Review Article

Clinical manifestation, laboratory and radiology finding, treatment and outcomes of COVID-19: A systematic review and meta-analysis

Nahid Dehghan Nayeri[1], Javad Nadali[2], Anahita Divani[1], Mohammad Hasan Basirinezhad[3], Mohsen Meidani[4]

[1]School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran, [2]School of Nursing and Midwifery, Shahroud University of Medical Sciences, Shahroud, Iran, [3]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran, [4]Department of Infectious Diseases and Tropical Medicine, Imam-Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

Background: Since December 2019, coronavirus (COVID-19) spread throughout the world. The high rate of infection and its unknown nature led specialists to report the condition of patients. The aim of this study is to systematically review of symptoms, laboratory and radiologic findings, treatment, and outcomes of patients with COVID-19. **Materials and Methods:** Databases such as PubMed, Embase, Scopus, Web of Science, Google Scholar, and Cochrane were searched. Finally, 46 articles were appropriate for the aim of the study. After quality evaluation, the necessary data were extracted and meta-analysis was performed. **Results:** 4858 articles were retrieved until March 30, 2020. After screening, the full-text of 46 articles was assessed. Of the reported cases, 31.7% had no comorbidities, 21.4% had high blood pressure, 70.6% had fever, and lymphopenia was reported in 55.2% of patients. For 16% bilateral patchy shadowing in radiography and for 51% ground-glass opacity was reported. Outcomes were remarkable for recover to death. **Conclusion:** COVID-19 leads to healthcare problems for countries. Nonspecific symptoms have made it difficult for differential diagnoses without computed tomography-scan or corona Test, but they are not available in many countries. Therefore, this systematic review can help health care staff to make decisions based on symptoms, treatments, and outcomes..

Key words: COVID-19, coronavirus, meta-analysis, SARS-CoV-2

How to cite this article: Dehghan Nayeri N, Nadali J, Divani A, Basirinezhad MH, Meidani M. Clinical manifestation, laboratory and radiology finding, treatment and outcomes of COVID-19: A systematic review and meta-analysis. J Res Med Sci 2021;26:41.

INTRODUCTION

Recently, a family of viruses with developed and special genome called human coronaviruses has been responsible for a large number of respiratory system diseases. Currently, these viruses are known as one of the main causes of severe respiratory diseases such as bronchitis and bronchiolitis and pneumonia in children, young people, and adults.[1] Six types of coronaviruses have already been identified.[2] Over the past two decades, many people have died from these viruses, ranging from 10% severe acute respiratory syndrome-related coronavirus (SARS-CoV) to 37% Middle East respiratory syndrome-related coronavirus (MERS-CoV).[3] Furthermore, these viruses are known as nosocomial infection agents and impose exorbitant costs to health systems.[1]

Despite the world's familiarity with these types of viruses, in December 2019, a series of cases of pneumonia with unknown etiology emerged in Wuhan, China, which the early symptoms were greatly similar to viral pneumonia. However, a closer examination and analysis of lower lung samples revealed that a type of coronavirus (nCOV) is the cause of the symptoms. This virus is named new coronavirus 2019 or COVID-19 by the WHO.[3] This time, the issue was quite different from previous times. The concern was not related to the

Access this article online

Quick Response Code:

Website: www.jmsjournal.net

DOI: 10.4103/jrms.JRMS_900_20

Address for correspondence: Dr. Mohsen Meidani, Department of Infectious Diseases and Tropical Medicine, Imam-Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran. E-mail: mohsenmeidani53@gmail.com

Submitted: 12-Aug-2020; **Revised:** 04-Oct-2020; **Accepted:** 19-Jan-2021; **Published:** 30-Jun-2021

mortality rate (MR) from the virus, rather it was about the high rate of its transmission. Furthermore, it was not known how to deal with this disease because of a lack of knowledge.

Despite the lower MR of this virus in comparison with its families, it is worrying due to its high prevalence and contagion so that the number of deaths and infections is very remarkable. Among 1,039,158 people have been infected with this virus in the world until April 4, 2020, 55,163 participants of them died.[4]

Coronaviruses exhibit high resistance in the environment. This feature has made it difficult to control and prevent the disease.[1] Furthermore, the rapid spread and transmission of this virus have caused worldwide concern. Until now more than 200 countries reported to have been infected by this virus and many patients have died.[5] On the other hand, according to the Centers for Disease Control and Prevention report, the incubation period of 2019-nCov is 2–14 days and has recently mentioned this period can also be very momentous in the virus transmission.[6]

Due to the mentioned features of this virus, this worldwide outbreak calls for faster and wisely control by countries.[7] For more effective control and prevention, recognizing the sign and symptoms of the patients in different periods of illness and isolating them plays an important role.[8] However, a variety of symptoms have been mentioned so far, some only just have been added such as Anosmia, hyposmia, and ageusia.[9,10] Furthermore, symptoms of fever, dry cough, and fatigue in the early stages without the typical symptoms of acute respiratory disease, and later pneumonia-like symptoms, gastrointestinal symptoms such as diarrhea with virus excretion (up to several weeks) and in some cases, central nervous system involvement such as multiple sclerosis has been reported.[1] Although some of the clinical manifestations of SARS, MERS, and COVID appears to be similar, distinct symptoms have also been reported in some patients, so faster differential diagnosis is required for treatment.[3,11-13]

Laboratory findings of patients infected by COVID-19 showed lymphopenia and leukopenia. Furthermore, findings of chest computed tomography (CT) scan showed bilateral abnormalities in lung lobes, which are very similar to symptoms of influenza and other respiratory viruses. This pattern made it more difficult to early differential diagnosis.[3,13] Other laboratory findings showed increased prothrombin time, increased D-dimer, increased liver enzymes, and increased cardiac enzymes in some cases. Pro calcitonin level was reported mostly normal, although these reports were contradictory in different studies.[13-15]

Although viral diseases usually have an overestimated MR in the early stages, issues are different this time. MRs are rising rapidly as a result of severe contagion, world outbreak, and lack of differential diagnosis and lack of appropriate and specific treatment.[15]

However, many countries are facing lack of facilities such as laboratory testing and sampling, hence priority is given only to subjects with very severe symptoms while recognizing symptoms and their incidence and frequency can have an effective role in the subsequent control of the disease. Since various symptoms have been mentioned in the studies, a systematic review is required to provide a conclusion for health and policymakers.

Likewise, there is no specific treatment for the disease so far, and various countries are trying different drugs and sometimes combinations therapy.[13,14] The efficacy of these drugs has not been systematically investigated by using patient-centered outcomes such as MR, discharge of hospital, and remission. Therefore, this study was conducted with the aim of recognizing the specific symptoms of COVID-19 as well as its treatments and outcomes as a systematic review with meta-analysis.

METHODS

Data sources and search strategy

Based on the PRISMA guide[16] (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), we used an evidence-based model for framing a PICO question model (PICO: Participants, Intervention, Comparison, and Outcomes). The questions posed was the following: What are the symptoms of patients with patients with COVID-19? What are laboratory and radiologic findings in patients with COVID-19? What are the treatments for COVID-19? What are the outcomes of patients with COVID-19? (P) Participants: Patients with COVID-19.(I) Intervention: Treatments performed in patients with COVID-19.© Comparison: Not applicable. (O) Outcomes: Hospitalization, recovery, death.

Since the primary purpose of this study was to conclude of the articles that listed the symptoms or treatments of COVID-19, all valid databases were searched. A broad search was attempted and the search restrictions were moved to include the maximum number of articles in the study without missing any valuable and related article. Then, duplicate entering studies from various databases were removed. After that, all of the titles were read and unrelated articles were deleted.

We search databases- PubMed, Embase, Scopus, Google Scholar, web of sciences, and Cochrane with keywords included coronavirus, COVID 19, symptoms, signs,

treatments, outcomes. No time limits were set for searches. However, since the emergence of the disease was in January 2020; the first articles were found on this time; and no studies had been done before. Therefore, all studies before that time were excluded after evaluating the titles. Diagram 1 shows the flow of assessing studies. Selection criteria and data extraction. Due to the emergence of the disease and to obtain the maximum possible knowledge, there was no restriction on the type of articles in the searching level. However, all the descriptive and analytical studies as well as the observationally reported interventional studies were included in the study. The search keywords and how each site was searched along with the number of articles are listed in Table 1. All studies were included until March 30, 2020.

All articles were assessed based on authors, place of study, sample number, study design, patient characteristics, and symptoms. Furthermore, laboratory findings and treatments used for patients were evaluated completely. Studies lacking the essential components required by the current study objective were excluded from the systematic review; such as being a case report; not mention the definitive diagnosis of COVID-19 with either laboratory tests or definitive symptoms. Furthermore, some articles were removed because they have not assessed symptoms entirely or only, they mentioned one or two nonspecific symptoms.

Quality assessment

Finally, all of 46 remaining articles were reviewed by two reviewers (J. N, A, D) independently and screened studies to identify all potentially eligible studies using the JBI Quality Assessment Tool, whose ratings are included in the Supplementary Table 1.

Statistical analysis

In this stage, data extracted from all articles were entered into STATA Version 16.0 software (StataCorp LLC Production, College Station, Texas, USA) software for meta-analysis and providing general conclusions about the symptoms and treatments. It should be noted that the heterogeneity of the studies was evaluated according to different symptoms, laboratory findings and treatments, and most of the criteria were heterogeneous in the studies. The Q and tests were used to investigate heterogeneity. Since the articles are heterogeneous, the random model has been used by the maximum likelihood estimation method. To describe each of the signs and symptoms, the ratio and confidence interval (CI) of 95% have been reported.

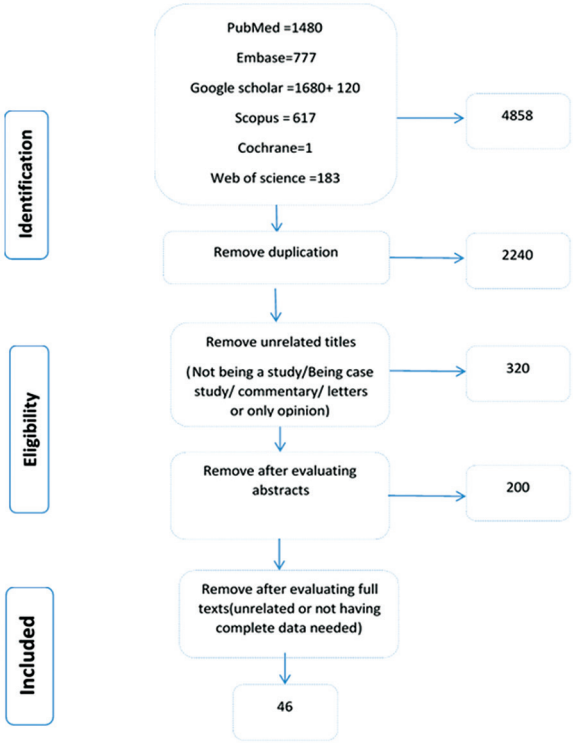

Diagram 1: Flow diagram of literature search and study selection (PRISMA flow chart)

Table 1: Databases and the results of searches

Databases	Search results
PubMed	Search (corona virus [Title]) OR COVID 19[Title]=918 Search (treatment [Title/Abstract]) AND ((corona virus [Title]) OR COVID 19[Title])=97 Search (corona virus [Title]) OR COVID 19[Title]) AND symptom [Title/Abstract]=22
Embase	'corona virus':ab, ti AND (symptoms: ab, ti OR signs: ab, ti)=41 ('corona virus':ti OR 'covid 19':ti) AND (symptoms: ab, ti OR signs: ab, ti)=67
Google scholar	allintitle: "corona virus"=113 (limit to after 2019) allintitle: "corona virus"=103 (without citation) (limit to after 2019) allintitle: symptoms "covid 19"=15 (limit to after 2019) allintitle: covid-19=1680 (limit to after 2019)
Scopus	(TITLE-ABS-KEY (*"covid 19"*) OR TITLE-ABS-KEY (*"corona virus"*))=617 (year: 2020)
Cochrane from Ovid	"corona virus".m_titl=0 COVID 19.m_titl=0 "corona virus".mp. [mp=ti, ot, ab, tx, kw, ct]=3
Cochrane	1 COVID 19 in Title Abstract Keyword 9 corona viruses in Title Abstract Keyword (not related)
Web of science	TITLE: ("corona virus") *OR* TITLE: (covid-19)=183

COVID 19=Coronavirus disease 2019

Table 2: Baseline characteristics of all the studies included in the meta-analysis

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
Chen N	Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China	Descriptive study retrospective single center *n*=99	-	Oxygen therapy 75 Mechanical ventilation: Noninvasive (ie, face mask) 13 Invasive 4 CRRT 9 ECMO 3 Antibiotic 70 Antifungal 15 Antiviral 75 Glucocorticoids 19 IVIG 27	Cephalosporins, quinolones, carbapenems, tigecycline against methicillin-resistant Staphylococcus aureus, linezolid, and antifungal drugs The duration of antibiotic treatment was 3-17 days (median 5 days [3-7]) Methylprednisolone sodium succinate, methylprednisolone, and dexamethasone for 3-15 days (median 5 [3-7])	Hospitalized 57 Discharged 31 Died 11	ARDS 25 AKI 3 Septic shock 4 VAP 1	RT-PCR
Weiliang Cao	Clinical features and laboratory inspection of novel coronavirus pneumonia (COVID-19) in Xiangyang, Hubei	Retrospective study *n*= 128	-	-	-	-	-	RT-PCR
Wei-jie Guan	Clinical characteristics of 2019 novel coronavirus infection in China	Retrospective study *n*= 1099	Median (3) Range (0-24)	Oxygen therapy 418 Mechanical ventilation 67 Invasive 24 Noninvasive 56 IV antibiotics 632 Oseltamivir 393 Antifungal 30 Systemic corticosteroids 204 ECMO 5 CRRT 9 IV IgG 143	Maximal daily dose of corticosteroids (mg/kg) 1.5 (0.7-40.0)	Discharged 55 Death 15 Recovered 9 Hospitalized 1029	ICU admitted 55 Septic shock 11 Acute respiratory distress syndrome 37 AKI 6 DIC 1 Rhabdomyolysis 1 Pneumonia 869	RT-PCR
Zhiliang Hu	Clinical Characteristics of 24 Asymptomatic Infections with COVID-19 Screened among Close Contacts in Nanjing, China	Case series *n*=24	8 (6-9)	Antiviral 21 Antibiotics and Antifungal 1 IVIG 3 Interferon atomization 24 Corticosteroids 0 Mechanical ventilation 0	Lopinavir/ritonavir Darunavir/cobicistat	Hospitalized 15 Discharge 9 No death	18 cases (75.0%) had the virus cleared admission to ICU 0	RT-PCR
Chaolin Huang	Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China	Prospectively *n*=41	-	O2 therapy: Nasal 27 NIV 10 Invasive mechanical ventilation 2 ECMO 2 Antiviral 38 Antibiotic 41 Glucocorticoid 9	-	Hospitalized 7 Discharged 28 Died 6	ARDS 12 AKI 3 Shock 3 Acute cardiac injury 5 Secondary infection 4	RT-PCR

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Table 2: Contd...

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
Ying Huang	Clinical characteristics of 36 non-survivors with COVID-19 in Wuhan, China	Retrospectivesingle-centered study *n*=36	-	O2 therapy 35 Mechanical ventilation Noninvasive 19 Invasive 9 Antibiotic 36 Antiviral 35 Glucocorticoids 25 IVIG 20 α-IFN 6	-	Dead 36	ARDS 36 Electrolyte disturbance 16 Acute renal injury 1	RT-PCR
Lei Liu	Clinical characteristics of 51 patients discharged from hospital with COVID-19 in Chongqing, China	Retrospective, single-center case series *n*=51	14	Oseltamivir (po) 7 Interferon (po) 51 Kaletra (po) 51 Thymopentin (IM) 48 Traditional Chinese medicine decoction (po) 28 Antibiotic 11 IV IgG 4 High-flow oxygen 8 noninvasive ventilation 6 Invasive ventilation 1	-	Discharged 50 Died 1	Average hospitalization day was 12 days	laboratory confirmed
Zuojiong Gong1	Clinical characteristics of 25 death cases with COVID-19: A retrospective review of medical records in a single medical center, Wuhan, China	Retrospective review of medical records *n*=25	Mean±SD 10.56±4.42 days	-	-	-	-	RT-PCR
Jie Xu	Prevalence and clinical features of 2019 novel COVID-19 in the Fever Clinic of a teaching hospital in Beijing	A single-center, retrospective study *n*=21	2-10 days	-	-	-	-	RT-PCR
Hong-Jian Zhang	Epidemiological and Clinical Characteristics of 124 Elderly Outpatients with COVID-19 in Wuhan, China	Retrospective study *n*= 124	7-11	-	-	-	-	RT-PCR
Bo Hu	Neurological Manifestations of Hospitalized Patients with COVID-19 in Wuhan, China	A retrospective case series study *n*=214	-	-	-	-	-	RT-PCR
Xiao-Min Chen	Epidemiologic and Clinical Characteristics of 91 Hospitalized Patients with COVID-19 in Zhejiang, China	Retrospective case series *n*=91	6 (3-8) days	-	-	Remained in hospital: 60 (65.93) Discharged: 31 (34.07) Died: 0 ICU: 9 (9.89)	-	RT-PCR

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Table 2: Contd...

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
Jun Liu	Clinical characteristics and treatment of patients infected with COVID-19 in Shishou, China	Single-center case series *n*=89	-	Noninvasive ventilation: 31 (35%) IMV: 4 (4%)	IFN: 89 (100%) 85 (96%) were treated with moxifloxacin Other antibiotics: 4 (4%) Immunoglobulins: 35 (39%) Lopinavir/ritonavir 84 (94%) Other antivirals: 5 (6%) Methylprednisolone: 35 (39%)	At present, of the 89 patients admitted, 16 have been discharged, 1 has died, 2 have deteriorated, and the remaining patients have improved or stabilized	ICU: 35 Non-ICU: 53	RT-PCR
Jianlei Cao	Clinical features and short-term outcomes of 18 patients with COVID-19 in intensive care unit	Retrospective case series *n*=102	3 (2-6) days	Antiviral: 100 (98.0) Antibiotic: 101 (99.0) Glucocorticoid: 51 (50.0) Immunoglobulin: 11 (10.8) Chinese medicine: 3 (2.9) Oxygen: 76 (74.5) NIV: 5 (4.9) IMV: 14 (13.7) ECMO: 3 (2.9) CRRT: 6 (5.9)	-	Hospital admission: 6 Discharge: 85 Died: 17	MODS: 10 ARDS: 1 Cardiac arrest: 4 Respiratory failure: 2	laboratory-confirmed
Sibylle Bernard Stoecklin, France	First cases of COVID-19 in France: Surveillance, investigations and control measures, January 2020	Case series *n*=3	-	-	-	Death: 0 Hospitalized: 3 Discharge: 2	-	RT-PCR
Simon Petrie, Australia	2019-nCoV acute respiratory disease, Australia Epidemiology Report	Epidemiology report *n*=12	-	-	-	Death: 0 Hospitalized 12	ICU admitted 1	PCR
Zhiyong Peng	Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China	Single-center case series *n*=138	-	Antiviral therapy: 124 (89.9) Glucocorticoid therapy: 62 (44.9) CKRT: 2 (1.45) Oxygen inhalation: 106 (76.81) NIV: 15 (10.9) IMV: 17 (12.32) ECMO: 4 (2.9)	Oseltamivir: 124 (89.9%) Moxifloxacin: 89 (64.4%) Ceftriaxone: 34 (24.6%) Azithromycin: 25 (18.1%) glucocorticoid therapy: 62 (44.9%)	34.1% were discharged 6 died (4.3%) 61.6% hospitalized	ICU: 36 Non-ICU: 102	RT-PCR
Jian Wu	Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province	Multicenter descriptive retrospective *n*=80	-	Oxygen therapy 36 Immunoglobulin therapy 16 Chinese medicine 3 Antibiotic treatment 73 Antiviral treatment 80 Hormone therapy 12	All patients were treated empirically with a single antibiotic, mainly moxifloxacin. The duration was 3-12 days. All patients received ribavirin antiviral therapy for 3-12 days	Hospitalized 61 Discharged: 721 Died 0	-	RT-PCR

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Table 2: Contd...

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
Wenjie Yang	Clinical characteristics and imaging manifestations of the 2019 novel COVID-19	Retrospective multi-center cohort study *n*=149	-	Oxygen therapy: 134 Antibiotic: 34 Antifungal: 0 Antiviral: 140 Interferon: 144 Glucocorticoids: 5 Immunoglobulin: 19	-	Hospitalized 76 Discharged: 73 Died 0	-	RT-PCR
Bicheng Zhang	Clinical characteristics of 82 death cases with COVID-19	Cohort *n*=82	5-10 days	Antibiotics: 82 Corticosteroids: 29 Anti-virus: 82 Oxygen therapy: 82 Mechanical ventilation: 33	-	Death: 82	ICU: 14	RT-PCR
Matt Arentz, USA	Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State	Case series *n*=21	-	Oxygen therapy 1 Invasive 15 Non-invasive 4	-	Hospitalization 10 Death 11	ARDS 20 Septic shock 4 Cardiac injury 7 AKI 4 Hepatic injury 3	RT-PCR
Pingzheng Mo	Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China	Descriptive Retrospective *n*=155	-	Oxygen therapy 102 Invasive 36 IVIG 9 α-IFN 30 Antiviral treatment 45 Arbidol 31 Lopinavir 27 Thymalfasin 11	-	-	-	laboratory confirmation
Yihui Huang	Clinical characteristics of laboratory confirmed positive cases of SARS-CoV-2 infection in Wuhan, China: A retrospective single center analysis	Descriptive Retrospective *n*=34	—	Oxygen therapy 25 Invasive 3 Non-invasive 2 Antibiotic therapy 31 Antiviral treatment 41 Glucocorticoids 21 Lopinavir/ritonavi 9	—	—-	ICU care 8 No-ICU car 26	laboratory confirmation
Kunhua Li	The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia	Descriptive retrospective *n*=83	-	-	-	-	-	—
Shuchang Zhou	CT Features of COVID-19 Pneumonia in 62 Patients in Wuhan, China	Descriptive retrospective *n*=65	-	-	-	-	-	Laboratory confirmed and the CT
Jin-jin Zhang	Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China	Descriptive retrospective *n*=140	-	In this study, data in regard to the treatment and outcome of these patients were not finalized, since most of these patients are remaining hospitalized	-	-	-	RT-PCR

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Table 2: Contd...

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
Jiong Wu	Chest CT Findings in Patients with COVID-19 and its Relationship with Clinical Features	Descriptive retrospective *n*=80	-	-	-	-	-	RT-PCR
Z Wang	Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China	Case series *n*=69	-	Oxygen therapy 43 Antibiotic therapy 66 Antiviral treatment 36 Arbidol 36 Glucocorticoids 10	-	Discharge 18 Hospitalization 44 Death 5	-	RT-PCR
S Tian	Characteristics of COVID-19 infection in Beijing." J Infect 80 (4): 401-406	Descriptive Retrospective *n*=262	-	-	-	Discharge 45 Hospitalization 214 Recovered 3	-	RT-PCR
Suxin Wan	Clinical Features and Treatment of COVID-19 Patients in Northeast Chongqing	Descriptive retrospective *n*=135		Oxygen therapy 90 IMV 1 NIV 34 Antibiotic therapy 59 Antiviral treatment 135 Glucocorticoids 36	-	Discharge 15 Hospitalization 150 Death 1	ARDS 21 Septic shock 1 Cardiac 10	RT-PCR
Tianmin Xu	Clinical Features and Dynamics of Viral Load in Imported and Non-imported Patients with COVID-19	Descriptive retrospective *n*=51	4-14	-	-	-	-	RT-PCR
Aixin Li	Clinical characteristics and durations of hospitalized patients with COVID-19 in Beijing: A retrospective cohort study	Retrospective cohort study *n*=77	4 (3-7)	-	-	Discharged 64 Hospitalization 8 Death 5	Nonsevere 57 Severe 20 Any 28 ARDS 3 Shock 1 Acute heart failure 2 AKI 2 Liver dysfunction 25 MODS 1 Secondary infection 3	RT-PCR
Tao Yao	Clinical characteristics of 55 cases of deaths with COVID-19 pneumonia in Wuhan, China	Retrospective case series *n*=55	-	Antifungal therapy 2 Antibiotic therapy 53 Glucocorticoid therapy 35 IVIG therapy 39 CRRT 4 Invasive mechanical ventilation 12 ECMO 1	55 patients received antiviral therapy for 5-14 days, and all of them received arbidole, 38 received Oseltamivir 10 received ribavirin, 1 received Lopinavir and ritonavir.	Death 55	-	RT-PCR

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Table 2: Contd...

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
De JIN	Clinical findings of 100 Mild Cases of COVID-19 in Wuhan: A	Retrospective, single center study *n*=100	-	Oxygen therapy 58 NIV 10 No respiratory support 32 Antibiotic treatment 95 Antiviral treatment 100 Antifungal treatment 1 Glucocorticoids 59 IVIG therapy 43 Chinese herbal medicine 67	All patients received Oseltamivir (75 mg/twice daily), Ganciclovir Sodium (5 mg/kg), Ribavirin (500 mg/twice daily), Arbidol hydrochloride (200 mg/twice daily), recombinant human interferon-alpha-2b (300/IU), Lopinavir (200 mg/day), Ganciclovir (600 mg/twice daily) and Traditional Chinese Medicine (200 ml/twice daily). 12 (12%) patients were treated with a single antiviral treatment, and 88 (88%) patients were given combination therapy The antibiotics used were Lacefofax, Moxifloxacin, Piracillin and Tazobactam, Azithromycin, Imipenem and Cilastatin, Voriconazole, Levofloxacin, Cefoperazone and Sulbactam, Meropenem and Minocycline	Hospitalized 96 Discharged 1 Died 33	-	RT-PCR
Tiejun Wu	Clinical characteristics and reasons of different duration from onset to release from quarantine for patients with COVID-19 Outside Hubei province, China	Descriptive retrospective *n*=37	-	Antibiotics 27 Antifungal drugs 1 Antiviral drugs 37 Glucocorticoids 8 Albumin 12 immunoglobulin 7 Thymosin 24 Oxygen therapy 15 Chinese Medicine 37	Daily dose of Glucocorticoids 40 mg 6/8 80 mg 1/8 120 mg 1/8 IV antibiotics 17/27 Oral antibiotics 10/27 Two antiviral 25/37 Three antiviral 12/37	-	Mild 5 Moderate 30 Severe 1 Critical 1 Complications 1 ARDS 2	RT-PCR
Kazuo Imai, Japan	Non-severe vs severe symptomatic COVID-19: 104 cases from the outbreak 1 on the cruise ship 2 “Diamond Princess” in Japan	Descriptive Retrospective *n*=104	-	Oxygen therapy 13 Mechanical ventilation 1	-	Died 0 Recovered 104	-	RT-PCR
Fan Yang	Epidemiological, Clinical Characteristics and Outcome of Medical Staff Infected with COVID-19 in Wuhan, China: A Retrospective Case Series Analysis	A Retrospective Case Series Analysis *n*=64	-	Oxygen therapy 34 Electrocardiograph monitoring 9 Antibiotics treatment 55 Antiviral treatment 64 Traditional Chinese medicine 13 Immune globulin 23 Thymosin 33	-	Hospital discharge 34 Continued hospitalization 30 Death 0	-	RT-PCR

Contd..

Table 2: Contd...

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
Xiaoyan Ming	Association of Cardiovascular Manifestations with In-hospital Outcomes in Patients with COVID-19: A Hospital Staff Data	Retrospective, single-center case series *n*=41	-	Oxygen therapy: 23 ECMO 1 Antibiotics treatment: 39 Antiviral treatment 40 Glucocorticoids 32 Traditional Chinese medicine 8 Immune globulin 33 Thymosin 16 Kaletra 16	-	-	ARDS 2 Septic shock 20 Hepatic 8 Infection 20	RT-PCR
Iek Long Lo Macau	Evaluation of SARS-CoV-2 RNA shedding in clinical specimens and clinical characteristics of 10 patients with COVID-19 in Macau	Retrospective study *n*=10	-	Oxygen therapy: 4 Antibiotics treatment: 10 Antiviral treatment 10 Glucocorticoids 3	-	Hospitalization 10 Discharge 5	Mild 2 Moderate 4 Severe 4 Critical 0	RT-PCR
Tao Chen	Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study	Retrospective study *n*=274	-	Oxygen therapy: 251 Antibiotics treatment: 249 Antiviral therapy 236 Glucocorticoid therapy 217 Immunoglobulin 54 IFN 89 CRRT 3 ECMO 1	-	Death 113 Recovered 161	ARDS 196 Sepsis 179 AKI 29 Liver injury 13 DIC 21 Electrolyte 93 Cardiac 132 Shock 46	RT-PCR
Yuhong Chen	Clinical characteristics and current treatment of critically ill patients with COVID-19 outside Wuhan, China	Multicenter, retrospective, observational *n*=37	-	Oxygen therapy: 24 Antibiotics treatment: 33 Antiviral therapy 37 Glucocorticoid therapy 41 Chinese medicine 35 Immunoglobulin 19 CRRT 2 Thymosin 32 Kaletra 34	-	-	Cardiac 6 AKI 4 Hepatic 1	laboratory confirmation
Peng peng	Treatment Outcomes, Influence Factors of 116 Hospitalized COVID-19 Patients with Longer/ Prolonged Treatment Course in Wuhan, China	Single center retrospective observational study *n*=116	-	Oxygen therapy: 83 Antibiotics treatment 109 Antiviral therapy 116 Glucocorticoid therapy 94 Immunoglobulin 58 ECMO 5	-	Recovered 72	None-severe 87 Severe 29 Any 49 Shock 5 ARDS 38 AKI 21 Cardiac 32 VAP 30	RT-PCR
Tao Guo	Cardiovascular Implications of Fatal Outcomes of Patients with COVID-19	Retrospective single-center case series *n*=187	-	Antivirus 166 Antibiotic 183 Glucocorticoid 106 Immune globulin 21 Mechanical ventilation 45	-	Death 43	ARDS 46 Coagulopathy 42 Liver injury 19 Kidney injury 18 Cardiac 11	Interim guidance of the WHO

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Table 2: Contd...

Author	Title	Type of study and number of samples	Incubation period (days)	Treatment	Detail	Outcome	Complications	Detection method
Vietnam	Featuring COVID-19 cases via screening symptomatic patients with epidemiologic link during flu season in a medical center of central Taiwan	Retrospective *n*=2	-	Not mentioned	-	Hospitalization 2	Not mentioned	RT-PCR
Japan	Chest CT Findings in Cases from the Cruise Ship "Diamond Princess" with COVID-19	Retrospective *n*=112	-	Not mentioned	-	Not mentioned	Not mentioned	RT-PCR
Yida Yang	Epidemiological, clinical and virologic characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms	Retrospective *n*=5	5	Antibiotic 277 Antivirus 546 Glucocorticoid 74	-	ICU admit 17	Liver injury 64 ARDS 17 Shock 2	RT-PCR

NIV=Noninvasive ventilation; IMV=Invasive mechanical ventilation; CRRT=Continuous renal replacement therapy; ECMO=Extracorporeal membrane oxygenation; IV=Intravenous; IVIG=IV immunoglobulin; ARDS=Acute respiratory distress syndrome; AKI=Acute kidney injury; VAP=Ventilator-associated pneumonia; RT-PCR=Real time reverse transcription polymerase chain reaction; ICU=Intensive care unit; COVID 19=Coronavirus disease 2019; α-IFN=Alpha interferon; SARS-CoV-2=Severe acute respiratory syndrome-related coronavirus-2; CT=Computed tomography; DIC=Disseminated intravascular coagulation; MODS=Multiple organ dysfunction syndrome

RESULTS

In this systematic review, 46 articles remained after the final evaluation.[3,12-15,17-57] The majority of articles were case series (73.3%), 25.7% were descriptive retrospective and <1% were descriptive prospective or epidemiological reports. Although most of the articles were originated in China, other articles–about 5%-were from countries such as Japan, the USA, Australia, France, and Taiwan. Besides, 44.5% of articles were published in March 2020. The characteristics of the studies have presented in Table 2.

The total number of patients reported in these articles was 5570. Slightly more than half of the patients were male (52.74%); and the mean age of the patients was 53.2 (CI: 50.17–56.33) year. The incubation period was reported between 0 and 24 days. Half of the patients reported contact with Chinese people, 15.56% had contact with patients, and 5.94% were exposed to the Huanan seafood market. Moreover, only 1.79% mentioned that they haven't had any contact.

It should be noted that only some articles have dealt with coexisting disorders or clinical characteristics. For example, 16 articles cited coexisting disorders, in which 38% (n = 2969) subjects were present, of which 31.7% had no coexisting disorders. About 21.4% of patients had hypertension (CI = 0.18–0.27); 10.8% had endocrine disorder especially diabetes mellitus (CI = 0.009–0.13); 8.1% had cardiovascular disease (CI = 0.08–0.13); 3.8% had chronic obstructive pulmonary disease or other respiratory diseases (CI = 0.03–0.05); 4.7% had cerebrovascular disease (CI = 0.04–0.07);12.6% had a history of previous surgery (CI = 0.02–0.10); and 6.3% had digestive system disease.

Clinical characteristics

The highest clinical characteristic (about 96% of the total number of patients surveyed) assessed was coughs. They reported that 60.5% of subjects (CI = 0.53–0.63) had dry coughs. However, expectoration and Sputum production was reported in 23.3% (CI = 0.18–0.31). As well as, about 15.8% reported chest pain (n = 225/1419). In this section, the sensitivity of the symptoms was not considered and only the prevalence of symptoms in patients was examined.

The second clinical characteristic (about 94%, equivalent to 5234 people) studied was the temperature which 70.6% of them fever was reported. However, only 5% of subjects had fever >39°. The forest plot of fever is shown in Figure 1.

Moreover, 21.1% had a fever <37.5°. Feeling ill, malaise or severe fatigue and weakness had 35.7% prevalence. Shortness of breath/dyspnea existed only in 22.2%. Poor appetite and anorexia were prevalent in about one fourth of

patients (23.6%), although, this symptom was examined in only 24% of subjects. Also, 18.5% reported myalgia and 11.1% had headache. Sore throat or pharyngalgia was about 12.2%.

Other signs and symptoms were rigor/chill (12%); diarrhoea/loose bowel movement (9.5%); rhinorrhoea/nasal congestion or sneezing/snotty nose (6.9%); nausea/vomiting (7.5%); dizziness (10.1%). Confusion/loss of consciousness was another important symptom that only assessed 7.7% of patients and 11.65% reported it. Other symptoms reported were tonsils well (2.09%); hmoptysis (1.8%); and hypogeusia/hyposmia (5.1%).

Other signs and symptoms were examined in few patients or they had a lower prevalence including conjunctivitis, abdominal pain, back pain, ataxia, and wheeze. The results of the sensitivity analysis are shown in Supplementary Table 2.

Laboratory findings

One of the most important laboratory findings in COVID-19 is SpO_2. However, only one study has reported this measure with 82 samples that 32.9% had Spo_2 between 85% and 94% and 10.1% had Spo_2 <85. No one had normal Spo_2.

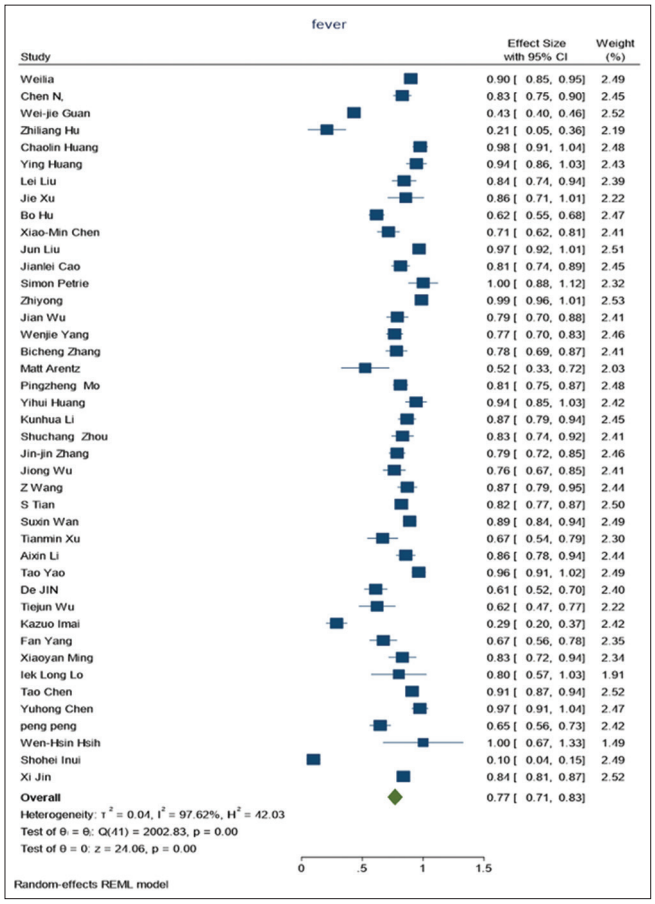

Figure 1: Forest plot of fever

WBC counts were among the most important laboratory criteria; studies reported 58.7% of samples had normal range (3.5–9.5 count, $\times 10^9$/L) and 24% <3.5 and 10.2% more than 9.5. For half of the samples were reported lymphocytes counts in the normal range (1.1–3.2 count, $\times 10^9$/L) and 55.2% below normal and only 13.7% above normal. Half of the patients had normal platelet counts, 21.9% had less than normal; and 5.5% (38/681) had platelet more than >350.

As well, ten articles measured Creatine kinase-about 2000 patients-and reported that 10% have been above creatine kinase normal range (171 U/L). In 15 articles which evaluated 2276 patients reported that D-dimer of 26.5% of patients has been >500 mg/l., but an article reported D-dimer in a normal range when they measured 51 people.

Criteria such as erythrocyte sedimentation rate (ESR), Fibrinogen, creatine kinase MB, PT, PTT, BUN, Na, K, and Chloride were reported in a small number of articles, the abnormal rate of which was not noteworthy. Other laboratory findings are shown in Table 3. The forest plot of C-reactive protein has displayed in Figure 2.

Radiologic findings

Because one of the organs involved in the COVID-19 disease is the lungs, chest radiography and CT-Scan can show the involvement of this tissue. Therefore, some studies have addressed this issue in addition to laboratory findings and symptoms. However, various studies showed different features. Three studies reported bilateral patchy shadowing in 16% (193/1202) in radiology and 18 studies showed Ground glass opacity (GGO) on 51.6% (1579/3055) patients in the CT-scan. The forest plot of GGO is presented in Figure 3. Other radiologic features are shown in Table 4.

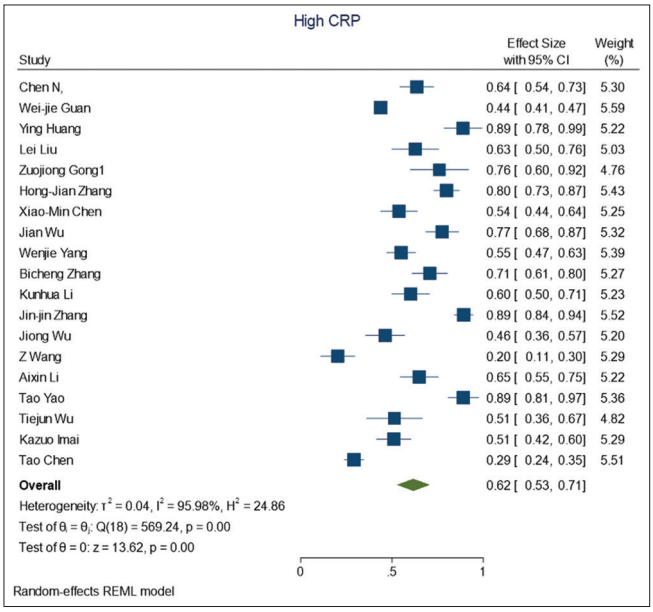

Figure 2: Forest plot of C-reactive protein

Table 3: Laboratory findings and abnormalities in patients with coronavirus disease 2019

Laboratory findings (normal range)	Number of patients examined	Number with the condition	Percent	Proportion	CI	I^2	P
Pro calcitonin (<0.5 ng/mL)							
NL	534	233	43.6	0.39	0.11-0.68	99.28	<0.001
≥0.5	2563	376	14.6	0.27	0.22-0.32	98.01	<0.001
Total bilirubin (5-21 mmol/L)							
NL	100	100	100				
≤5	149	7	4.6	0.05	0.02-0.09		
>21	1553	125	8.0	0.09	0.05-0.14	88.24	<0.001
Alanine aminotransferase (9-50 U/L)							
NL	94	70	74.4	0.75	0.66-0.84		
≤9	256	9	3.3	0.03	0.00-0.07	48.20	0.15
>50	2439	406	16.6	0.17	0.13-0.20	81.74	<0.001
Aspartate aminotransferase (15-40 U/L)							
NL	135	82	60.7	0.61	0.53-0.69	0	0.80
≤15	226	114	50.4	0.39	0.35-0.44		
>40	2607	499	19.1	0.22	0.17-0.27	90.63	<0.001
Albumin (3.4-5.4 g/dL)							
≤3.4	653	296	45.3	0.52	0.26-0.77	99.07	<0.001
>5.4	249	20	8.0	0.03	0.01-0.05		
Fibrinogen (2-4 g/L)							
≤2	91	3	3.2	0.03	0.01-0.09		
>4	128	26	20.3	0.18	0.12-0.25		
LDH (125-243 U/L)							
NL	41	11	26.8	0.27	0.16-0.42		
≤125	0	0	0				
>243	2361	802	33.9	0.43	0.31-0.55	97.35	<0.001
Creatine kinase (<171 U/L)							
NL	92	78	84.7	0.66	0.51-0.78		
<171	248	42	16.9	0.16	0.11-0.20		
≥171	1959	200	10.2	0.12	0.08-0.16	85.40	<0.001
Haemoglobin (115-150 g/L)							
NL	290	193	66.5	0.55	0.23-0.87	96.75	<0.001
≤115	644	253	39.2	0.42	0.29-0.55	92.55	<0.001
Creatinine (64-104 μmol/L)							
NL	25	7	28	0.28	0.14-0.48		
≤64	434	60	13.8	0.16	0.06-0.25	92.69	<0.001
>104	980	140	14.2	0.13	0.08-0.19	90.51	<0.001

LDH=Lactate dehydrogenase; CI=Confidence interval

Treatment

COVID-19 is an emergent disease and no specific treatment has been well-known for it, therefore different drugs were used in combination. Oxygen therapy is the first and popular treatment as mentioned Spo_2 is decreased in the patients. Antiviral such as oseltamivir, lopinavir/ritonavir (Kaletra), darunavir/cobicistat, and Arbidol were used. Other medications used for COVID-19 are shown in Table 5.

Complications

Although medical staff have tried to provide the best available treatment for patients with COVID-19 severe complications that happened in some of the patients, and has even led to mortality. Some of the most important complications mentioned in the articles are: 22.9% acute respiratory injury/acute respiratory distress syndrome (448/1995); 11.2% septic shock (93/826); 35.1% electrolyte disorder (109/310); 13.6% Disseminated intravascular coagulation (63/461); 10.3% liver disorder (133/1288), and 14.4% ventilator-associated pneumonia (31/215).

Outcomes

Different outcomes have been recorded after getting the disease in the studies including discharge 23% (549/2381); hospitalization 76.9% (1767/2297); recovery 24.1% (493/2042); death 12.4% (311/2502).

DISCUSSION

This study investigated systematically physical symptoms and signs, as well as laboratory and radiological findings

Table 4: Radiologic findings in patients with coronavirus disease 2019

Radiologic findings	Number of patients examined	Number with the condition	Percent	Proportion	CI	I^2	*P*
Abnormalities on chest radiograph							
Bilateral patchy shadowing	1202	193	16.0	0.09	0.08-0.11		
Local patchy shadowing	1313	78	5.9	0.02	0.01-0.03		
Ground-glass opacity	1120	65	5.8	0.05	0.04-0.06		
Interstitial abnormalities	1101	13	1.1	0.01	0.00-0.02		
Normal	674	76	11.2	0.10	0.04-0.16	35.59	0.21
Abnormalities on chest CT							
GGO[1]	3055	1579	51.6	0.58	0.42-0.73	99.26	<0.001
Bilateral patchy shadowing	1539	904	58.7	0.75	0.47-1.03	99.13	<0.001
Local Patchy shadowing	1324	437	33.0	0.16	0.00-0.31	96.52	<0.001
Bilateral pneumonia	1730	1086	62.7	0.73	0.60-0.87	97.83	<0.001
Unilateral pneumonia	1258	247	19.6	0.18	0.12-0.24	87.20	<0.001
Pulmonary consolidation or exudation	484	190	39.2	0.38	0.23-0.53	93.26	<0.001
Interstitial abnormalities	1335	173	12.9	0.10	0.01-0.19	96.63	<0.001

GOO=Ground glass opacity; CI=Confidence interval; CT=Computed tomography

Table 5: Treatments used for patients with coronavirus disease 2019

Treatment	Number of patients examined	Number of patients with this condition	Percent	Proportion	CI	I^2	*P*
Oxygen therapy	2994	1726	57.6	0.59	0.47-0.71	98.48	<0.001
NIV	2361	293	12.4	0.12	0.09-0.15	93.22	<0.001
IMV	2807	262	9.3	0.14	0.09-0.19	92.10	<0.001
Antibiotic	3411	2212	64.8	0.72	0.61-0.83	99.19	<0.001
Moxifloxacin	37	26	70.2	0.70	0.54-0.83		
Levofloxacin	37	8	21.6	0.22	0.11-0.37		
Ceftriaxone	37	2	5.4	0.05	0.01-0.18		
Linezolid	37	2	5.4	0.05	0.01-0.18		
Carbapenems	37	6	16.2	0.16	0.08-0.31		
Antiviral	2581	2284	88.4	0.87	0.80-0.94	97.03	<0.001
Oseltamivir	1228	444	36.1	0.40	0.09-0.71	98.64	<0.001
Lopinavir/Rritonavir (Kaletra)	342	158	2.83	0.52	0.17-0.88	98.31	<0.001
Darunavir/Cobicistat	24	21	87.5	0.88	0.69-0.96		
Arbidol	261	93	35.6	0.47	0.16-0.78	96.09	<0.001
Other treatments							
Thymosin/Thymopentin	264	164	2.94	0.62	0.40-0.84	95.20	<0.001
Antifungal	1459	57	3.9	0.04	0.02-0.07	75.40	<0.001
Glucocorticoids	3629	1188	32.7	0.41	0.30-0.52	98.63	<0.001
Chines medicine	432	191	44.2	0.43	0.08-0.79	99.20	<0.001
IVIG	2589	526	20.3	0.30	0.23-0.38	96.10	<0.001
α-IFN	689	344	49.9	0.41	0.05-0.88	99.64	<0.001
CRRT	1702	29	1.7	0.02	0.00-0.03	61.88	0.02
ECMO	1863	22	1.1	0.01	0.00-0.02	41.62	0.10

NIV=Noninvasive ventilation; IMV=Invasive mechanical ventilation; CRRT=Continuous renal replacement therapy; ECMO=Extracorporeal membrane oxygenation; IVIG=Intravenous immunoglobulin; α-IFN=Alfa interferon; CI=Computed tomography

and treatment in published studies on patients with COVID-19. Despite the new emergence and lack of confirmed knowledge of the symptoms of the disease and the ways of treatment, many studies have been done on patients with COVID-19 during their physical examination and treatment. In addition to their therapeutic duties, specialists from different countries have provided detailed reports on the patients' condition and their outcomes, as evidenced by the publication of several thousand articles in this field. Despite a lot of articles in this regard, it was tried to observe all of the principles and procedures of systematic review with high quality; so that the studies were evaluated carefully in terms of quality and relevance with the intention of the studies that remained for the final review be valid and invaluable. Hence, 46 articles remained in the final stage. These articles were all reviewed for quality and they were worthy to study.

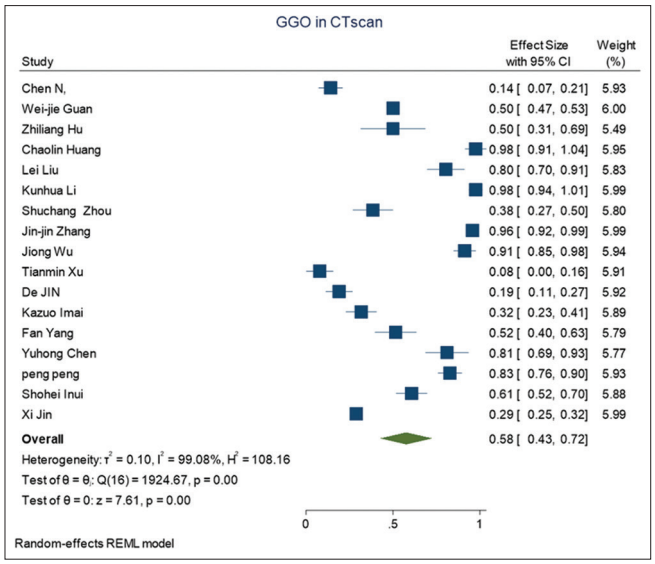

Figure 3: Forest plot of ground-glass opacity in computed tomography scan

Slightly more than half of the patients were male. However, studies were heterogeneous (CI = 0.49–0.54; $P < 0.001$). Given that men have social attendance and COVID-19 is contagious, this can be a possible sensible explanation. Contact with Chinese people was the most reason of transmission, which was expected due to the initial emergence of the disease in China and the most of published papers were from this country.

In this study, most of the studies confirmed the presence of comorbidities in patients with COVID-19. The comorbidities were confirmed not only in COVID-19 but also in previous influenza viral infections such as MERS and H1N1.[58,59]

The most common symptoms reported were dry cough and fever. These symptoms and the extent of involvement contain important messages. The fact that fever has been reported in two-thirds of patients, and only one-tenth of patients had a fever above 39°C, raises doubts about the use of temperature to separate and quarantine of patients.

Many of the other symptoms are not specific to COVID-19, and they are similar to other virus infections in this family and other viruses that make it difficult to differentiate. However, it is recommended that protective measures be taken even in suspicious cases and the symptoms be considered corona to prevent further spread. Symptoms such as feeling ill, malaise or severe fatigue or weakness, and dyspnea are also seen in other flu and pneumonia.[60-62] Sore throat or pharyngalgia and rhinorrhea, Nasal congestion, sneezing and snotty nose, as well as rigor/chill are also nonspecific symptoms and have been reported with other influenza and common cold.[63-65]

Myalgia and headache have also been reported in other pneumonia with other origin.[66] Furthermore, symptoms such as dizziness and confusion/loss of consciousness have been reported before the emergence of COVID-19.[67-69] Poor appetite, anorexia, nausea/vomiting, and diarrhea/loose bowel movement are also common symptoms of other viral infections and pneumonia.[70-72]

Laboratory findings suggest that arterial blood saturation is significantly reduced. This finding has also been observed in other pneumonia due to lung tissue damage.[73] Both lymphopenia and lymphocytosis were found in patients. Meanwhile, half of the patient had lymphopenia, while slightly more than one-tenth had Lymphocytosis. This discrepancy can go back to the time of measurement. As the disease progresses, the risk of lymphopenia increases. Some studies confirmed that lymphopenia is a frequent finding in hospitalized patients with community-acquired pneumonia (CAP), affecting approximately 50% of the patients[74] and it is associated with a deregulated immune response, increased severity, and mortality.[75] Some authors suggested that is lymphocytosis evidence of active inflammation in pneumonia.

Although other studies have shown that monocyte was positively correlated with ESR and negatively with body temperature,[76] in the current studies, this correlation has not been evaluated.

The study revealed the platelet counts of one-fifth of evaluated people were lower than normal; it has been noted in other studies so that a study indicated that an increase in mean platelet measurements during admission can predict the prognoses of patients with pneumonia and related to poor outcomes.[77] However, in the current study, only 5.5% had more platelet.

Creatine kinase was also reported to be high in 10% of those measured. This is consistent with other infections that lead to pneumonia.[78] D-dimer was measured in only one article; however, more than a quarter of patients had a high rate of that. However, a study has shown in CAP patients, a D-dimer >2 μg/mL was risk factor associated with in-hospital mortality.[79]

Radiological findings included chest X-ray (CXR) and CT scan of patients in current studies have shown lung tissue involvement. Chest CT scan can be performed after the detection of abnormalities in CXR. Combination of radiological findings with clinical manifestations can lead to better clinical judgment.[80] In current studies, some have shown bilateral patchy shadowing or GGO in CT scans of the lungs. In a multicentre study, this feature has also been confirmed. It showed a mixed and diverse pattern with both lung parenchyma and the Interstitial involved.[81] Another modality is chest CT-scan. It can be

ordered in suspected cases with typical symptoms at the first step, or it can be performed after the detection of any abnormalities in CXR.

Therapies in the studies indicated that specialists have used various combination therapies in addition to oxygen therapy. They were usually a combination of antiviral, antibiotic, and miscellaneous treatments. Nevertheless, more specific treatments have been given for other pneumonia or viral infections because of more comprehensive knowledge and broader research.[82,83]

CONCLUSIONS

Up to the present, the studies of COVID-19 usually have been observational, and experts have reported them along with their medical prescriptions. Nevertheless, research is ongoing and new signs and symptoms of the disease are being identified. However, the results of the current study could be useful because it showed the most popular symptoms and the validity of them for identifying and isolating patients. Because some symptoms, such as fever, occur in only two-thirds of people, they are not a good measure of isolation and more measures should be done. Although CT scan is a valid test for detecting the typical pattern of COVID-19 pneumonia, in the early stages of the disease is not recommended since in this period CT scan of lungs may be completely normal. Furthermore, in other forms of COVID-19 which affect organs other than the respiratory system, CT scan is not a valuable diagnostic test.

Further studies in European countries, the United States, and Asia are needed to identify new dimensions of the disease; therefore, systematic reviews can be done regularly.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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SUPPLEMENTARY TABLES

Supplementary Table 1: JBI quality assessment tool

ID	Author name	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total score
1	Weiliang Cao	✓	✓	✓	✓	no	✓	✓	✓	✓	8
2	Nanshan Chen	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
3	Wei-jie Guan	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
4	Zhiliang Hu	✓	✓	✓	✓	No	No	✓	✓	✓	7
5	Chaolin Huang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
6	Ying Huang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
7	Lei Liu	✓	✓	No	UN	✓	✓	✓	✓	✓	7
8	Zuojiong Gong	✓	✓	No	✓	✓	✓	✓	✓	✓	8
9	Ying Liang	✓	✓	✓	✓	UN	✓	✓	✓	✓	8
10	Hong-Jian Zhang	✓	✓	✓	No	✓	✓	✓	✓	✓	8
11	Ling Mao	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
12	Guo-Qing Qian	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
13	Jun Liu	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
14	Jianlei Cao	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
15	Sibylle Bernard Stoecklin	UN	UN	UN	UN	UN	UN	UN	UN	UN	0
16	Simon Petrie	UN	UN	UN	UN	UN	UN	UN	UN	UN	0
17	DaweiWang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
18	Hongcui Cao	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
19	Wenjie Yang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
20	Bicheng Zhang	✓	✓	✓	UN	✓	✓	✓	✓	✓	8
21	Matthew Arentz	✓	✓	✓	UN	✓	UN	✓	✓	✓	7
22	Pingzheng Mo	✓	✓	✓	✓	✓	UN	✓	✓	✓	8
23	Yihui Huang	✓	✓	✓	UN	✓	✓	✓	✓	✓	8
24	Kunhua Li	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
25	Shuchang Zhou	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
26	Jin-jin Zhang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
27	Jiong Wu,	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
28	ZhongliangWang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
29	SijiaTian	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
30	Suxin Wan	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
31	Yuan Xue	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
32	Wen Zhao	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
33	Tao Yao	✓	✓	✓	No	✓	✓	✓	✓	✓	8
34	De JIN	✓	✓	✓	No	✓	✓	✓	✓	✓	8
35	Suochen Tian	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
36	Sakiko Tabata	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
37	Jie Liu	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
38	Jiaming Zhang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
39	Chin Ion Lei	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
40	Tao Chen	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
41	Yuhong Chen	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
42	peng peng	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
43	Zhibing Lu	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
44	Wen-Hsin Hsih	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
45	Shohei Inui	✓	✓	✓	✓	✓	✓	✓	✓	✓	9
46	Yida Yang	✓	✓	✓	✓	✓	✓	✓	✓	✓	9

UN=Unknown; ✓=Yes; Q1=Was the sample frame appropriate to address the target population?; Q2=Were study participants sampled in an appropriate way?; Q3=Was the sample size adequate?; Q4=Were the study subjects and the setting described in detail?; Q5=Was the data analysis conducted with sufficient coverage of the identified sample?; Q6=Were valid methods used for the identification of the condition?; Q7=Was the condition measured in a standard, reliable way for all participants?; Q8=Was there appropriate statistical analysis?; Q9=Was the response rate adequate, and if not, was the low response rate managed appropriately?; JBI= Joanna Briggs Institute

Supplementary Table 2: Egger test (publication bias)

Variable	B1	SE	*Z*	*P*
High CRP	1.22	2.971	0.41	0.681
GGO	−2.14	3.929	−0.54	0.586
Fever	−2.60	1.546	−1.68	0.092

SE=Standard error; GGO=Ground glass opacity; CRP=C-reactive protein