	0.96	(0.87, 1.00)	93.01	0.00	524	563
Platelet count (Decrease)	0.27	(0.12, 0.45)	93.13	0.00	83	436
Platelet count (Increase)	0.05	(0.02, 0.08)	0.00	0.79	14	279
Aspartate Aminotransferase (Normal)	0.90	(0.71, 1.00)	96.86	0.00	528	608
Aspartate Aminotransferase (Increase)	0.29	(0.18, 0.41)	84.10	0.00	135	449
Lactate Dehydrogenase (Normal)	0.95	(0.72, 1.00)	97.02	0.00	321	370
Lactate Dehydrogenase (Increase)	0.69	(0.36, 0.95)	98.04	0.00	300	478
	0.80	(0.73, 0.85)	*	*	126	177

Table 2

Meta-analysis results.

Characteristic	Value	(-CL, +CL)	I ²	P	Positive	Number of patients
Epidemiology						
Male	0.54	(0.51, 0.56)	68.34	0.00	4647	8815
Female	0.46	(0.44, 0.49)	68.34	0.00	4168	8815
Contact with another person with respiratory symptoms	0.27	(0.15, 0.42)	95.94	0.00	328	1289
History of travel from china (Wuhan, and ...)	0.58	(0.41, 0.73)	99.02	0.00	1917	4208
Exposure to source of transmission	0.30	(0.16, 0.45)	98.51	0.00	719	3583
Smoking history	0.17	(0.00, 0.53)	99.18	0.00	1001	1559
Admission to ICU	0.16	(0.08, 0.27)	94.70	0.00	175	1843
Diabetes	0.11	(0.08, 0.14)	68.64	0.00	250	2505
Hypertension	0.19	(0.12, 0.27)	94.35	0.00	484	2403
Malignancy	0.05	(0.02, 0.08)	82.12	0.00	72	2250
Cardiovascular	0.12	(0.06, 0.20)	95.16	0.00	207	2301
Other comorbidity	0.16	(0.11, 0.22)	75.84	0.00	598	2897
COPD	0.03	(0.01, 0.06)	75.84	0.00	48	1900
Clinical symptoms						
Fever	0.83	(0.77, 0.89)	95.15	0.00	3273	4370
Cough	0.59	(0.48, 0.69)	97.33	0.00	2100	4308
Myalgia or fatigue	0.31	(0.23, 0.39)	94.28	0.00	1051	3029
Sputum production	0.29	(0.21, 0.39)	84.96	0.00	478	1497
Headache	0.10	(0.06, 0.14)	70.94	0.00	306	3557
Hemoptysis	0.02	(0.00, 0.05)	70.94	0.00	21	1370
Diarrhea	0.08	(0.06, 0.11)	80.05	0.00	203	3690
Dyspnea	0.19	(0.12, 0.26)	93.99	0.00	495	2651
Acute respiratory distress syndrome (ARDS)	0.22	(0.00, 0.60)	96.19	0.00	49	173
Vomiting	0.03	(0.02, 0.05)	65.12	0.00	105	2961
Sore throat	0.12	(0.07, 0.18)	91.85	0.00	287	2996
Rhinorrhea	0.09	(0.03, 0.17)	87.72	0.00	64	1455
Chest pain	0.11	(0.04, 0.21)	95.44	0.00	108	1834
Laboratory						
WBC(Normal)	0.81	(0.69, 0.91)	95.56	0.00	958	1260
WBC (Decrease)	0.21	(0.16, 0.27)	70.65	0.00	180	785
WBC(Increase)	0.14	(0.08, 0.21)	84.85	0.00	109	760
Neutrophil (Normal)	0.95	(0.87, 1.00)	93.15	0.00	721	797
Neutrophil (Decrease)	0.16	(0.12, 0.21)	*	*	39	229
Neutrophil (Increase)	0.17	(0.05, 0.34)	92.34	0.00	67	380
Albumin (Normal)	0.95		86.35	0.00	243	259

(continued on next page)

Table 2 (continued)

Characteristic	Value	(-CL, +CL)	I ²	P	Positive	Number of patients
Erythrocyte Sedimentation rate (Increase)						
Alanine Aminotransferase (Normal)	0.90	(0.77, 0.98)	92.20	0.00	459	500
Alanine Aminotransferase (Decrease)	0.01	(0.00, 0.05)	*	*	2	149
Alanine Aminotransferase (Increase)	0.18	(0.12, 0.25)	54.18	0.00	65	358
Creatine kinase (Normal)	0.94	(0.81, 1.00)	93.92	0.00	427	467
Creatine kinase (Decrease)	0.17	(0.12, 0.22)	*	*	42	248
Creatine kinase (Increase)	0.12	(0.03, 0.24)	85.74	0.00	32	320
Lymphocyte (Normal)	0.61	(0.46, 0.75)	93.25	0.00	385	701
Lymphocyte (Decrease)	0.58	(0.40, 0.75)	97.86	0.00	826	1431
Lymphocyte (Increase)	0.14	(0.06, 0.24)	0.00	0.00	9	63
Hemoglobin (Normal)	1.00	(0.98, 1.00)	*	*	69	69
Hemoglobin (Decrease)	0.98	(0.95, 1.00)	*	*	162	179
Radiology						
Multiple mottling and ground-glass opacity	0.60	(0.50, 0.70)	95.37	0.00	1399	2951
Bilateral patchy shadowing	0.50	(0.44, 0.57)	40.60	0.17	592	1257
Crazy paving	0.16	(0.06, 0.29)	85.09	0.00	47	324
Discrete nodules	0.10	(0.00, 0.30)	93.19	0.00	15	305
Peripheral distribution	0.61	(0.45, 0.75)	91.16	0.00	327	517
Unilateral Pneumonia	0.61	(0.45, 0.75)	91.16	0.00	61	249
Local patchy shadowing	0.36	(0.34, 0.39)	*	*	411	1114
Consolidation	0.37	(0.24, 0.51)	94.74	0.00	650	1594
Cavitation	0.00	(0.00, 0.02)			4	141
Lymphadenopathy	0.02	(0.00, 0.05)	59.24	0.02	18	523
Bilateral pneumonia	0.70	(0.59, 0.79)	90.99	0.00	1330	1644
Pneumothorax	0.01	(0.00, 0.05)	*	*	1	99
Interstitial abnormalities	0.13	(0.11, 0.15)	*	*	143	1099
Linear	0.08	(0.04, 0.13)	*	*	12	142
Pleural effusion	0.05	(0.02, 0.09)	69.66	0.00	39	615
Supportive treatment						
Antiviral therapy	0.90	(0.74, 0.99)	98.61	0.00	1374	2205
Antibiotic therapy	0.68	(0.49, 0.84)	97.80	0.00	1094	1806
Use of corticosteroid	0.32	(0.19, 0.47)	96.97	0.00	498	2028
Immunotherapy	0.39	(0.13, 0.69)	98.92	0.00	428	1674
Oxygen support	0.56	(0.32, 0.78)	98.95	0.00	1003	2141
Non-invasive ventilation or	0.11	(0.05, 0.19)	93.91	0.00	163	1858

Table 2 (continued)

Characteristic	Value	(-CL, +CL)	I ²	P	Positive	Number of patients
high-flow nasal canula						
Invasive mechanical ventilation	0.08	(0.01, 0.19)	96.06	0.00	88	1643
Invasive mechanical ventilation and ECMO	0.02	(0.00, 0.05)	71.69	0.00	15	576
Nasal cannula	0.55	(0.24, 0.84)	97.00	0.00	218	339
Continuous renal replacement therapy	0.06	(0.01, 0.13)	79.86	0.00	23	361
Clinical outcomes						
Recovered	0.53	98.63	0.00		788	2952
Staying in hospital	0.67	97.93	0.00		1791	2355
Death	0.05	89.08	0.00		151	3054

Thus, DerSimonian and Laird random effects models were used [8]. All statistical interpretations were reported on a 95% confidence interval (CI) basis.

3. Results

3.1. Search results

We evaluated 5 electronic databases and categorized 2095 articles published until 10 March 2020 (Fig. 1). Of these, after initial screening of the title and abstract, 1795 articles were excluded due to their irrelevance and duplication and the full text of remaining 300 articles were reviewed (Fig. 1). Among the 250 articles, were excluded again for specific reasons: case reports, conference papers, repeat articles, letters, editorials, expert opinions, animal, *in vitro* studies, and unusable data sets. Finally, 50 studies were included in this systematic review and meta-analysis. Supplementary data 1 depicts the main characteristics of 50 included studies.

3.2. Characteristics of studies

A total of 50 articles were included in this meta-analysis [2,4,5,9–20], [21–30, 31–55] including data from 8815 patients. Study size ranged from 4 to 1719 subjects. The methodological quality of the included studies was high for observational studies (Table 1). The highest quality of the literature was 8 stars and the lowest 3 stars.

3.3. Publication bias detection

The results of the Egger test are displayed in Table 3. There was a publication bias in the meta-analysis of the bilateral pneumonia group (P = 0.004).

3.4. Epidemiological characteristics

A total of 50 studies including 8815 patients were included in this study, the mean age was 46 years and 4647 (0.54%) were male. Among studies been reported that data on the epidemiological characteristics, evidence of heterogeneity was present in the history contact with another person with respiratory symptoms (I² = 95.94, P = 0.00), history of travel from China (Wuhan) (I² = 99.02, P = 0.00), exposure to source of transmission (COVID-19 infected patients, wildlife) within 14 days (I² = 98.51, P = 0.00), admission to ICU (I² = 94.70, P = 0.00), smoking history (current or past) (I² = 99.18, P = 0.00) (Table 2). Among eligible literatures, 26 studies reported that hypertension, diabetes, and cardiovascular illness were more prevalent in patients. Detailed results of Meta-analysis are shown in Table 2.

Table 3
Results of Egger test.

Group	Fever	Cough	Myalgia or fatigue	Acute respiratory distress syndrome	Death	COPD	Multiple mottling and ground-glass opacity	Bilateral patchy shadowing	Bilateral pneumonia
P	0.103	0.054	0.592	0.868	0.197	0.127	0.155	0.238	0.004

3.5. Clinical characteristics

There were 13 symptoms of 2019-nCoV in infected patients which were reported. Among studies been reported that data on the clinical symptoms, evidence of heterogeneity was present in the symptoms of fever ($I^2 = 95.15$, $P = 0.00$), cough ($I^2 = 97.33$, $P = 0.00$), myalgia or fatigue ($I^2 = 94.28$, $P = 0.00$), sputum production ($I^2 = 84.96$, $P = 0.00$), headache or hemoptysis ($I^2 = 70.94$, $P = 0.00$), and diarrhea ($I^2 = 80.05$, $P = 0.00$) (Table 2). Among been reported clinical symptoms, the pooled incidence rate was calculated for four symptoms: acute respiratory distress syndrome (ARDS) (22%, 95% CI: 0.00, 0.60), dyspnea (19%, 95% CI: 0.12, 0.26), sore throat (12%, 95% CI: 0.07, 0.18), chest pain (11%, 95% CI: 0.04, 0.21), rhinorrhea (9%, 95% CI: 0.03, 0.17), vomiting (3%, 95% CI: 0.02, 0.05) (Table 2).

3.6. Laboratory characteristics

Among been reported laboratory characteristics, white blood cells were decreased in 180 patients (the pooled incidence rate was 21%, $I^2 = 70.65$, $P = 0.00$) and increased in 109 patients (the pooled incidence rate was 14%, $I^2 = 84.85$, $P = 0.00$) (Table 3). Lymphocyte were decreased in 826 patients (the pooled incidence rate was 58%, $I^2 = 97.86$, $P = 0.00$) and increased in 9 patients (the pooled incidence rate was 14%, $I^2 = 0.00$, $P = 0.00$) (Table 2). The increased neutrophils observed in 67 patients, evidence of heterogeneity was present in it ($I^2 = 92.34\%$, $P = 0.00$). Albumin were decreased in 121 patients (the pooled incidence rate was 54%, $I^2 = 99.38$, $P = 0.00$). The D-Dimer and thromboplastin time were increased in 254 and 72 patients (the pooled incidence rates were 48%; 20%, $I^2 = 99.24$; 94.02, $P = 0.00$). Procalcitonin, C-reactive protein, alanine aminotransferase, aspartate aminotransferase, Lactate Dehydrogenase and creatine kinase were increased in 276, 865, 65, 135, 300 and 32 patients (the pooled incidence rates were 60%, 72%, 18%, 29%, 69% and 12%, $P = 0.00$) (Table 3). Prothrombin time were decreased in 35 patients (the pooled incidence rate was 10%, $I^2 = 95.30$, $P = 0.00$) and increased in 177 patients (the pooled incidence rate was 44%, $I^2 = 99.44$, $P = 0.00$) (Table 2).

3.7. Radiological characteristics

The radiological characteristics of 2019-nCoV infected patients were described differently. By reviewing the literature, there are different common manifestations as follows: multiple mottling and ground-glass opacity, bilateral pneumonia, consolidation, and bilateral or local patchy shadowing. Among been reported radiological characteristics, evidence of heterogeneity were reported in the multiple mottling and ground-glass opacity (60%, $I^2 = 95.37$, $P = 0.00$), bilateral pneumonia (70%, $I^2 = 90.99$, $P = 0.00$), consolidation (37%, $I^2 = 94.74$, $P = 0.00$), and bilateral patchy shadowing (50%, $I^2 = 40.60$, $P = 0.17$). Additionally, pneumothorax happened in one patient [13].

3.8. Treatment

Among been reported treatment, 1374, 1094 patients were treated

with antiviral and antimicrobial agents (the pooled incidence rates and heterogeneities were 90%; 68%, $I^2 = 98.61$; 97.80). The pooled incidence rates were 32% and 39% in use of corticosteroids and immunotherapy. Totally, 1510 patients used oxygen therapy. Among these studies, there were 218 patients who used nasal cannula, the pooled incidence was 55% (95% CI: 0.24, 0.84) for five studies. 11% (95% CI: 0.32, 0.78) patients used non-invasive ventilation or high-flow nasal cannula. Additionally, 88 and 15 patients were treated with invasive mechanical ventilation and invasive mechanical ventilation or extra-corporeal membrane oxygenation (ECMO), the pooled incidence were 8% and 2% (Table 2). Three articles had no detailed data on oxygen therapy [12, 55]. There were 23 patients who used continuous renal replacement therapy, the pooled incidence was 6% (95% CI: 0.01, 0.13) for five studies.

3.9. Clinical outcomes

Among been reported clinical outcomes, unfortunately, 151 died cases were reported, the pooled incidence of mortality was 53% with significant heterogeneity ($I^2 = 89.08\%$, $P = 0.00$). Subsequently the course of treatment of patients is about several weeks until some articles published, some patients still staying in the hospital, the statistics on mortality may be inaccurate. Incidence rate correlation is shown in Table 4. In addition, 1791 and 788 cases were reported as staying in hospital and recovered with significant heterogeneity ($I^2 = 97.93\%$; 98.63, $P = 0.00$) (Table 2).

Pooled incidence rate for characters is shown in Fig. 2.

4. Discussion

2019-nCoV is one type of coronaviruses are enveloped non-segmented positive-sense RNA viruses belonging to the β -coronavirus cluster like SARS and Middle East respiratory syndrome (MERS) and now it had diseased more than half millions of people worldwide [12, 13,55,56]. It is assumed that 2019-nCoV to be a recombinant virus between bat coronavirus and coronavirus of another unknown origin [57]. Up to now, unfortunately, there is no detailed and precise treatments presented for 2019-nCoV. Symptomatic and supportive treatment is the basis of therapy for patients infected by 2019-nCoV. Our meta-analysis was based on data from 50 retrospective studies in 8815 patients of 2019-nCoV. The Most of the cases were from hospitals in China. Several clinical predictors of mortality were found including increased age, male sex and underlying illness, including hypertension, diabetes, renal disease, heart disease and respiratory disease. In our meta-analysis, the frequency of males more than females (52.7% vs 47.3%). The similar findings with the gender distribution have been reported in MERS and SARS [13,15]. It may be related to the occupational risk factors for males [4]. There are some possible reasons in the reduced susceptibility of females to 2019-nCoV such as Gender-specific effects and X chromosome in infectious disease susceptibility, and their more strong immune responses [58,59]. Although, a recent study that revealed there was no divergence with the gender distribution of males and females between ICU patients and

Table 4
Summary of Pearson Correlation Coefficient Values between deaths with other variable.

Pearson r	Death vs. Age mean	Death vs. History of travel from china (Wuhan and ...)	Death vs. Fever ($\geq 37.3^\circ\text{C}$) or ($\geq 38^\circ\text{C}$)	Death vs. Cough	Death vs. Diarrhea	Death vs. thromboplastin time (Increase)	Death vs. lymphocyte (Normal)	Death vs. Cavitation	Death vs. Linear	Death vs. Antiviral therapy
r	0.5376	-0.5368	0.5784	0.3752	0.5155	-0.7788	0.7483	0.7989	0.8951	0.8801
95% confidence interval	0.2383 to 0.7437	-0.8228 to -0.03390	0.3037 to 0.7643	0.01724 to 0.6479	0.09454 to 0.7801	-0.9578 to -0.1643	0.4456 to 0.8975	0.1152 to 0.9690	0.5158 to 0.9810	0.5938 to 0.9686
R squared	0.289	0.2882	0.3345	0.1408	0.2657	0.6065	0.56	0.6383	0.8012	0.7747
P value	0.0013	0.0391	0.0003	0.0411	0.02	0.0228	0.0002	0.0311	0.0027	0.0004
P (two-tailed)	**	*	***	*	*	*	***	*	**	***
P value summary	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Significant? (alpha = 0.05)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Number of XY Pairs	33	15	35	30	20	8	19	7	8	11

non-ICU patients [34]. However, we suggest that more investigations are required in order to identify potential risk factors, their relation to different populations, and their mechanisms involved. Older adults and severe patients with comorbidities are as high-risk group to 2019-nCoV [45]. A study performed on influenza illness demonstrated the higher risk of mortality for severe patients with chronic obstructive pulmonary disease (COPD) (OR 1.49, 95% CI: 1.10–2.01), cardiovascular disease (OR 2.92, 95% CI: 1.76–4.86), hypertension (OR 1.49, 95% CI: 1.10–2.10) [60]. The comorbidities effect had also been observed to have similar effects in 2019-nCoV and MERS [61]. Age and comorbidities are major predictors of numerous adverse outcomes in SARS [62]. SARS cases were mostly occurred in younger people; while half of the cases of MERS infection seen in people older than 50 years [63]. Compared with SARS patients, comorbidities, such as diabetes, hypertension, chronic heart disease and chronic pulmonary disease, were more common in MERS cases [64]. Based on the outcomes of meta-analysis, incidence rates of clinical characteristic includes fever, cough, myalgia or fatigue, and sputum production were 83, 59, 31, and 29% respectively. The incidence of ARDS was 22%, and the case mortality rate of patients with 2019-nCoV infection was 5% which is lower than to SARS and MERS [65]. Several reports propose that pulmonary fibrosis will become one of the severe problems in cases with 2019-nCoV infection [66–68]. How to stop and decrease the incidence of pulmonary fibrosis in cases with 2019-nCoV infection are crucial complications in the treatment of 2019-nCoV [66–68]. Additionally, we observed that hemoptysis, vomiting, diarrhea rhinorrhea, headache chest pain and sore throat are less than occurred in patients with 2019-nCoV. Air-space opacities (unilateral focal and both unilateral multifocal or bilateral involvement) are the key radiological characters in SARS cases [69,70]. Although, ground-glass opacities and consolidation were the most frequent radiological characters in MERS patients [71,72]. Guan W and colleagues [17] observed that the frequent radiographic features were ground-glass opacity (50%) and bilateral patchy shadowing (46%) in 1099 cases with 2019-nCoV infection. Huang C and colleagues [4] reported that the normal radiographic feature of severe patients with 2019-nCoV were bilateral multiple lobular and subsegmental areas of consolidation. The pooled incidences of the bilateral pneumonia multiple mottling and ground-glass opacity bilateral patchy shadowing and consolidation were 70%, 60%, 50%, and 37%. Based on the laboratory characters, the pooled incidence rate of lymphocytes decrease and increase were 58% and 14%. Otherwise, the pooled incidence rate of increasing and decreasing Neutrophils was 17% and 16%. These defects are comparable to those previously detected in cases with MERS and SARS infection [73]. These outcomes more endorse that lymphocytes decrease along with increasing neutrophils was a characteristic of SARS, and 2019-nCoV might primarily effect on lymphocytes, especially T lymphocytes [74]. Additionally, the administration of glucocorticosteroids cause immunosuppression, decreasing the function and/or numbers of lymphocytes, and deregulated lymphocyte responses. Therefore, treatment with glucocorticoids difficult the concern about Lymphopenia [75]. On the other hand, immune insufficiency may be also a risk factor for poor outcome in patients with 2019-nCoV. Currently, outcomes on the death of 2019-nCoV are varying. The recent four reports include 138, 41, 507 and 41 cases, the mortality was 4.3%, 15%, 7.9% and 14.6% respectively [4,34,52,56]. However, the mortality rates of SARS (10%) and MERS (35%) are higher than to 2019-nCoV [76]. In our meta-analysis, the pooled incidence death was 5% respectively. Although, this result higher than the death reported by the previous reports [52,56]. The cause for this occurrence may be related with the absence of identifying information on data, and also deficient data on diagnosis approaches and treatment practices about 2019-nCoV. However, there were also some limitations of our meta-analysis: (1) all reports included had retrospective designed with high statistic heterogeneity (large variation in the sample size among studies; (2) often cases in

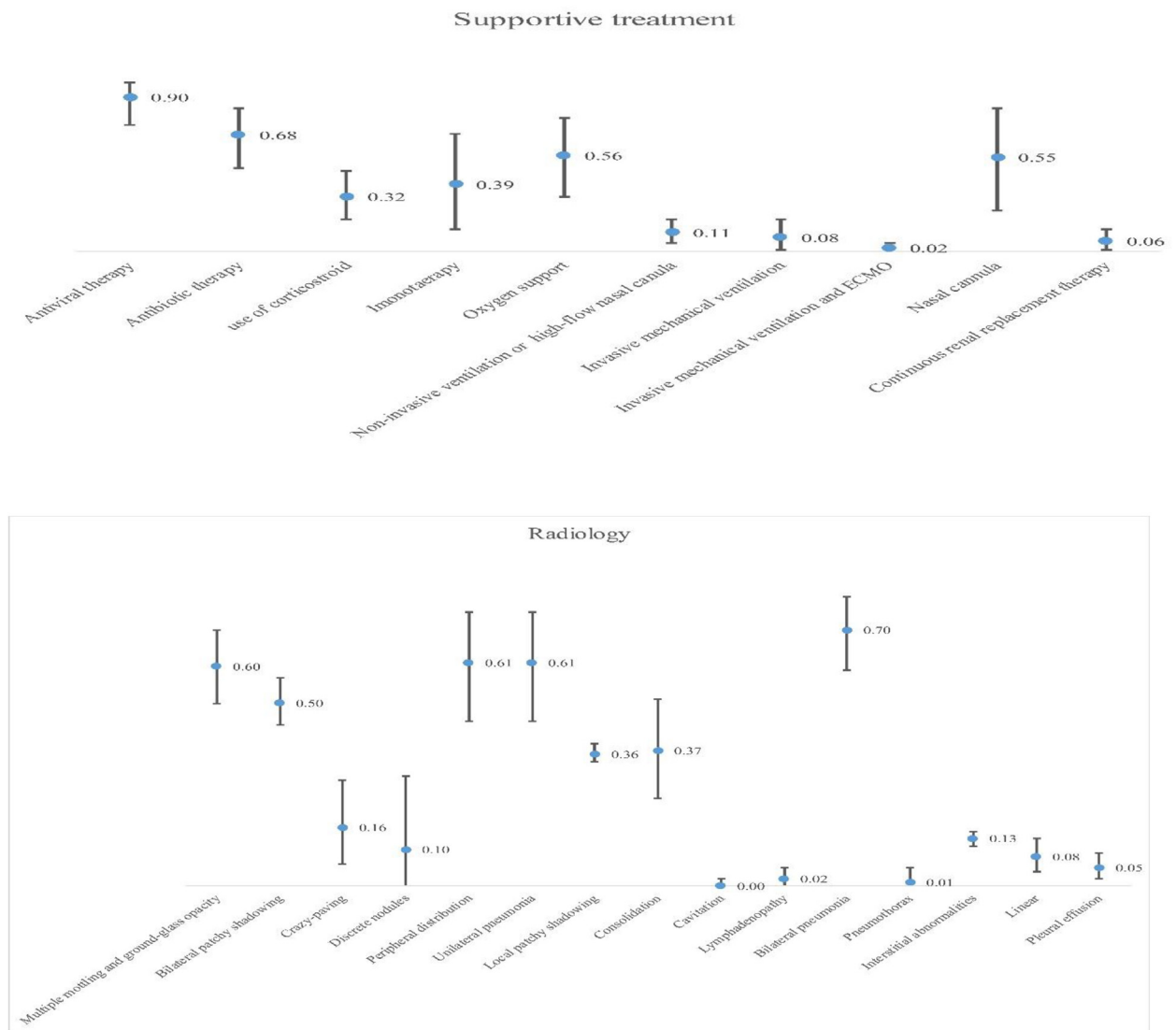


Fig. 2. Pooled incidence rate for characters in the study.

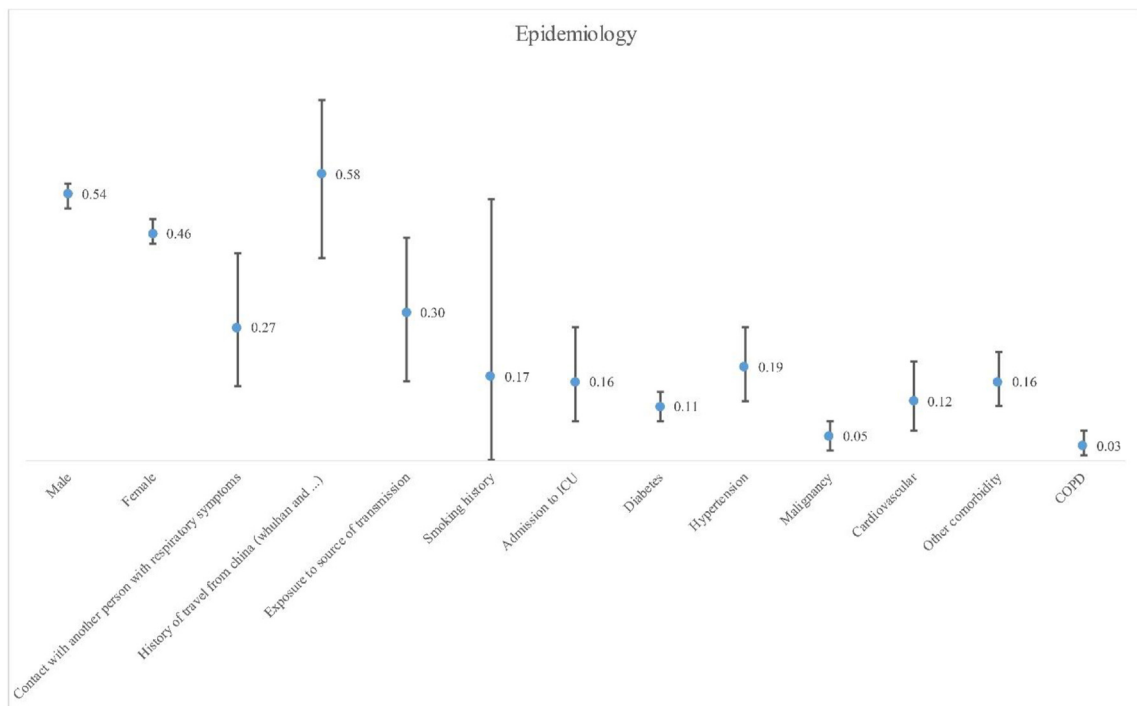
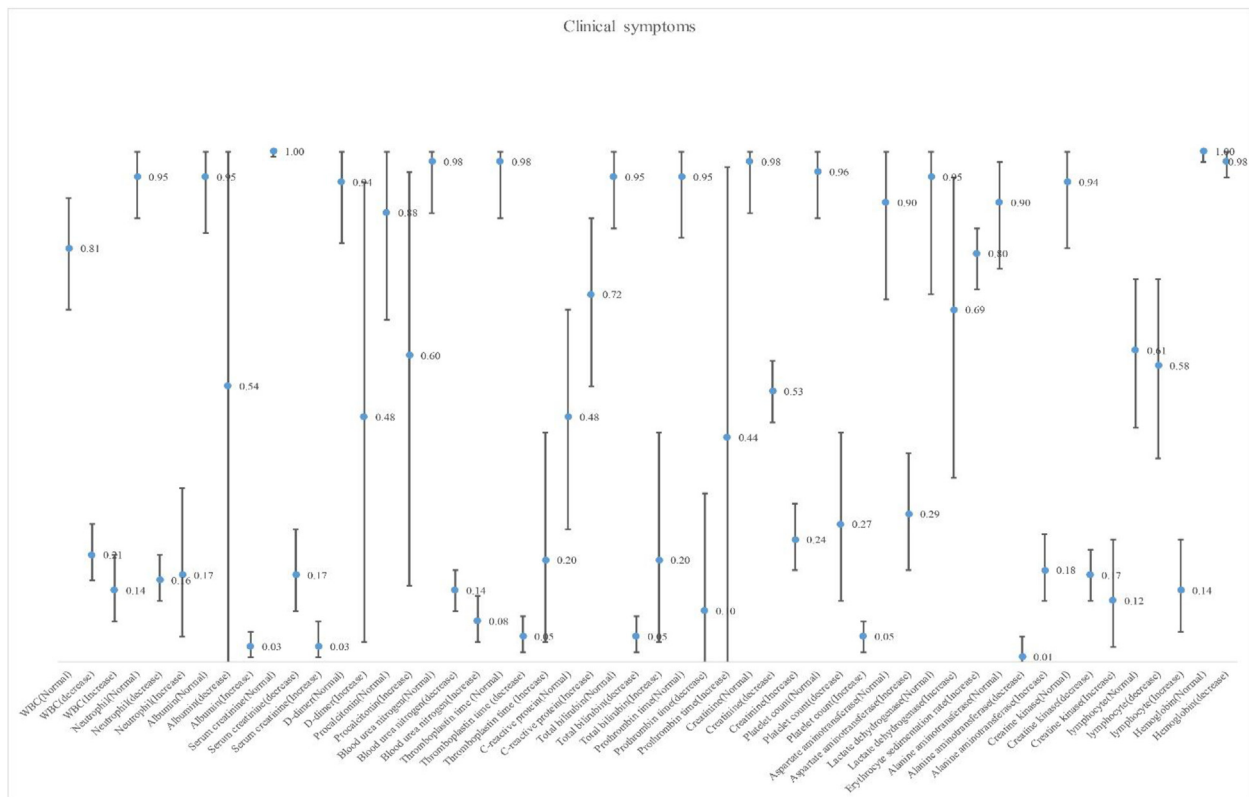
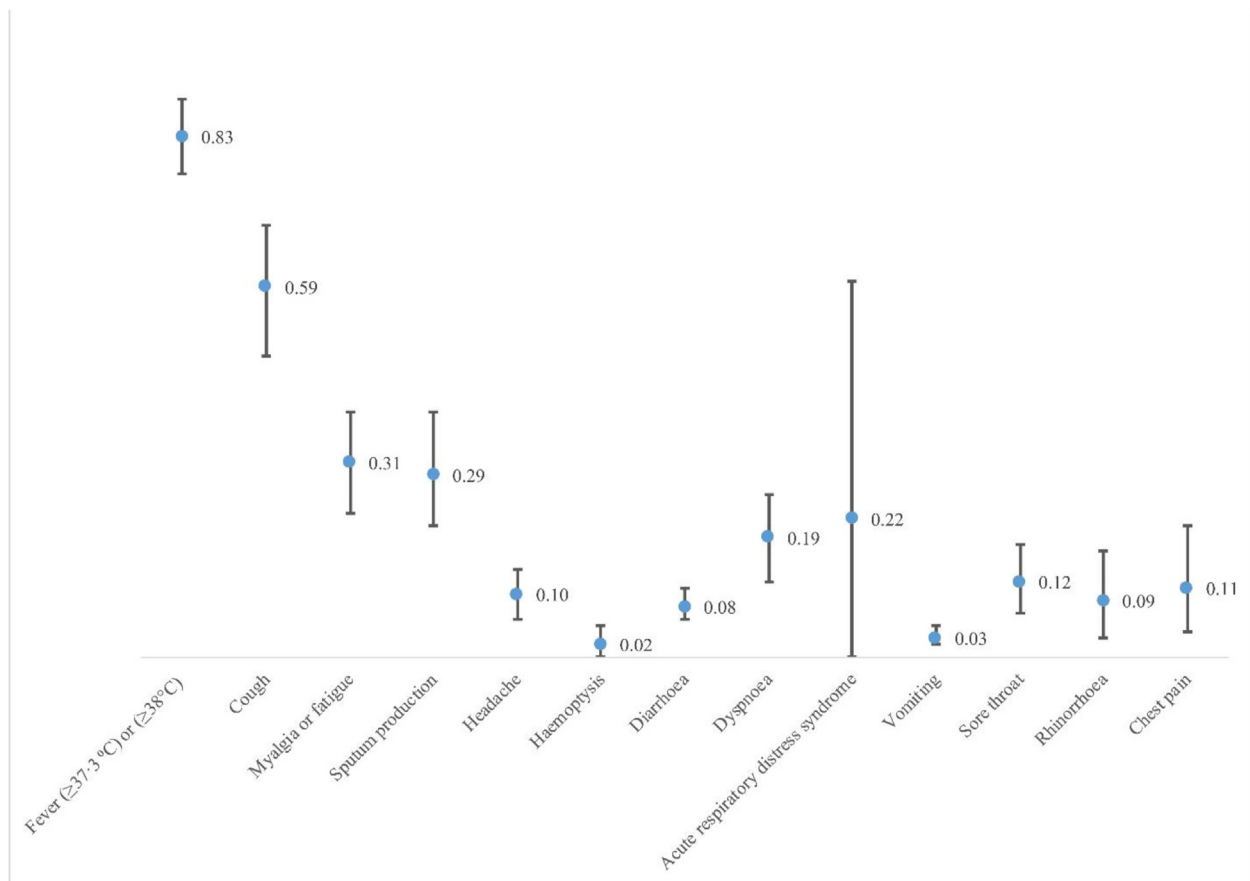


Fig. 2. (continued).



Clinical outcomes

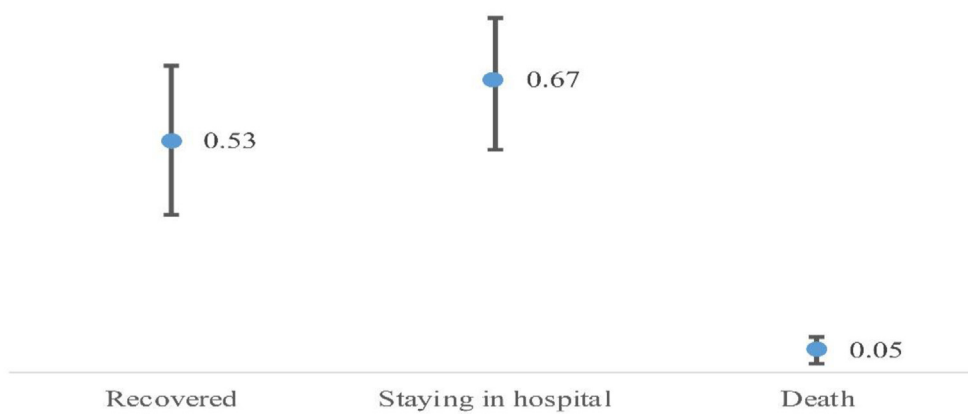


Fig. 2. (continued).

this meta-analysis are Chinese; (3) large variation in lengths of follow-up led to some cases may be still staying in hospital in the included studies. In conclusion, the outcomes of our systemic review and meta-analysis provide a quantitative pooled incidence rate of clinical, epidemiological, laboratory, and radiological features of 2019-nCoV and has great potential to develop diagnosis and patient's stratification in 2019-nCoV. However, this conclusions of this study

still requisite to be warranted by more careful design, larger sample size multivariate studies to corroborate the results of this meta-analysis.

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Declaration of competing interest

The authors declare that there are no conflict of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jmm.2020.10.004>.

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