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COVID-19 Clinical Characteristics, Complications and comorbidity: An updated Systemic Review and Meta-analysis

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Abstract:	Background COVID-19, a novel pneumonia associated with the 2019 coronavirus infected pneumonia suddenly broke out in the world. The aim of this study is to summaries and analysis the clinical characteristics of COVID-19. Methods Literatures have been systematically searched on Scopus, PubMed, Embase, Web of Science, and The Cochrane Library and also special databases prepared for COVID-19 such as LitCovid Hub, WHO, Elsevier, Medrxiv and CDC from inception up to May 1, 2020. Data searching, extracting and quality appraising were done by two researchers, independently. At last, Random-effects size based on Cochrane test and I 2 were used. The Newcastle-Ottawa Scale was used to assess quality, and publication bias was analyzed by Egger and Begg's test. The review protocol has been registered in PROSPERO with ID: CRD42020173639 and with ethical code IR.GUMS.REC.1398.542. Results Out of 2464 studies, 75(3.04%) were included. A total of 111490 patients with a mean age of 49.43 years [Confidence Interval(CI)95%: 47.44-51.42] were evaluated. Most of patients was male (52.65%). The body mass index (BMI) in the most was in normal rate (23.26). 33.5% of patients were health care workers. 62.71% of patients had direct exposure history. The most common clinical symptoms were fever, cough, myalgia and dyspnea (82.72%, 57.69%; 25.20% and 20.87%, respectively). The most common comorbidities were acute respiratory distress syndrome, chronic medical illness, hypertension, and diabetes (30.4%, 22.25%, 17.47%, and 11.19% respectively). Among the laboratory abnormalities, the most patients had high levels of leucocytes (24.76%), lymphocyte (39.56%), increasing of neutrophil (14.48%), platelet (39.81%), D-dimer (30.89%), AST (22.09%), Creatinine (48.21%), troponin I (4.12%), urea nitrogen (22.94%), Creatine Kinase (48.21%), and C-reactive proteins (56.8%). About 37.35% of patients had a decreasing in the hemoglobin. CT-Scan funding shows that three fourths of patients had bilateral pneumonia involvement (78.25%), and 58.37% had GGO. Crazy-paving, vascular enlargement, air bronchus gram sign, and air trapping were seen in 22.55%, 61.79%, and 11.76%, respectively. The most common regions of the lung involvement were lower lobe 91.70%. Also, 66.34% of patients had peripheral involvement, and had punctate ground glass opacities (64.73%). Conclusion

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	COVID-19 is still a leading epidemic infection with comorbidities, clinical, laboratory and radiological findings, and its specific demographic characteristics. We found the rate of mortality of patients with COVID-19 is also decreasing, gradually. It could be related to the early recognition, early intervention, and early centered-quarantine of people in the world.

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COVID-19 Clinical Characteristics, Complications and comorbidity: An updated Systemic Review and Meta-analysis

Running title: Clinical Characteristics of 2019 coronavirus

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ABSTRACT

Background: COVID-19, a novel pneumonia associated with the 2019 coronavirus infected pneumonia suddenly broke out in the world. The aim of this study is to summaries and analysis the clinical characteristics of COVID-19.

Methods: Literatures have been systematically searched on Scopus, PubMed, Embase, Web of Science, and The Cochrane Library and also special databases prepared for COVID-19 such as LitCovid Hub, WHO, Elsevier, Medrxiv and CDC from inception up to May 1, 2020. Data searching, extracting and quality appraising were done by two researchers, independently. At last, Random-effects size based on Cochrane test and I^2 were used. The Newcastle-Ottawa Scale was used to assess quality, and publication bias was analyzed by Egger and Begg's test. The review protocol has been registered in PROSPERO with ID: CRD42020173639 and with ethical code IR.GUMS.REC.1398.542**.**

Results: Out of 2464 studies, 75(3.04%) were included. A total of 111490 patients with a mean age of 49.43 years [Confidence Interval(CI)95%: 47.44-51.42] were evaluated. Most of patients was male (52.65%). The body mass index (BMI) in the most was in normal rate (23.26). 33.5% of patients were health care workers. 62.71% of patients had direct exposure history. The most common clinical symptoms were fever, cough, myalgia and dyspnea (82.72%, 57.69%; 25.20% and 20.87%, respectively). The most common comorbidities were acute respiratory distress syndrome, chronic medical illness, hypertension, and diabetes (30.4%, 22.25%, 17.47%, and 11.19% respectively). Among the laboratory abnormalities, the most patients had high levels of leucocytes (24.76%), lymphocyte (39.56%), increasing of neutrophil (14.48%), platelet (39.81%), D-dimer (30.89%), AST (22.09%), Creatinine (48.21%), troponin I (4.12%), urea nitrogen (22.94%), Creatine Kinase (48.21%), and C-reactive proteins (56.8%). About 37.35% of patients

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INTRODUCTION

In late December 2019, a pneumonia case of unknown cause was reported in Wuhan, Hubei Province, the People's Republic of China, which changed the lives of people all over the world. [1], which the virus was recognized as SARS-CoV-2 [2]. The researchers confirmed that the prevalence of coronavirus disease 2019 (COVID-19) is a continuous prevalence of the SARS-CoV-2 [2]. On 26 February 2020, the WHO reported an increase in the new cases of Italy, Iran, and South Korea[3], and until - 2 March 2020- more than 89,000 cases were confirmed, of which more than 90% of them were from China[4]. Recently, more than 2,900 people have died in China and more than 130 have died in other countries, also more than 45,000 people have recovered[4].

Based on the researches, the COVID-19 spreads via respiratory droplets produced from the airways during coughing or sneezing [5,6], and the time between exposure and symptom ranges from two to fourteen days [7]. Fever, cough, diarrhea, and shortness of breath may be symptoms of the COVID-19 [7]. It is confirmed that serious complications may be pneumonia and acute respiratory distress syndrome (ARDS). Until now, no vaccine or specific antiviral treatment was discovered, and to manage symptoms of the COVID-19 physicians advised supportive therapy for fourteen days [7]. There is not data about the typical degree of immunity, re-infection of COVID-19, and immunity of COVID-19 [8]. The time range of progress of symptoms of COVID-19 and death has been shown between 6 and 41 days [9]. Most of the people who died were over the age of 60 and most patients suffered from cardiovascular diseases and diabetes [10,11]. Unfortunately, as of 28 February 2020, more than a dozen deaths have been recorded in each of Iran, South Korea, and Italy [3]. Transmission of the COVID-19 human-to-human via respiratory droplets [69], and is able transmission if people touch a surface [12]. The COVID-19 virus could stay viable surface for up to nine days at room temperature [6]. It is confirmed that the disinfection of surfaces by 62–71% ethanol

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could be useful for one minute [6]. Temporally, there is no specific antiviral medication [13]. To control of severity of the disease, intravenous fluids, and breathing support especially oxygen therapy may be useful [14]. Researchers are investigating the Favipiravir, Ribavirin, Remdesivir, and Galidesiviras as potential drugs against the COVID-19 virus [15-17].

Until May 1, 2020, about 2464 manuscripts have been reported regarding the epidemiology and clinical features of pneumonia caused by the COVID-19 virus via researchers in the world. In this study we reviewed main PubMed, Embase, Web of Science, Scopus, and The Cochrane Library, and also special databases prepared for COVID-19 such as LitCovid Hub, WHO, Elsevier, Medrxiv and CDC data bases from inception up to May 1, 2020. We analyzed the prevalence of various clinical symptoms have been proposed as the typical features for the COVID-19 virus, furthermore, some features are controversial in different clinic environments. Therefore, update evidence-based medical clinical characters are required urgently and Vital. In this study, we try to did a systemic review and a meta-analysis of the clinical features and significance demographics characters of patient with the COVID-19 virus pneumonia.

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2. Method

2.1. Study Protocol

This review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses. Data searching, extracting and quality appraising were done by two researchers (MH.YK & A.J), independently. Any encounters were solved by consensus between the team and a third researcher. The protocol for the review was registered with PROSPERO ((https://www.crd.york.ac.uk/PROSPERO/) Identifier(ID): CRD42020173639[18]. Also, the ethics committee approval of this study is IR.GUMS.REC.1398.542 (S1-2 File).

2.2. Search Strategy

An advanced relevant search was conducted in international databases, such as Scopus, PubMed, Embase, Web of Science, and The Cochrane Library and also special databases prepared for COVID-19 such as as LitCovid Hub, WHO, Elsevier, Medrxiv and CDC from inception up to May 1, 2020 were searched for articles published. Articles on COVID-19, severe acute respiratory syndrome coronavirus 2, novel coronavirus, SARS-CoV-2, nCoV disease, SARS2, COVID19, Wuhan coronavirus, 2019-nCoV, coronavirus disease-19, coronavirus disease 2019, 2019 novel 201 coronavirus and Wuhan pneumonia were also manually retrieved. To maximize search sensitivity, no filters or limits on language were applied. To identify further studies, the reference lists of included articles and review articles were hand-searched.

To search a combination of words, Boolean operators (AND & OR) were used. Also, searching was done through medical subject heading (MeSH) terms. The authors independently analyzed the manuscript contained in the title and abstract.

2.3. Selection Criteria

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The duplicates records were removed using EndNote X7 (Thomson Reuters, New York, NY, USA). Two reviewers (MH.YK and A.J) independently screened the records by title and abstract. A third reviewer were evaluated the full texts of potentially eligible records. Included studies were patients who diagnosed with RT-PCR; the raw data for clinical, radiological, CT-scan, laboratory findings, and the outcomes. Studies were excluded which had insufficient information about patients' characteristics and outcomes. Case reports, reviews, repeat articles, letters, editorials, and expert opinions; studies without usable data; and animal studies were also excluded. Only studies are written in English and Chinese were selected.

2.4. Quality assessment

The Newcastle-Ottawa Scale was used to assess quality. Assessment scores of 0-3, 4-6, and 7-9 indicated poor, fair, and good studies, respectively. Disagreements were resolved by consensus. After excluding irrelevant studies in the screening and eligibility stages, the Newcastle-Ottawa Scale (NOS) [19] were used to assessing the quality of the final studies. The Checklist (S3 File) was used which consists of 8 sections, and divides the studies with a scale score of 0 to 8 from poor to high quality, respectively. The studies are divided into three levels of scoring: 1- Studies with a score of 5: poor quality; 2- studies with a score of 5–6: medium quality; 3- studies with a score of 7 to 8: high quality. Finally, medium to high quality articles were entered into the next stage (Fig 1).

Fig 1. A flow diagram following the PRISMA (Depicted by MH-YK).

2.5. Data extraction

A data extraction form was designed by two reviewers (MH.YK and A.J) which were blind for the name of the author, institute and journal. In necessary cases, further information and raw data were requested by contacting the author (the first author or responsible or the authors' department). The

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reviewers extracted the data from all eligible studies and disagreements were resolved by discussion with a third researcher. The following data were extracted: first author name; year of publication; type of study, the country where the study was conducted; distribution of age and sex in the population, number of patients investigated, exposure history, comorbid conditions, symptoms at admission, clinical, radiological, CT-scan and laboratory findings, therapies, and discharge, recovery, and death outcomes (S4 File).

2.6. Statistical analysis

All data was considered as a binomial distribution probability, and the variance was calculated by a binomial distribution. The Cochran test (Q) and I^2 index were used to evaluate its heterogeneity [20,21]. The I^2 index less than 25% is low heterogeneity, between 75% -25% is the average heterogeneity and more than 75% are considered as heterogeneous[22,23]. To examine publication bias, the Begg's test and Egger's test were carried out using a funnel plot. Data analysis was examined by the comprehensive meta-analysis (Ver. 2 Englewood, NJ 07631, USA), and the level of significance was considered as $p<0.05$.

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3. RESULTS

3.1. Study characteristics and methodological quality

Out of 2464 studies, 75(3.04%)[24-92] were included with a total of 111490 patients (Fig 1). All possible data were meta-analyzed (S4 File)(Table 1)(S1-144 Fig).

Fig 1. A flow diagram following the PRISMA (Depicted by MH-YK).

3.2. General characteristics

As shown in (S1-3 Fig), 62.71% of patients had direct exposure history with infected people in Wuhan or Hubei province [CI95%: 52.22-72.12]. The mean age of the patients was 49.43 years [CI95%: 47.44-51.42] (S4 Fig). Most of patients (52.65%) was male [Cl95%: 51-54.3], and 47.28% was female [CI95%: 45.56-49] (S5 Fig). The body mass index (BMI) in most of patients was in normal rate (23.26) [CI95%: 22.28-24.23] (S6 Fig). About 33.5% of patients who suffer from 2019 novel infected coronavirus pneumonia were health care workers (HCWs) [CI95%: 12-64.9] (S7 Fig).

3.3. The prevalence of 2019 coronavirus based on the comorbidities

The most common comorbidities were acute respiratory distress syndrome (ARDS) 30.4% [CI 95%: 14.4-53.1]; chronic medical illness 22.25% [CI 95%: 10.62-40.79], hypertension 17.47% [CI 95%: 13.55-22.24], and diabetes 11.19% [CI 95%: 9.19-13.55] respectively. The low common comorbidities were chronic kidney diseases 3.05% [CI 95%: 1.59-6.78]; malignancies 3.2% [CI 95%: 2.33-4.38]; nervous system 3.5% [CI 95%: 1.26-9.31], and chronic obstructive pulmonary disease (COPD) 3.56% [CI 95%: 2.38-5.32] (S8-23 Fig).

3.4. The prevalence of 2019 coronavirus based on the clinical symptoms

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The more than three fourths of patients (82.72%) had fever [CI 95%: 77.87-86.68]; 57.69% had cough [CI 95%: 50.72-64.37]; 25.20% had myalgia/fatigue [CI 95%: 19.62-31.73], and 20.87% had dyspnea [CI 95%:13.94-30.04]. The other clinical symptoms of patients were respectively, chill 15.02% [CI 95%: 7.57-27.61]; sore throat 10.18% [CI 95%: 6.83-14.91]; rhinorrhea 5.9% [CI 95%: 3.47-9.17]; shortness of breath 13.61% [CI 95%: 5.98-28.06]; chest tightness 14.55% [CI 95%: 9.73-21.19]; chest pain 3.19% [CI 95%: 1.02-9.54]; sputum production 19.93% [CI 95%: 13.38-28.63]; headache 9.08% [CI 95%: 7.08-11.58]; hemoptysis 3.55% [CI 95%: 2.00-6.22]; nausea and vomiting 6.00% [CI 95%: 4.54-7.90], and diarrhea 7.49% [CI 95%: 5.87-9.51] (S24-42 Fig).

3.5. The prevalence of 2019 coronavirus based on the timing

The incubation period of patients was estimated 5 days [CI95%: 5.008-6.073]. Duration of illness to dyspnea, first hospital to ICU, onset of symptom to hospital, and first symptom to death were reported 13 days [CI95%: 11.025-15.581], 5 days [CI95%: 3.438-6.158], 6 days [CI95%: 4.664-7.201], and 17 days [CI95%: 13.772-19.523] (S43-9 Fig).

3.6. General Examination of COVID-19 plus Patients'

The systolic to diastolic blood pressure was 87.887 (mm Hg) [CI95%: 82.570-93.205] \ 126.56 (mm Hg) [CI95%: 123.696-129.423], which was normal. The oxygen pressure of patients was between 49 (kpa) and 128 (kpa), (Mean 87.887 kpa) [CI95%: 82.570-93.205]. The oxygen saturation of patients was between 92 (kpa) and 97 (kpa), (Mean 95.141 kpa) [CI95%: 92.991-97.291]. The heart rate of patients was between 87 and 90 beats per minute (Mean 89.272 beats per minute) [CI95%: 87.870-90.674]. The respiratory rate of patients was between 10 and 18.7 breaths per minute (Mean 14.335 breaths per minute) [CI95%: 9.938-18.731] (S50-6 Fig).

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3.7. The prevalence of 2019 coronavirus based on the laboratory findings

The mean of white blood cell (WBC) of patients was reported 5.063 ($\times 10^9$ per L) [CI 95%: 4.74-5.37]. The most patients with COVID-19 (54.36%) were in the range of 4 and 10 (count, $\times 10^9$ per L) of WBC [CI 95%: 41.11-67.00]. The mean of leucocytes was reported 5.93 ($\times 10^9$ per L) [CI 95%: 5.11-6.74]. The most patients with COVID-19 (24.76%) were in the range of more than 10 ($\times 10^9$ per L) of leucocytes [CI 95%: 17.39-33.96]. The mean of lymphocyte was found 1.01 ($\times 10^9$ per L) [CI 95%: 0.9509-1.0872]. In this study, the most patients with COVID-19 (39.56%) were in the range of more than 1.0 ($\times 10^9$ per L) of lymphocyte [CI 95%: 30.32-49.61]. The mean of neutrophil was shown 3.94 ($\times 10^9$ per L) [CI 95%: 3.599-4.283]. As shown in …, 13.14% of patients with COVID-19 had an increasing in the neutrophil [CI 95%: 5.71-1.50], and 9.37% had a decreasing in the neutrophil [CI 95%:7.61-21.73]. The mean of hemoglobin was reported 134.96 (g/L) [CI 95%: 131.981-137.947]. As shown in …, 37.35% of patients with COVID-19 had a decreasing in the hemoglobin [CI 95%: 24.62-52.11]. The mean of platelet was reported 202.75 ($\times 10^9$ per L) [CI 95%: 191.530-213.982]. The most patients with COVID-19 (39.81%) had range higher than 100 ($\times 10^9$ per L) of platelet [CI 95%: 16.68-68.59]. The mean of prothrombin time was reported 12.18 s [CI 95%: 11.62-12.74]. Although, the mean of activated partial thromboplastin time was found 32.21 s [CI 95%: 29.40-35.02]. About 14.48% of patients with COVID-19 had an increasing in the neutrophil [CI 95%: 7.42-26.36], and 7.38% had a decreasing in the neutrophil [CI 95%: 10.14-32.15]. The mean of the D-dimer was found 0.548 μg/L [CI 95%: 0.478-0.618]. About 30.89% of patients with COVID-19 had an increasing in the D-dimer [CI 95%: 21.09-42.77]. The mean of aspartate aminotransferase (AST) was reported 28.95 IU/L [CI 95%: 25.243-32.659]. In this regards, 22.09 % of patients with COVID-19 had an increasing in the AST [CI 95%: 17.43-27.58]. Another frequent abnormal laboratory finding in patients with

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COVID-19 had increasing levels in the creatinine (48.21%) [CI 95%: 19.61-78.03]. Other hands, 4.12 % of patients with COVID-19 had high levels of troponin I [CI 95%: 2.78-5.46]. According to confirmed COVID-19 subjects, the mean of urea nitrogen was reported 4.702 mmol/L [CI 95%: 4.39-5.01]. Among the patients, 22.94% had high levels of the urea nitrogen [CI 95%: 6.26-57.03]. Procalcitonin levels lower than 0.25 ng/mL was seen in 64.97% of the patients. Also, the patients with high levels of C-reactive proteins was estimated 56.8% [CI 95%: 33.75-77.23]. The mean of creatine kinase was 105.34 U/L [CI 95%: 95.258-115.421]. In fact, 38.53% of patients had lower than 185 U/L of creatine kinase [CI 95%: 12.81-72.79]. Based on confirmed COVID-19 subjects, the means of myoglobin, glucose, potassium, alanine aminotransferase, sodium, albumin, and lactate dehydrogenase were 43.42 ng/mL [CI 95%: 26.458-60.385], 6.415 mmol/L [CI 95%: 6.061-6.769], 3.905 mmol/L [CI 95%: 3.803-4.008], 26.358 U/L [CI 95%: 24.062-28.654], 138.56 mmol/L [CI 95%: 138.123-139.001], 37.488 g/L [CI 95%: 34.812-40.165], and 284.265 U/L [CI 95%: 262.114-306.415], respectively (S58-101 Fig).

3.8. The prevalence of 2019 coronavirus based on the radiologic findings

To diagnoses of COVID-19, imaging of chest X-Ray (CXR) and chest CT-scan were common. The study shows that the most common pattern of parenchymal involvement was bilateral pneumonia involvement and ground-glass opacification/opacity (GGO). In fact, three fourths of patients (78.25%) had bilateral pneumonia involvement [CI 95%: 60.59-8938], and 58.37% had GGO [CI 95%: 45.11-70.52]. This study shows that 46.83% of patients had both of consolidation and GGOs [CI 95%: 34.26-59.82]. Absence of both GGOs and consolidation were seen in 12.78% of patients [CI 95%: 4.72-30.24]. Also, consolidation was seen in 29.43% of patients [CI 95%: 20.2-40.71]. Based on CT-Scan findings, crazy-paving, vascular enlargement, air bronchus gram sign, and air trapping were seen in 22.55% [CI 95%: 14.26-33.76], 43.59% [CI 95%: 6.34-89.82],

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61.79% [CI 95%: 50.02-72.32], and 11.76% [CI 95%: 5.38-23-81], respectively. This study also shows that patients who suffer from nodular opacities, reversed halo sign, bronchus deformation due to fibrosis and strip like lesions, pleural retraction sign, and pleural effusion were 13.99% [CI 95%: 5.53-31.13], 2.54% [CI 95%: 0.96-6.58], 47.62% [CI 95%: 27.85-68.16], 56.45% [CI 95%: 43.97-68.17], and 7.15% [CI 95%: 4.65-10.84], respectively. The most common sites of the lung involvement were lower lobe 91.70% [CI 95%: 82.70-96.23]. Also, 66.34% of patients had peripheral involvement [CI 95%: 47.89-80.86], and 64.73% had punctate ground glass opacities [CI 95%: 15.97-94.66]. Five affected lobes were involved in the most of patients 34.59% [CI 95%: 27.32-42.66] (S102-127 Fig).

3.9. The prevalence of 2019 coronavirus based on the therapies

To treatment of COVID-19, the most common patients (86.45%) took antiviral drugs [CI 95%: 76.34-92.65] and 75.09% took antibiotic [CI 95%: 61.65-84.97]. As shown in …, oxygen therapy and interferon therapy were seen in 72% [CI 95%: 47.85-87.82], and 68.78% [CI 95%: 10.63-97.61] of patients. Corticosteroid therapy and Intravenous immunoglobulin therapy were seen in about 27% of patients, [CI 95%: 20.54-35], and [CI 95%: 14.6-46.43], respectively (S128-140 Fig).

3.10. Outcomes

Remained in hospital was required in 62.38% of patients with COVID-19 [CI 95%: 47.43-76.06]. The pooled mortality rate of the patients was about 4.55% [CI 95%: 2.49-8.15]. The discharge and recovery rates of patients with COVID-19 were estimated 25.88% [CI 95%: 15.91-39.18], and 6.49% [CI 95%: 0.11-80.93]. The subgroup analysis shows that there was no significant difference between male and female in the patients with COVID-19 (P = 0.9008), direct and indirect exposure of patients (P =0.1094), hemoglobin (P =0.092), urea nitrogen (P = 0.1121), and CRP (P = 0.5716).

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On the other hands, there was a significant difference between increasing and decreasing of the body temperature (P = 0.004), PO_2 (P = 0.034), WBC (P = 0.0001), leucocytes (P=0.0001), and lymphocyte (P=0.0006). Meanwhile there was a significant difference between increasing and decreasing of the neutrophil (P=0.0001), platelet (P=0.0001), prothrombin time (P=0.0001), activated partial thromboplastin time (P=0.0001), d-dimer (P=0.002), AST (P=0.0001), creatinine (P=0.0001), bilirubin (P=0.0001), Creatine kinase (P=0.0001), myoglobin (P=0.0001), glucose (P=0.877), albumin (P=0.0165), and lactate dehydrogenase (P=0.745) (S141-4 Fig).

3.11. Publication bias

The publication bias in this study was evaluated by Begg's and Egger's tests. The publication bias by Begg's test was calculated 0.68, and the Egger's test was calculated 0.87. The probability of the publication bias in this study was not significant (Fig 2).

Fig 2. Publication bias of studies included.

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4. Discussion

This study has evaluated the COVID-19 clinical characteristics, complications, and comorbidity to the comparison of the latest information about the COVID-19 pandemic. The mean age of patients with COVID-19 was estimated 49.43 years. Most of patients was male. The BMI of patients was in normal rate. 33.5% of patients were health care workers. More half of the patients had direct exposure history. The most common clinical symptoms were fever, cough, myalgia and dyspnea. The most common comorbidities were acute respiratory distress syndrome, chronic medical illness, hypertension, and diabetes. In the terms of the laboratory abnormalities, the most patients had high levels of leucocytes, lymphocyte, neutrophil, platelet, D-dimer, AST, Creatinine, troponin I, urea nitrogen, Creatine Kinase, and C-reactive proteins. Majority of patients had a decreasing in the hemoglobin. CT-Scan imaging showed that most of patients involved with bilateral pneumonia, and GGO. Crazy-paving, vascular enlargement, air bronchus gram sign, and air trapping were also seen. The most common regions of the lung involvement were lower lobe. Also, majority of patients had peripheral involvement, and had punctate ground glass opacities.

This study showed that fever (82.72%), cough (57.69%), (25.20%) myalgia or fatigue, and dyspnea (20.87%) were the most common symptoms. Nasiri et al fund that fever (83.0%), cough (65.2%) and dyspnea (27.4%) were the most common symptoms [93]. Chen et al estimated fever and cough were the most common clinical finding in 87.1% and 36.5% of patients, respectively [88]. Chen et al showed the cardiovascular and cerebrovascular diseases at 21.7% of the patients [88]. Our study showed the most common comorbidities were ARDS, (30.4%), chronic medical illness (22.25%), hypertension (17.47%), and diabetes (11.19%). In this respect, the results of our study were inconsistent with those of Nasiri et al [93]. They found that the most common comorbidities were hypertension (18.5 %), cardiovascular diseases (14.9 %) and diabetes (10.8 %) [93]. Yang et al, also

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showed that hypertension (17 ± 7%), diabetes (8 ± 6%), and cardiovascular diseases (5 ± 4%) were the most common comorbid findings [10]. The high prevalence of ARDS among patients with COVID-19 may be a case of the role of these viruses in inducing of the ARDS [94]. The high prevalence of hypertension and cardiovascular comorbidities may be regarding the important role of angiotensin-converting enzyme inhibitors (ACEI) in COVID-19. Based on researches angiotensin-converting enzyme 2 (ACE2) receptor was identified as the receptor used by COVID-19 to infect human cells. Previous studies showed that the function of ACEI results in the upregulation of ACE2 [95]. Therefore, the increase in ACE2 levels may result in a greater risk of infection with the COVID-19 [31].

Based on the laboratory abnormalities, the most patients had high levels of the C-reactive proteins (56.8%), Creatine Kinase (48.21%), Creatinine (48.21%), platelet (39.81%), lymphocyte (39.56%), leucocytes (24.76%), D-dimer (30.89%), neutrophil (14.48%), AST (22.09%), troponin I (4.12%), and urea nitrogen (22.94%). Wang observed that the C-reactive protein levels in the early stage of COVID-19 may show lung lesions and disease severity. C-reactive protein levels also could show disease changes, especially for patients in critical condition [96]. Wang et al also demonstrated that most patients with severe acute respiratory syndrome (SARS) had high levels of the CRP [97]. However, Carlos Lopez-Delgado previously showed that thrombocytopenia and lymphopenia strongly increased a higher risk of mortality in SARS and H1N1 influenza [98].

The incubation period of patients was estimated at 5 days. Duration of illness to dyspnea was reported 13 days, the first hospital to ICU was reported 5 days, the onset of symptom to the hospital was estimated 6 days, and the first symptom to death was reported 17 days. In this respect, the results of our study were consistent with those of Nasiri et al [93]. Nasiri showed that the mean

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duration between hospitalization and death was 17.5 days [93]. Feng et al showed that duration between hospitalization and death was 17.4 days in patients with SARS [99].

This study has limitations. Most of the clinical findings were from observational studies. This study not only Chinese studies, but also needs other countries for comprehensive results globally. The pooled mortality rate of the patients was about 4.55%. Guan reported the mortality rate of the patients with COVID-19 was 1.4% [100]. In this respect, the results of our study were inconsistent with those Li et al (7%) [93], Qian et al (8.9%) [101], and Rodriguez et al (13.9%) [102]. In the current study, early recognition, early intervention, and early centered-quarantine may be contributing factors in the low mortalities [103].

5. Limitations

the inclusion of studies with different inclusion and exclusion criteria, and there is no consensus definition of COVID-19 expressed is one of the main limitations of this meta-analysis to be mentioned. Otherwise most of the information is for China and the results cannot be generalized to the whole world because of nationality, ethnicity, race, lifestyle and etc. Also, data were accessed by using Guilan University of Medical Sciences' -Iran Ministry of Health & Medical Education- VPN which some databases are not fully accessible. Most of the articles were preprinted and not reviewed. This will be challenging the accuracy and precision of the results of the original articles, and the use of previous articles. However, the research team reviewed each article carefully.

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6. Conclusion

COVID-19 has turned the new leaf in the world people's lives with various cultures, languages, and traditions. The mortality rate in our study was 4.55% and the mean duration between hospitalization and death was 17 days. It seems to be the rate of mortality of patients with COVID-19 is decreasing, gradually. It could be related to the early recognition, early intervention, and early centered-quarantine in the world.

7. Supporting information

S1 File. PRISMA Checklist

S2 File. The review protocol which has been registered in PROSPERO International Prospective Register of Systematic Reviews.

S3 File. Newcastle-Ottawa scale checklist.

S4 File. Data characteristics (Full details) (MS Excel).

S1 Fig. The percentage of direct exposure history in patients with COVID-19

S2 Fig. The percentage of indirect exposure history in patients with COVID-19

S3 Fig. The percentage of total exposure history in patients with COVID-19

S4 Fig. The prevalence of age in patients with COVID-19

S5 Fig. The percentage of gender age in patients with COVID-19

S6 Fig. The prevalence of BMI in patients with COVID-19

S7 Fig. The percentage of occupation (HCWs) in patients with COVID-19

S8 Fig. The percentage of acute respiratory distress syndrome (ARDS) in patients with COVID-19

S9 Fig. The percentage of acute cardiac injury in patients with COVID-19

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S10 Fig. The percentage of acute kidney injury in patients with COVID-19

S11 Fig. The percentage of acute respiratory injury in patients with COVID-19

S12 Fig. The percentage of sptic shock in patients with COVID-19

S13 Fig. The percentage of diabetes in patients with COVID-19

S14 Fig. The percentage of hypertension in patients with COVID-19

S15 Fig. The percentage of cardiovascular diseases (CVD) in patients with COVID-19

S16 Fig. The percentage of COPD in patients with COVID-19

S17 Fig. The percentage of nervous system in patients with COVID-19

S18 Fig. The percentage of malignancies in patients with COVID-19

S19 Fig. The percentage of chronic medical illness in patients with COVID-19

S20 Fig. The percentage of endocrine system diseases in patients with COVID-19

S21 Fig. The percentage of digestive system diseases in patients with COVID-19

S22 Fig. The percentage of chronic kidney diseases in patients with COVID-19

S23 Fig. The percentage of chronic liver diseases in patients with COVID-19

S24 Fig. The percentage of Fever in patients with COVID-19

S25 Fig. The percentage of Chill in patients with COVID-19

S26 Fig. The percentage of Temperature (°C) in patients with COVID-19

S27 Fig. The percentage of Cough in patients with COVID-19

S28 Fig. The percentage of Sore throat in patients with COVID-19

S29 Fig. The percentage of Rhinorrhea in patients with COVID-19

S30 Fig. The percentage of Shortness of breath in patients with COVID-19

S31 Fig. The percentage of Chest tightness in patients with COVID-19

S32 Fig. The percentage of Chest pain in patients with COVID-19

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S33 Fig. The percentage of Dyspnea in patients with COVID-19

S34 Fig. The percentage of Myalgia in patients with COVID-19

S35 Fig. The percentage of Sputum production in patients with COVID-19

S36 Fig. The percentage of Headache in patients with COVID-19

S37 Fig. The percentage of Hemoptysis in patients with COVID-19

S38 Fig. The percentage of Nausea and vomiting in patients with COVID-19

S39 Fig. The percentage of Diarrhea in patients with COVID-19

S40 Fig. The percentage of Anosemia in patients with COVID-19

S41 Fig. The percentage of Anorexia in patients with COVID-19

S42 Fig. The percentage of Rash in patients with COVID-19

S43 Fig. Mean of days Incubation period in patients with COVID-19

S44 Fig. Mean of days Illness onset to dyspnea in patients with COVID-19

S45 Fig. Mean of days First hospital to ICU in patients with COVID-19

S46 Fig. Mean of days Onset of symptom to hospital in patients with COVID-19

S47 Fig. Mean of days Onset of symptom to ICU in patients with COVID-19

S48 Fig. Mean of days ARDS and needed ICU in patients with COVID-19

S49 Fig. Mean of days symptom to death in patients with COVID-19

S50 Fig. Mean Diastolic pressure in patients with COVID-19

S51 Fig. Mean Systolic pressure in patients with COVID-19

S52 Fig. Mean PO2 (kpa, range80-100) in patients with COVID-19

S53 Fig. Decreased PO2 (kpa, range80-100) in patients with COVID-19

S54 Fig. Mean O2 sat (range ≥95%) in patients with COVID-19

S55 Fig. Mean Heart rate (Beats per minute) in patients with COVID-19

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S56 Fig. Mean Respiratory rate in patients with COVID-19

S57 Fig. Mean WBC (count, × 10^9 per L Range) in patients with COVID-19

S58 Fig. Sub grouped analysis of WBC (count, × 10^9 per L Range) in patients with COVID-19

S59 Fig. Mean Leucocytes (× 10^9 per L; normal range 3·5–9·5) range in patients with COVID-19

S60 Fig. Sub grouped analysis of Leucocytes (× 10^9 per L; normal range 3·5–9·5) range in patients with COVID-19

S61 Fig. Mean Lymphocyte (× 10^9 per L) (range 1.1–3.2) range in patients with COVID-19

S62 Fig. Sub grouped analysis of Lymphocyte (× 10^9 per L) (range 1.1–3.2) range in patients with COVID-19

S63 Fig. Mean Neutrophil (count, × 10^9 per L range) in patients with COVID-19

S64 Fig. Sub grouped analysis of Neutrophil (count, × 10^9 per L range) in patients with COVID-19

S65 Fig. Mean Hemoglobin (g/L; normal range 130·0–175·0) range in patients with COVID-19

S66 Fig. Sub grouped analysis of Hemoglobin (g/L; normal range 130·0–175·0) range in patients with COVID-19

S67 Fig. Mean Platelet (count, × 10^9 per L range) in patients with COVID-19

S68 Fig. Sub grouped analysis of Platelet (count, × 10^9 per L range) in patients with COVID-19

S69 Fig. Mean Prothrombin time (s Range) in patients with COVID-19

S70 Fig. Sub grouped analysis of Prothrombin time (s Range) in patients with COVID-19

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S71 Fig. Mean Activated partial thromboplastin time (s Range) in patients with COVID-19

S72 Fig. Sub grouped analysis of Activated partial thromboplastin time (s Range) in patients with COVID-19

S73 Fig. Mean D-dimer (μg/L; normal range 0·0–1·5) Range in patients with COVID-19

S74 Fig. Sub grouped analysis of D-dimer (μg/L; normal range 0·0–1·5) Range in patients with COVID-19

S75 Fig. Mean AST (IU/L, range 8–40) Range in patients with COVID-19

S76 Fig. Sub grouped analysis of AST (IU/L, range 8–40) Range in patients with COVID-19

S77 Fig. Mean Creatinine (μmol/L range) in patients with COVID-19

S78 Fig. Sub grouped analysis of Creatinine (μmol/L range) in patients with COVID-19

S79 Fig. Mean Troponin in patients with COVID-19

S80 Fig. Total Bilirubin (U/L; normal range 50·0–310·0) in patients with COVID-19

S81 Fig. Sub grouped analysis of Increased bilirubin in patients with COVID-19

S82 Fig. Mean Urea nitrogen (mmol/L, range 2.6–7.5) in patients with COVID-19

S83 Fig. Sub grouped analysis of Decreased Urea nitrogen in patients with COVID-19

S84 Fig. Mean Procalcitonin (ng/mL) in patients with COVID-19

S85 Fig. Sub grouped analysis of Procalcitonin in patients with COVID-19

S86 Fig. Mean CRP (mg/dL) in patients with COVID-19

S87 Fig. Sub grouped analysis of CRP in patients with COVID-19

S88 Fig. Mean Erythrocyte in patients with COVID-19

S89 Fig. Mean Creatine kinase (U/L; normal range 50·0–310·0) in patients with COVID-19

S90 Fig. Sub grouped analysis of Creatine kinase in patients with COVID-19

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S91 Fig. Mean Myoglobin (ng/mL; normal range 0·0–146·9) in patients with COVID-19

S92 Fig. Sub grouped analysis of Myoglobin in patients with COVID-19

S93 Fig. Mean Glucose (mmol/L; normal range 3·9–6·1) in patients with COVID-19

S94 Fig. Sub grouped analysis of Glucose in patients with COVID-19

S95 Fig. Mean Potassium (mmol/L) in patients with COVID-19

S96 Fig. Mean Alanine aminotransferase/ALT (U/L) in patients with COVID-19

S97 Fig. Mean Sodium (mmol/L) in patients with COVID-19

S98 Fig. Mean Albumin (g/L, range 35–57) in patients with COVID-19

S99 Fig. Sub grouped analysis of Albumin in patients with COVID-19

S100 Fig. Mean Lactate dehydrogenase/LDH in patients with COVID-19

S101 Fig. Sub grouped analysis of Lactate dehydrogenase/LDH in patients with COVID-19

S102 Fig. The percentage of CXR Unilateral Pneumonia in patients with COVID-19

S103 Fig. The percentage of Chest X-Ray Bilateral Pneumonia in patients with COVID-19

S104 Fig. The percentage of Absence of both GGOs and consolidation in patients with COVID-19

S105 Fig. The percentage of Presence of GGOs with consolidation in patients with COVID-19

S106 Fig. The percentage of GGOs in patients with COVID-19

S107 Fig. The percentage of consolidation in patients with COVID-19

S108 Fig. The percentage of Crazy-paving in patients with COVID-19

S109 Fig. The percentage of Vascular enlargement in patients with COVID-19

S110 Fig. The percentage of Interlobular septal thickening in a crazy-paving pattern in patients with COVID-19

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S111 Fig. The percentage of Air Broncho gram sign in patients with COVID-19

S112 Fig. The percentage of Air trapping in patients with COVID-19

S113 Fig. The percentage of Nodular opacities in patients with COVID-19

S114 Fig. The percentage of Reversed halo sign in patients with COVID-19

S115 Fig. The percentage of Discrete pulmonary Nodules with halo sign in patients with COVID-19

S116 Fig. The percentage of Discrete pulmonary Nodules without halo sign in patients with COVID-19

S117 Fig. The percentage of Bronchus deformation due to fibrosis and strip like lesions in patients with COVID-19

S118 Fig. The percentage of Lymphadenopathy in patients with COVID-19

S119 Fig. The percentage of Pleural retraction sign in patients with COVID-19

S120 Fig. The percentage of Pleural effusion in patients with COVID-19

S121 Fig. The percentage of fibrous stripes in patients with COVID-19

S122 Fig. The percentage of patchy Consolidation at CT in patients with COVID-19

S123 Fig. The percentage of Peripheral, Central, Both of lung in patients with COVID-19

S124 Fig. The percentage of Upper, Middle, Lower lobe in patients with COVID-19

S125 Fig. The percentage of Patchy or punctate ground glass opacities in patients with COVID-19

S126 Fig. The percentage of Patients number affected lobe in patients with COVID-19

S127 Fig. The percentage of Interstitial abnormality in patients with COVID-19

S128 Fig. The percentage of Corticosteroid in patients with COVID-19

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S129 Fig. The percentage of Intravenous immunoglobulin therapy in patients with COVID-19

S130 Fig. The percentage of Interferon in patients with COVID-19

S131 Fig. The percentage of Non-Invasive ventilation in patients with COVID-19

S132 Fig. The percentage of Invasive Mechanical Ventilation in patients with COVID-19

S133 Fig. The percentage of Immunoglobulin therapy in patients with COVID-19

S134 Fig. The percentage of Nasal cannula in patients with COVID-19

S135 Fig. The percentage of Oxygen therapy in patients with COVID-19

S136 Fig. The percentage of CRRT in patients with COVID-19

S137 Fig. The percentage of ECMO in patients with COVID-19

S138 Fig. The percentage of Antifungal in patients with COVID-19

S139 Fig. The percentage of Antibiotic in patients with COVID-19

S140 Fig. The percentage of Antiviral in patients with COVID-19

S141 Fig. The percentage of Discharge in patients with COVID-19

S142 Fig. The percentage of Recovery in patients with COVID-19

S143 Fig. The percentage of Remained in hospital in patients with COVID-19

S144 Fig. The percentage of Death in patients with COVID-19

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9. Conflict of interests

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The authors have declared that no competing interests exist.

10. Data Availability Statement

All relevant data are within the paper and its Supporting Information files.

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12. Author Contributions

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785 Table 1- A Systemic Review and Meta-analysis COVID-19 Clinical Characteristics, Complications and
786 comorbidity

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		NO Study	(CI-95%)	P-value	I^2 (%)	P-value Subgroup	I^2(%) Subgroup	Supplementary Data/ Figures
Exposure History	Direct	37	62.71% (52.22-72.12)	0.0181	96.39	0.1094	97.18	S1 Fig
	Indirect	12	41.01% (24.47-59.87)	0.3507	97.42			S2 Fig
	Total	49	57.6% (48.3-66.4)	---	--			S3 Fig
Age		64	49.43 (47.44-51.42)	0.0001	98.10	--	--	S4 Fig
Gender	Male	68	52.65% (51-54.3)	0.0016	58.56	0.9008	69.57	S5 Fig
	Female	67	47.28% (45.56-49)	0.0019	62.31			
	Total	136	---	--	---			
BMI		4	23.26 (22.28-24.23)	0.0001	85.61	--	--	S6 Fig
Occupation	HCWs	5	33.5% (12-64.9)	0.302	96.72	--	--	S7 Fig
Comorbid conditions	Acute respiratory distress syndrome (ARDS)	8	30.4% (14.4-53.1)	0.088	91.48	--	--	S8 Fig
	Acute Cardiac Injury	6	10.16% (6.34-15.9)	0.0001	65.47	--	--	S9 Fig
	Acute Kidney Injury	7	4.4% (1.46-12.54)	0.0001	92.1	--	--	S10 Fig
	Acute Respiratory Injury	7	5.49% (3.26-9.09)	0.0001	63.65	--	--	S11 Fig
	Septic Shock	7	4.61% (1.97-10.41)	0.0001	80.86	--	--	S12 Fig
	Diabetes	35	11.19% (9.19-13.55)	0.0001	66.95	--	--	S13 Fig
	Hypertension	34	17.47% (13.55-22.24)	0.0001	88.64	--	--	S14 Fig
	Cardiovascular diseases (CVD)	23	11.16% (6.87-17.65)	0.0001	94.79	--	--	S15 Fig
	COPD	20	3.56% (2.38-5.32)	0.0001	61.75	--	--	S16 Fig
	Nervous system	4	3.5% (1.26-9.31)	0.0001	71.3	--	--	S17 Fig
	Malignancies	23	3.2% (2.33-4.38)	0.0001	26.56	--	--	S18 Fig
	Chronic medical illness	5	22.25% (10.62-40.79)	0.0053	90.33	--	--	S19 Fig

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		Endocrine system diseases	3	8.3% (5.4-12.4)	0.0001	6.44 (Fixed effect size)	--	--	S20 Fig
		Digestive system diseases	7	4.62% (2.47-8.46)	0.0001	75.85	--	--	S21 Fig
		Chronic kidney diseases	12	3.05% (1.59-6.78)	0.0001	67.87	--	--	S22 Fig
		Chronic liver diseases	14	5.94% (3.51-9.9)	0.0001	80.77	--	--	S23 Fig
Sign and symptoms	Fever		60	82.72% (77.87-86.68)	0.0001	95.24	--	--	S24 Fig
	Chill		11	15.02% (7.57-27.61)	0.001	95.13	--	--	S25 Fig
	Temperature (°C)	<37.3	10	19.16% (10.55-32.26)	0.0001	96.3	0.004	91.87	S26 Fig
		>39	15	14.1% (8.12-23.35)	0.0001	94.02			
		37.3-38	14	32.38% (25.7-39.87)	0.0001	87.12			
		38.1-39	14	33.39% (22.96-40.51)	0.0001	86.39			
			53	--	--	--			
	Cough		62	57.69% (50.72-64.37)	0.0307	95.62	--	--	S27 Fig
	Sore throat		23	10.18% (6.83-14.91)	0.0001	90.59	--	--	S28 Fig
	Rhinorrhea		7	5.9% (3.47-9.17)	0.0001	0 (Fixed effect size)	--	--	S29 Fig
	Shortness of breath		11	13.61% (5.98-28.06)	0.0001	94.17	--	--	S30 Fig
	Chest tightness		14	14.55% (9.73-21.19)	0.0001	89.31	--	--	S31 Fig
	Chest pain		11	3.19% (1.02-9.54)	0.0001	93.64	--	--	S32 Fig
	Dyspnea		22	20.87% (13.94-30.04)	0.0001	92.86	--	--	S33 Fig
	Myalgia		52	25.20% (19.62-31.73)	0.0001	94.19	--	--	S34 Fig
	Sputum production		20	19.93% (13.38-28.63)	0.0001	94.59	--	--	S35 Fig
	Headache		42	9.08% (7.08-11.58)	0.0001	83.10	--	--	S36 Fig
	Hemoptysis		9	3.55% (2.00-6.22)	0.0001	61.99	--	--	S37 Fig
	Nausea and vomiting		21	6.00% (4.54-7.90)	0.0001	35.81	--	--	S38 Fig
	Diarrhea		43	7.49% (5.87-9.51)	0.0001	72.42	--	--	S39 Fig
	Anosemia		2	6.65%	0.0001	78.44	--	--	S40 Fig

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				20.1-19.84					
	Anorexia		2	32.59% 20.02-48.27	0.0303	80.45	--	--	S41 Fig
	Rash		1	8.33% 2.09-27.88	0.0012	68.89	--	--	S42 Fig
Timing(days)		Incubation period	8	5.540 (5.008-6.073)	0.0001	98.07	--	--	S43 Fig
		Illness onset to dyspnea	11	13.303 (11.025-15.581)	0.0001	99.32	--	--	S44 Fig
		First hospital to ICU	12	4.798 (3.438-6.158)	0.0001	99.47	--	--	S45 Fig
		Onset of symptom to hospital	11	5.935 (4.664-7.201)	0.0001	98.90	--	--	S46 Fig
		Onset of symptom to ICU	4	6.092 (1.594-10.590)	0.007	99.78	--	--	S47 Fig
		ARDS and needed ICU	2	9.5 (6.56-12.44)	0.0001	100	--	--	S48 Fig
		Days symptom to death	3	16.647 (13.772-19.523)	0.0001	97.73	--	--	S49 Fig
Pressure (mmHg)		Diastolic pressure	5	87.887 (82.570-93.205)	0.0001	96.62	--	--	S50 Fig
		Systolic pressure	6	126.56 (123.696-129.423)	0.0001	63.17	--	--	S51 Fig
PO_2 (kpa, range80-100)		Mean	7	88.690 (49.211-128.169)	0.0001	99.93	--	--	S52 Fig
		Decreased	3	26.72% (12.52-48.15)	--	--	0.034	83.779	S53 Fig
		Total		26.72% (12.52-48.15)	--	--	0.034		
O_2 sat ((range ≥95%))			3	95.141% (92.991-97.291)	0.0001	99.08	--	--	S54 Fig
Heart rate (beats per minute)			9	89.272 (87.870-90.674)	0.0001	60.06	--	--	S55 Fig
Respiratory rate			13	14.335 (9.938-18.731)	0.0001	99.84	--	--	S56 Fig
Laboratory	WBC count, × 10^9 per L Range	Mean	22	5.063 (4.74-5.37)	0.0001	85.18	--	--	S57 Fig
		<4	12	17.97% (10.17-29.78)	0.0001	94.18	0.0001	93.21	S58 Fig
		>10	10	14.45% (10.28-19.94)	0.005	61.43			
		4-10	5	54.36% (41.11-67.00)	0.0001	82.43			

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		Total		**23.53% (18.81-29.00)**	**--**	**--**			
	Leucocytes (× 10⁹ per L; normal range 3·5–9·5) range	**Mean**	**10**	**5.93 (5.11-6.74)**	**0.0001**	**95.82**	**--**	**--**	**S59 Fig**
		<10	**10**	**16.25% (6.05-36.89)**	**0.003**	**97.55**	**0.0001**	**95.88**	**S60 Fig**
		>10	**11**	**24.76% (17.39-33.96)**	**0.0001**	**88.73**			
		Total		**23.40% (16.80-31.61)**	**--**	**--**			
	Lymphocyte (× 10 9 per L) (range 1.1–3.2) range	**Mean**	**34**	**1.0190 (0.9509-1.0872)**	**0.0001**	**97.98**	**--**	**--**	**S61 Fig**
		<1.0	**23**	**32.89% (22.65-45.07)**	**0.0001**	**93.43**	**0.0006**	**92.34**	**S62 Fig**
		>1.0	**15**	**39.56% (30.32-49.61)**	**0.001**	**90.55**			
		Total		**43.04% (40.93-45.18)**	**--**	**--**			
	Neutrophil count, × 10⁹ per L range	**Mean**	**34**	**3.941 (3.599-4.283)**	**0.0001**	**94.18**	**--**	**--**	**S63 Fig**
		Decreased	**9**	**9.37% (5.71-1.50)**	**0.0001**	**76.05**	**0.0001**	**85.64**	**S64 Fig**
		Increased	**12**	**13.14% (7.61-21.73)**	**0.0001**	**88.42**			
		Total	**21**	**10.88% (7.55-15.42)**	**--**	**--**			
	Hemoglobin (g/L; normal range 130·0–175·0) range	**Mean**	**21**	**134.964 (131.981-137.947)**	**0.0001**	**90.36**	**--**	**--**	**S65 Fig**
		Decreased	**5**	**37.35% (24.62-52.11)**	**0.092**	**78.07**	**0.092**	**90.36**	**S66 Fig**
		Total	**21**	**37.35% (24.62-52.11)**	**--**	**--**			
	Platelet count, × 10⁹ per L range	**Mean**	**30**	**202.756 (191.530-213.982)**	**0.0001**	**98.62**	**--**	**--**	**S67 Fig**
		<100	**12**	**11.48 (06.49-19.49)**	**0.0001**	**91.89**	**0.0001**	**93.82**	**S68 Fig**
		≥100	**12**	**39.81 (16.68-68.59)**	**0.4974**	**95.09**			
		Total	**24**	**15.54 (9.56-24.24)**	**--**	**--**			
	Prothrombin time (s Range)	**Mean**	**16**	**12.18 (11.62-12.74)**	**0.0001**	**98.59**	**--**	**--**	**S69 Fig**
		Decreased	**3**	**8.28 (1.28-38.59)**	**0.0151**	**93.75**	**0.0001**	**53.35**	**S70 Fig**
		Increased	**5**	**8.65 (5.56-13.22)**	**0.0001**	**57.88**			
		Total	**8**	**8.63 (5.62-13.04)**	**--**	**--**			
	Activated partial thromboplastin time	**Mean**	**11**	**32.21 (29.40-35.02)**	**0.0001**	**98.93**	**--**	**--**	**S71 Fig**
		Decreased	**3**	**7.38% (10.14-32.15)**	**0.000**	**92.55**	**0.0001**	**91.75**	**S72 Fig**

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	(s Range)	Increased	6	14.48% (7.42-26.36)	0.0001	91.25			
		Total	9	13.14% (7.05-23.17)	--	--			
	D-dimer (µg/L; normal range 0·0–1·5) Range	Mean	16	0.548 (0.478-0.618)	0.0001	99.92			S73 Fig
		Increased	8	30.89% (21.09-42.77)	0.002	92.47	0.002	92.47	S74 Fig
		Total		30.89% (21.09-42.77)	--	--			
	AST (IU/L, range 8–40) Range	Mean	10	28.951 (25.243-32.659)	0.0001	97.06	--	--	S75 Fig
		Increased	5	22.09% (17.43-27.58)	0.0001	56.10	0.0001	92.87	S76 Fig
		Total		22.09% (17.43-27.58)	--	--			
	Creatinine (µmol/L range)	Mean	23	68.47 (65.22-71.07)	0.0001	95.29	--	--	S77 Fig
		>133	7	48.21% (19.61-78.03)	0.916	95.18	0.0001	95.29	S78 Fig
		≤133	10	5.04% (2.55-9.73)	0.0001	81.71			
		Total	17	9.03% (5.04-15.66)	--	--			
	Troponin		4	4.12% (2.78-5.46)	0.0001	98.80	--	--	S79 Fig
	Bilirubin (U/L; normal range 50·0–310·0) range	Total bilirubin	21	10.23% (9.32-11.14)	0.0001	98.45	--	--	S80 Fig
		Increased bilirubin	9	6.61% (3.97-10.79)	--	--	0.0001	74.42	S81 Fig
	Urea nitrogen (mmol/L, range2.6–7.5)	Mean	17	4.702% (4.39-5.01)	0.0001	93.72	--	--	S82 Fig
		Decreased	4	22.94% (6.26-57.03)	--	--	0.1121	93.66	S83 Fig
	Procalcitonin (ng/mL)	Total	18	0.22% (0.18-0.53)	0.0001	99.93	--	--	S84 Fig
		<0.1	5	43.65% (20.04-70.54)	0.6575	88.59	0.0001	93.93	S85 Fig
		0.1 to <0.25	3	21.32% (14.1-30.92)	0.0001	1.35 (Fixed effect size)			
		0.25 to 0.5	5	17.78% (3.4-57.05)	0.093	87.89			
		>0.5	9	11.47% (3.45-31.98)	0.0002	96.08			
	CRP (mg/dL)	Mean	28	37.52% (34.16-40.87)	0.0001	99.9	--	--	S86 Fig
		CRP >60	14	56.8% (33.75-77.23)	--	--	0.5716	97.72	S87 Fig
	Erythrocyte	Mean	5	41.11	0.0007	87.09	--	--	S88 Fig

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				(17.21-65.02)					
	Creatine kinase (U/L; normal range 50·0–310·0) range	Mean	18	105.34 (95.25-115.42)	0.0001	99.70	--	--	S89 Fig
		≤185	6	38.53% (12.81-72.79)	0.520	96.32	0.0001	93.94	S90 Fig
		≥185	8	14.68% (9.55-21.91)	0.0001	81.91			
		Total	13	16.41% (10.99-23.78)	--	--			
	Myoglobin (ng/mL; normal range 0·0–146·9) range	Mean	4	43.421 (26.45-60.38)	0.0001	99.96	--	--	S91 Fig
		Increased	4	14.20% (11.79-17.00)	--	--	0.0001	0.000	S92 Fig
	Glucose (mmol/L; normal range 3·9–6·1)	Mean	7	6.415 (6.061-6.769)	0.0001	82.01	--	--	S93 Fig
		Increased	4	49.12% (38.10-60.22)	--	--	0.877	83.073	S94 Fig
	Potassium (mmol/L)		10	3.905 (3.803-4.008)	0.0001	32.07	--	--	S95 Fig
	Alanine aminotransferase/ALT (U/L)		18	26.358 (24.06-28.65)	0.0001	91.89	--	--	S96 Fig
	Sodium (mmol/L)		10	138.56 (138.12-139.00)	0.0001	70.66	--	--	S97 Fig
	Albumin (g/L, range 35–57)	Mean	12	37.488 (34.81-40.16)	0.0001	97.81	--	--	S98 Fig
		Decreased	6	14.77% (3.97-42.06)	--	--	0.0165	96.77	S99 Fig
	Lactate dehydrogenase/LDH	Mean	22	284.265 (262.11-306.41)	0.0001	95.57	--	--	S100 Fig
		≤245	5	37.73% (20.98-58.03)	0.234	87.19	0.745	89.57	S101 Fig
		245≥	10	56.43% (44.56-67.61)	0.287	91.14			
		Total	15	51.71% (41.47-61.81)	--	--			
Radiological Findings		CXR Unilateral Pneumonia	6	16.29% (9.26-27.04)	0.0001	83.78	--	--	S102 Fig
		Chest X-Ray Bilateral Pneumonia	21	78.25% (60.59-8938)	0.0032	97.72	--	--	S103 Fig
		Absence of both GGOs and consolidation	3	12.78% (4.72-30.24)	0.0005	71.58	--	--	S104 Fig
		Presence of GGOs with consolidation	10	46.83% (34.26-59.82)	0.0001	88.26	--	--	S105 Fig

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	GGOs	30	58.37% (45.11-70.52)	0.0001	97.03	--	--	S106 Fig
	consolidation	18	29.43% (20.2-40.71)	0.0006	93.83	--	--	S107 Fig
	Crazy-paving	7	22.55% (14.26-33.76)	0.0001	84.75	--	--	S108 Fig
	Vascular enlargement	4	43.59% (6.34-89.82)	0.8356	98.67	--	--	S109 Fig
	Interlobular septal thickening in a crazy-paving pattern	3	62.94% (56.24-69.18)	0.0002	0 (Fixed effect size)	--	--	S110 Fig
	Air Bronchogram sign	6	61.79% (50.02-72.32)	0.0497	79.89	--	--	S111 Fig
	Air trapping	1	11.76% (5.38-23-81)	0.0001	0 (Fixed effect size)	--	--	S112 Fig
	Nodular opacities	4	13.99% (5.53-31.13)	0.0005	80.12	--	--	S113 Fig
	Reversed halo sign	2	2.54% (0.96-6.58)	0.0001	0.0001	--	--	S114 Fig
	Discrete pulmonary Nodules with halo sign	1	17.65% (9.45-30.57)	0.0001	0 (Fixed effect size)	--	--	S115 Fig
	Discrete pulmonary Nodules without halo sign	1	3.92% (0.98-14.37)	0.0001	0 (Fixed effect size)	--	--	S116 Fig
	Bronchus deformation due to fibrosis and strip like lesions	1	47.62% (27.85-68.16)	0.8273	0 (Fixed effect size)	--	--	S117 Fig
	Lymphadenopathy	2	4.74% (2.48-8.85)	0.0001	0 (Fixed effect size)	--	--	S118 Fig
	Pleural retraction sign	1	56.45% (43.97-68.17)	0.3110	0 (Fixed effect size)	--	--	S119 Fig
	Pleural effusion	10	7.15% (4.65-10.84)	0.0001	53.92	--	--	S120 Fig

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	Number of fibrous stripes	2	34.65% (8.23-75.80)	0.4838	94.65	--	--	S121 Fig
	Number of patchy Consolidation at CT	2	24.2% (15.73-35.31)	0.0001	42.86	--	--	S122 Fig
	Peripheral	8	66.34% (47.89-80.86)	0.2821	92.40	0.0001	94.90	S123 Fig
	Central	3	1.47% (0.61-3.48)	0.0001	0 (Fixed effect size)			
	Both	5	36.2% (22.13-53.11)	0.0813	93.36			
	Upper	2	83.29% (73.31-90.05)	0.0001	0 (Fixed effect size)	0.0001	75.34	S124 Fig
	Middle	2	72.64% (40.62-91.16)	0.1582	80.69			
	Lower	2	91.70% (82.70-96.23)	0.0001	0 (Fixed effect size)			
	Number of Patchy or punctate ground glass opacities	2	64.73% (15.97-94.66)	0.5997	97.51	--	--	S125 Fig
	Patients number of 1 affected lobe	6	15.77% (9.11-25.91)	0.0001	76.24	0.0001	84.19	S126 Fig
	Patients number of 2 affected lobes	6	14.08% (11.01-17.83)	0.0001	0 (Fixed effect size)			
	Patients number of 3 affected lobes	6	9.82% (7.28-13.12)	0.0001	0 (Fixed effect size)			
	Patients number of 4 affected lobes	6	18.36% (14.89-22.43)	0.0001	0 (Fixed effect size)			
	Patients number of 5	6	34.59% (27.32-42.66)	0.0003	56.47			

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	affected lobes							
	Interstitial abnormality	1	13.01% (11.15-15.13)	0.0001	0 (Fixed effect size)			S127 Fig
Treatment	Corticosteroid	18	27.17% (20.54-35)	0.0001	91.77	--	--	S128 Fig
	Intravenous immunoglobulin therapy	8	27.79% (14.6-46.43)	0.021	96.66	--	--	S129 Fig
	Interferon	4	68.78% (10.63-97.61)	0.5958	96.99	--	--	S130 Fig
	Non-Invasive ventilation	16	21.48% (12.02-35.4)	0.0003	96.16	--	--	S131 Fig
	Invasive mechanical Ventilation	8	5.71% (2.91-10.93)	0.0001	76.19	--	--	S132 Fig
	Immunoglobulin therapy	9	25.93% (16.1-38.97)	0.0006	93.18	--	--	S133 Fig
	Nasal cannula	8	59.88% (51.54-67.69)	0.020	72.66	--	--	S134 Fig
	Oxygen therapy	7	72% (47.85-87.82)	0.0725	97.89	--	--	S135 Fig
	CRRT	6	7.92% (4.63-13.25)	0.0001	57.49	--	--	S136 Fig
	ECMO	4	2.06% (0.42-9.39)	0.0001	90.39	--	--	S137 Fig
	Antifungal	5	6.7% (1.98-2.033)	0.0001	94.56	--	--	S138 Fig
	Antibiotic	16	75.09% (61.65-84.97)	0.0006	94.81	--	--	S139 Fig
	Antiviral	18	86.45% (76.34-92.65)	0.0001	96.58	--	--	S140 Fig
Outcomes	Discharge	19	25.88% (15.91-39.18)	0.0008	97.08	--	--	S141 Fig
	Recovery	3	6.49% (0.11-80.93)	0.2036	97.68	--	--	S142 Fig
	Remained in hospital	24	62.87% (47.43-76.06)	0.1012	97.24	--	--	S143 Fig
	Death	25	4.55% (2.49-8.15)	0.0001	98.09	--	--	S144 Fig

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Table 1- A Systemic Review and Meta-analysis COVID-19 Clinical Characteristics, Complications and comorbidity

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		NO Study	(CI-95%)	P-value	I^2 (%)	P-value Subgroup	I^2(%) Subgroup	Supplementary Data/ Figures
Exposure History	Direct	37	62.71% (52.22-72.12)	0.0181	96.39	0.1094	97.18	S1 Fig
	Indirect	12	41.01% (24.47-59.87)	0.3507	97.42			S2 Fig
	Total	49	57.6% (48.3-66.4)	---	--			S3 Fig
Age		64	49.43 (47.44-51.42)	0.0001	98.10	--	--	S4 Fig
Gender	Male	68	52.65% (51-54.3)	0.0016	58.56	0.9008	69.57	S5 Fig
	Female	67	47.28% (45.56-49)	0.0019	62.31			
	Total	136	---	--	---			
BMI		4	23.26 (22.28-24.23)	0.0001	85.61	--	--	S6 Fig
Occupation	HCWs	5	33.5% (12-64.9)	0.302	96.72	--	--	S7 Fig
Comorbid conditions	Acute respiratory distress syndrome (ARDS)	8	30.4% (14.4-53.1)	0.088	91.48	--	--	S8 Fig
	Acute Cardiac Injury	6	10.16% (6.34-15.9)	0.0001	65.47	--	--	S9 Fig
	Acute Kidney Injury	7	4.4% (1.46-12.54)	0.0001	92.1	--	--	S10 Fig
	Acute Respiratory Injury	7	5.49% (3.26-9.09)	0.0001	63.65	--	--	S11 Fig
	Septic Shock	7	4.61% (1.97-10.41)	0.0001	80.86	--	--	S12 Fig
	Diabetes	35	11.19% (9.19-13.55)	0.0001	66.95	--	--	S13 Fig
	Hypertension	34	17.47% (13.55-22.24)	0.0001	88.64	--	--	S14 Fig
	Cardiovascular diseases (CVD)	23	11.16% (6.87-17.65)	0.0001	94.79	--	--	S15 Fig
	COPD	20	3.56% (2.38-5.32)	0.0001	61.75	--	--	S16 Fig
	Nervous system	4	3.5% (1.26-9.31)	0.0001	71.3	--	--	S17 Fig
	Malignancies	23	3.2% (2.33-4.38)	0.0001	26.56	--	--	S18 Fig
	Chronic medical illness	5	22.25% (10.62-40.79)	0.0053	90.33	--	--	S19 Fig

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		Endocrine system diseases	3	8.3% (5.4-12.4)	0.0001	6.44 (Fixed effect size)	--	--	S20 Fig
		Digestive system diseases	7	4.62% (2.47-8.46)	0.0001	75.85	--	--	S21 Fig
		Chronic kidney diseases	12	3.05% (1.59-6.78)	0.0001	67.87	--	--	S22 Fig
		Chronic liver diseases	14	5.94% (3.51-9.9)	0.0001	80.77	--	--	S23 Fig
Sign and symptoms	Fever		60	82.72% (77.87-86.68)	0.0001	95.24	--	--	S24 Fig
	Chill		11	15.02% (7.57-27.61)	0.001	95.13	--	--	S25 Fig
	Temperature (°C)	<37.3	10	19.16% (10.55-32.26)	0.0001	96.3	0.004	91.87	S26 Fig
		>39	15	14.1% (8.12-23.35)	0.0001	94.02			
		37.3-38	14	32.38% (25.7-39.87)	0.0001	87.12			
		38.1-39	14	33.39% (22.96-40.51)	0.0001	86.39			
			53	--	--	--			
	Cough		62	57.69% (50.72-64.37)	0.0307	95.62	--	--	S27 Fig
	Sore throat		23	10.18% (6.83-14.91)	0.0001	90.59	--	--	S28 Fig
	Rhinorrhea		7	5.9% (3.47-9.17)	0.0001	0 (Fixed effect size)	--	--	S29 Fig
	Shortness of breath		11	13.61% (5.98-28.06)	0.0001	94.17	--	--	S30 Fig
	Chest tightness		14	14.55% (9.73-21.19)	0.0001	89.31	--	--	S31 Fig
	Chest pain		11	3.19% (1.02-9.54)	0.0001	93.64	--	--	S32 Fig
	Dyspnea		22	20.87% (13.94-30.04)	0.0001	92.86	--	--	S33 Fig
	Myalgia		52	25.20% (19.62-31.73)	0.0001	94.19	--	--	S34 Fig
	Sputum production		20	19.93% (13.38-28.63)	0.0001	94.59	--	--	S35 Fig
	Headache		42	9.08% (7.08-11.58)	0.0001	83.10	--	--	S36 Fig
	Hemoptysis		9	3.55% (2.00-6.22)	0.0001	61.99	--	--	S37 Fig
	Nausea and vomiting		21	6.00% (4.54-7.90)	0.0001	35.81	--	--	S38 Fig
	Diarrhea		43	7.49% (5.87-9.51)	0.0001	72.42	--	--	S39 Fig

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	Anosemia		2	6.65% 20.1-19.84	0.0001	78.44	--	--	S40 Fig
	Anorexia		2	32.59% 20.02-48.27	0.0303	80.45	--	--	S41 Fig
	Rash		1	8.33% 2.09-27.88	0.0012	68.89	--	--	S42 Fig
Timing(days)		Incubation period	8	5.540 (5.008-6.073)	0.0001	98.07	--	--	S43 Fig
		Illness onset to dyspnea	11	13.303 (11.025-15.581)	0.0001	99.32	--	--	S44 Fig
		First hospital to ICU	12	4.798 (3.438-6.158)	0.0001	99.47	--	--	S45 Fig
		Onset of symptom to hospital	11	5.935 (4.664-7.201)	0.0001	98.90	--	--	S46 Fig
		Onset of symptom to ICU	4	6.092 (1.594-10.590)	0.007	99.78	--	--	S47 Fig
		ARDS and needed ICU	2	9.5 (6.56-12.44)	0.0001	100	--	--	S48 Fig
		Days symptom to death	3	16.647 (13.772-19.523)	0.0001	97.73	--	--	S49 Fig
Pressure (mmHg)		Diastolic pressure	5	87.887 (82.570-93.205)	0.0001	96.62	--	--	S50 Fig
		Systolic pressure	6	126.56 (123.696-129.423)	0.0001	63.17	--	--	S51 Fig
PO_2 (kpa, range80-100)		Mean	7	88.690 (49.211-128.169)	0.0001	99.93	--	--	S52 Fig
		Decreased	3	26.72% (12.52-48.15)	--	--	0.034	83.779	S53 Fig
		Total		26.72% (12.52-48.15)	--	--	0.034		
O_2 sat ((range ≥95%))			3	95.141% (92.991-97.291)	0.0001	99.08	--	--	S54 Fig
Heart rate (beats per minute)			9	89.272 (87.870-90.674)	0.0001	60.06	--	--	S55 Fig
Respiratory rate			13	14.335 (9.938-18.731)	0.0001	99.84	--	--	S56 Fig
Laboratory	WBC count, × 10^9 per L Range	Mean	22	5.063 (4.74-5.37)	0.0001	85.18	--	--	S57 Fig
		<4	12	17.97% (10.17-29.78)	0.0001	94.18	0.0001	93.21	S58 Fig
		>10	10	14.45% (10.28-19.94)	0.005	61.43			
		4-10	5	54.36%	0.0001	82.43			

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				(41.11-67.00)					
		Total		23.53% (18.81-29.00)	--	--			
	Leucocytes (× 10^9 per L; normal range 3·5–9·5) range	Mean	10	5.93 (5.11-6.74)	0.0001	95.82	--	--	S59 Fig
		<10	10	16.25% (6.05-36.89)	0.003	97.55	0.0001	95.88	S60 Fig
		>10	11	24.76% (17.39-33.96)	0.0001	88.73			
		Total		23.40% (16.80-31.61)	--	--			
	Lymphocyte (× 10 9 per L) (range 1.1–3.2) range	Mean	34	1.0190 (0.9509-1.0872)	0.0001	97.98	--	--	S61 Fig
		<1.0	23	32.89% (22.65-45.07)	0.0001	93.43	0.0006	92.34	S62 Fig
		>1.0	15	39.56% (30.32-49.61)	0.001	90.55			
		Total		43.04% (40.93-45.18)	--	--			
	Neutrophil count, × 10^9 per L range	Mean	34	3.941 (3.599-4.283)	0.0001	94.18	--	--	S63 Fig
		Decreased	9	9.37% (5.71-1.50)	0.0001	76.05	0.0001	85.64	S64 Fig
		Increased	12	13.14% (7.61-21.73)	0.0001	88.42			
		Total	21	10.88% (7.55-15.42)	--	--			
	Hemoglobin (g/L; normal range 130·0–175·0) range	Mean	21	134.964 (131.981-137.947)	0.0001	90.36	--	--	S65 Fig
		Decreased	5	37.35% (24.62-52.11)	0.092	78.07	0.092	90.36	S66 Fig
		Total	21	37.35% (24.62-52.11)	--	--			
	Platelet count, × 10^9 per L range	Mean	30	202.756 (191.530-213.982)	0.0001	98.62	--	--	S67 Fig
		<100	12	11.48 (06.49-19.49)	0.0001	91.89	0.0001	93.82	S68 Fig
		≥100	12	39.81 (16.68-68.59)	0.4974	95.09			
		Total	24	15.54 (9.56-24.24)	--	--			
	Prothrombin time (s Range)	Mean	16	12.18 (11.62-12.74)	0.0001	98.59	--	--	S69 Fig
		Decreased	3	8.28 (1.28-38.59)	0.0151	93.75	0.0001	53.35	S70 Fig
		Increased	5	8.65 (5.56-13.22)	0.0001	57.88			
		Total	8	8.63 (5.62-13.04)	--	--			
	Activated partial	Mean	11	32.21 (29.40-35.02)	0.0001	98.93	--	--	S71 Fig

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	thromboplastin time (s Range)	Decreased	3	7.38% (10.14-32.15)	0.000	92.55	0.0001	91.75	S72 Fig
		Increased	6	14.48% (7.42-26.36)	0.0001	91.25			
		Total	9	13.14% (7.05-23.17)	--	--			
	D-dimer (µg/L; normal range 0·0–1·5) Range	Mean	16	0.548 (0.478-0.618)	0.0001	99.92			S73 Fig
		Increased	8	30.89% (21.09-42.77)	0.002	92.47	0.002	92.47	S74 Fig
		Total		30.89% (21.09-42.77)	--	--			
	AST (IU/L, range 8–40) Range	Mean	10	28.951 (25.243-32.659)	0.0001	97.06	--	--	S75 Fig
		Increased	5	22.09% (17.43-27.58)	0.0001	56.10	0.0001	92.87	S76 Fig
		Total		22.09% (17.43-27.58)	--	--			
	Creatinine (µmol/L range)	Mean	23	68.47 (65.22-71.07)	0.0001	95.29	--	--	S77 Fig
		>133	7	48.21% (19.61-78.03)	0.916	95.18	0.0001	95.29	S78 Fig
		≤133	10	5.04% (2.55-9.73)	0.0001	81.71			
		Total	17	9.03% (5.04-15.66)	--	--			
	Troponin		4	4.12% (2.78-5.46)	0.0001	98.80	--	--	S79 Fig
	Bilirubin (U/L; normal range 50·0–310·0) range	Total bilirubin	21	10.23% (9.32-11.14)	0.0001	98.45	--	--	S80 Fig
		Increased bilirubin	9	6.61% (3.97-10.79)	--	--	0.0001	74.42	S81 Fig
	Urea nitrogen (mmol/L, range2.6–7.5)	Mean	17	4.702% (4.39-5.01)	0.0001	93.72	--	--	S82 Fig
		Decreased	4	22.94% (6.26-57.03)	--	--	0.1121	93.66	S83 Fig
	Procalcitonin (ng/mL)	Total	18	0.22% (0.18-0.53)	0.0001	99.93	--	--	S84 Fig
		<0.1	5	43.65% (20.04-70.54)	0.6575	88.59	0.0001	93.93	S85 Fig
		0.1 to <0.25	3	21.32% (14.1-30.92)	0.0001	1.35 (Fixed effect size)			
		0.25 to 0.5	5	17.78% (3.4-57.05)	0.093	87.89			
		>0.5	9	11.47% (3.45-31.98)	0.0002	96.08			
	CRP (mg/dL)	Mean	28	37.52% (34.16-40.87)	0.0001	99.9	--	--	S86 Fig

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		CRP >60	14	56.8% (33.75-77.23)	--	--	0.5716	97.72	S87 Fig
	Erythrocyte	Mean	5	41.11 (17.21-65.02)	0.0007	87.09	--	--	S88 Fig
	Creatine kinase (U/L; normal range 50·0–310·0) range	Mean	18	105.34 (95.25-115.42)	0.0001	99.70	--	--	S89 Fig
		≤185	6	38.53% (12.81-72.79)	0.520	96.32	0.0001	93.94	S90 Fig
		≥185	8	14.68% (9.55-21.91)	0.0001	81.91			
		Total	13	16.41% (10.99-23.78)	--	--			
	Myoglobin (ng/mL; normal range 0·0–146·9) range	Mean	4	43.421 (26.45-60.38)	0.0001	99.96	--	--	S91 Fig
		Increased	4	14.20% (11.79-17.00)	--	--	0.0001	0.000	S92 Fig
	Glucose (mmol/L; normal range 3·9–6·1)	Mean	7	6.415 (6.061-6.769)	0.0001	82.01	--	--	S93 Fig
		Increased	4	49.12% (38.10-60.22)	--	--	0.877	83.073	S94 Fig
	Potassium (mmol/L)		10	3.905 (3.803-4.008)	0.0001	32.07	--	--	S95 Fig
	Alanine aminotransferase/ALT (U/L)		18	26.358 (24.06-28.65)	0.0001	91.89	--	--	S96 Fig
	Sodium (mmol/L)		10	138.56 (138.12-139.00)	0.0001	70.66	--	--	S97 Fig
	Albumin (g/L, range 35–57)	Mean	12	37.488 (34.81-40.16)	0.0001	97.81	--	--	S98 Fig
		Decreased	6	14.77% (3.97-42.06)	--	--	0.0165	96.77	S99 Fig
	Lactate dehydrogenase/LDH	Mean	22	284.265 (262.11-306.41)	0.0001	95.57	--	--	S100 Fig
		≤245	5	37.73% (20.98-58.03)	0.234	87.19	0.745	89.57	S101 Fig
		245≥	10	56.43% (44.56-67.61)	0.287	91.14			
		Total	15	51.71% (41.47-61.81)	--	--			
Radiological		CXR Unilateral Pneumonia	6	16.29% (9.26-27.04)	0.0001	83.78	--	--	S102 Fig
		Chest X-Ray Bilateral Pneumonia	21	78.25% (60.59-8938)	0.0032	97.72	--	--	S103 Fig
		Absence of both GGOs and consolidation	3	12.78% (4.72-30.24)	0.0005	71.58	--	--	S104 Fig

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	Presence of GGOs with consolidation	10	46.83% (34.26-59.82)	0.0001	88.26	--	--	S105 Fig
	GGOs	30	58.37% (45.11-70.52)	0.0001	97.03	--	--	S106 Fig
	consolidation	18	29.43% (20.2-40.71)	0.0006	93.83	--	--	S107 Fig
	Crazy-paving	7	22.55% (14.26-33.76)	0.0001	84.75	--	--	S108 Fig
	Vascular enlargement	4	43.59% (6.34-89.82)	0.8356	98.67	--	--	S109 Fig
	Interlobular septal thickening in a crazy-paving pattern	3	62.94% (56.24-69.18)	0.0002	0 (Fixed effect size)	--	--	S110 Fig
	Air Bronchogram sign	6	61.79% (50.02-72.32)	0.0497	79.89	--	--	S111 Fig
	Air trapping	1	11.76% (5.38-23-81)	0.0001	0 (Fixed effect size)	--	--	S112 Fig
	Nodular opacities	4	13.99% (5.53-31.13)	0.0005	80.12	--	--	S113 Fig
	Reversed halo sign	2	2.54% (0.96-6.58)	0.0001	0.0001	--	--	S114 Fig
	Discrete pulmonary Nodules with halo sign	1	17.65% (9.45-30.57)	0.0001	0 (Fixed effect size)	--	--	S115 Fig
	Discrete pulmonary Nodules without halo sign	1	3.92% (0.98-14.37)	0.0001	0 (Fixed effect size)	--	--	S116 Fig
	Bronchus deformation due to fibrosis and strip like lesions	1	47.62% (27.85-68.16)	0.8273	0 (Fixed effect size)	--	--	S117 Fig
	Lymphadenopathy	2	4.74% (2.48-8.85)	0.0001	0 (Fixed effect size)	--	--	S118 Fig

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	Pleural retraction sign	1	56.45% (43.97-68.17)	0.3110	0 (Fixed effect size)	--	--	S119 Fig
	Pleural effusion	10	7.15% (4.65-10.84)	0.0001	53.92	--	--	S120 Fig
	Number of fibrous stripes	2	34.65% (8.23-75.80)	0.4838	94.65	--	--	S121 Fig
	Number of patchy Consolidation at CT	2	24.2% (15.73-35.31)	0.0001	42.86	--	--	S122 Fig
	Peripheral	8	66.34% (47.89-80.86)	0.2821	92.40	0.0001	94.90	S123 Fig
	Central	3	1.47% (0.61-3.48)	0.0001	0 (Fixed effect size)			
	Both	5	36.2% (22.13-53.11)	0.0813	93.36			
	Upper	2	83.29% (73.31-90.05)	0.0001	0 (Fixed effect size)	0.0001	75.34	S124 Fig
	Middle	2	72.64% (40.62-91.16)	0.1582	80.69			
	Lower	2	91.70% (82.70-96.23)	0.0001	0 (Fixed effect size)			
	Number of Patchy or punctate ground glass opacities	2	64.73% (15.97-94.66)	0.5997	97.51	--	--	S125 Fig
	Patients number of 1 affected lobe	6	15.77% (9.11-25.91)	0.0001	76.24	0.0001	84.19	S126 Fig
	Patients number of 2 affected lobes	6	14.08% (11.01-17.83)	0.0001	0 (Fixed effect size)			
	Patients number of 3 affected lobes	6	9.82% (7.28-13.12)	0.0001	0 (Fixed effect size)			
	Patients number	6	18.36% (14.89-22.43)	0.0001	0			

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	of 4 affected lobes				(Fixed effect size)			
	Patients number of 5 affected lobes	6	34.59% (27.32-42.66)	0.0003	56.47			
	Interstitial abnormality	1	13.01% (11.15-15.13)	0.0001	0 (Fixed effect size)			S127 Fig
Treatment	Corticosteroid	18	27.17% (20.54-35)	0.0001	91.77	--	--	S128 Fig
	Intravenous immunoglobulin therapy	8	27.79% (14.6-46.43)	0.021	96.66	--	--	S129 Fig
	Interferon	4	68.78% (10.63-97.61)	0.5958	96.99	--	--	S130 Fig
	Non-Invasive ventilation	16	21.48% (12.02-35.4)	0.0003	96.16	--	--	S131 Fig
	Invasive mechanical Ventilation	8	5.71% (2.91-10.93)	0.0001	76.19	--	--	S132 Fig
	Immunoglobulin therapy	9	25.93% (16.1-38.97)	0.0006	93.18	--	--	S133 Fig
	Nasal cannula	8	59.88% (51.54-67.69)	0.020	72.66	--	--	S134 Fig
	Oxygen therapy	7	72% (47.85-87.82)	0.0725	97.89	--	--	S135 Fig
	CRRT	6	7.92% (4.63-13.25)	0.0001	57.49	--	--	S136 Fig
	ECMO	4	2.06% (0.42-9.39)	0.0001	90.39	--	--	S137 Fig
	Antifungal	5	6.7% (1.98-2.033)	0.0001	94.56	--	--	S138 Fig
	Antibiotic	16	75.09% (61.65-84.97)	0.0006	94.81	--	--	S139 Fig
	Antiviral	18	86.45% (76.34-92.65)	0.0001	96.58	--	--	S140 Fig
Outcomes	Discharge	19	25.88% (15.91-39.18)	0.0008	97.08	--	--	S141 Fig
	Recovery	3	6.49% (0.11-80.93)	0.2036	97.68	--	--	S142 Fig
	Remained in hospital	24	62.87% (47.43-76.06)	0.1012	97.24	--	--	S143 Fig

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	Death	**25**	**4.55% (2.49-8.15)**	**0.0001**	**98.09**	**--**	**--**	**S144 Fig**

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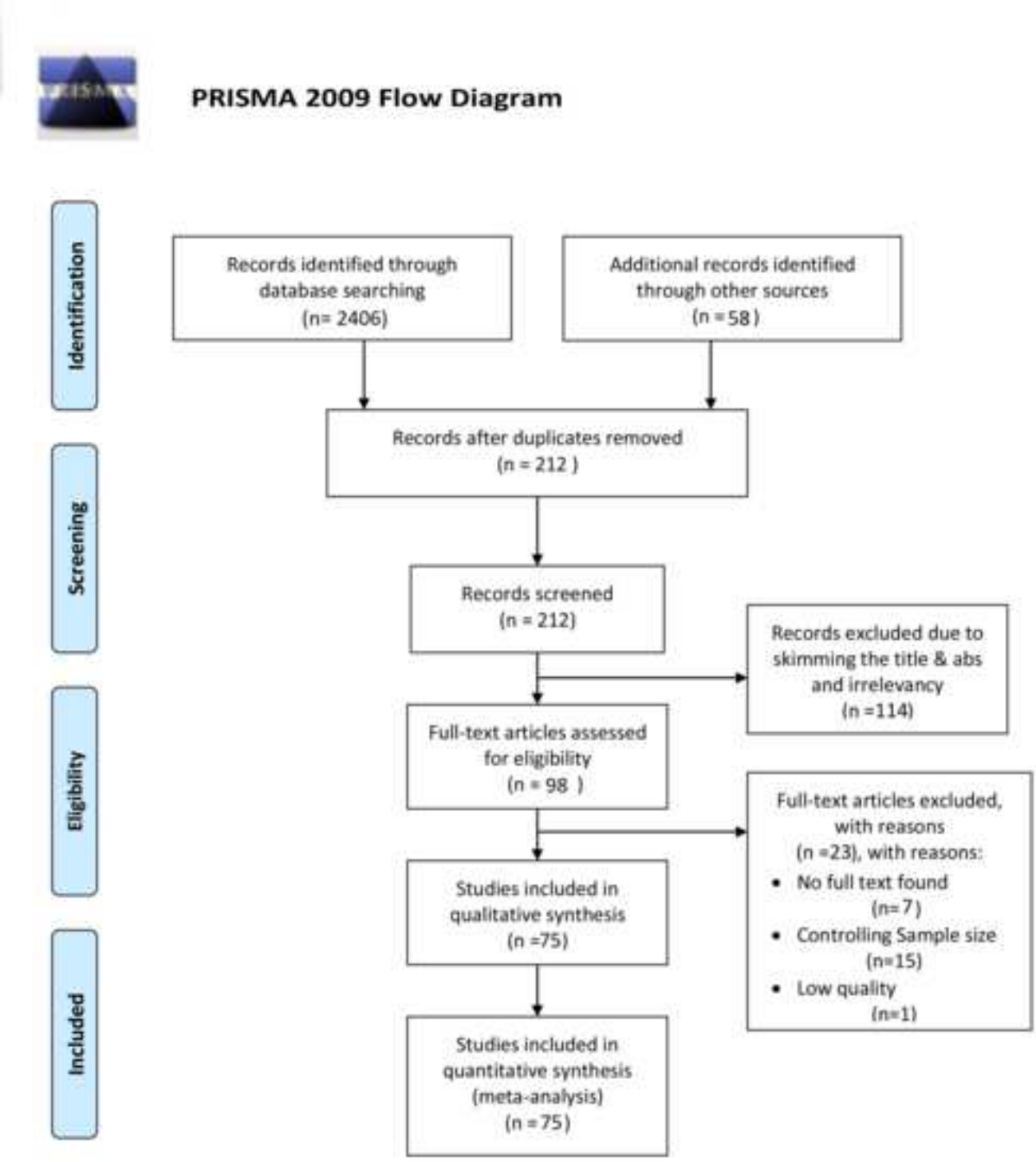
Fig 1. A flow diagram following the PRISMA (Depicted by MH-YK). Click here to download Figure Fig 1.tif



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.* PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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Fig 2. Publication bias of studies included.

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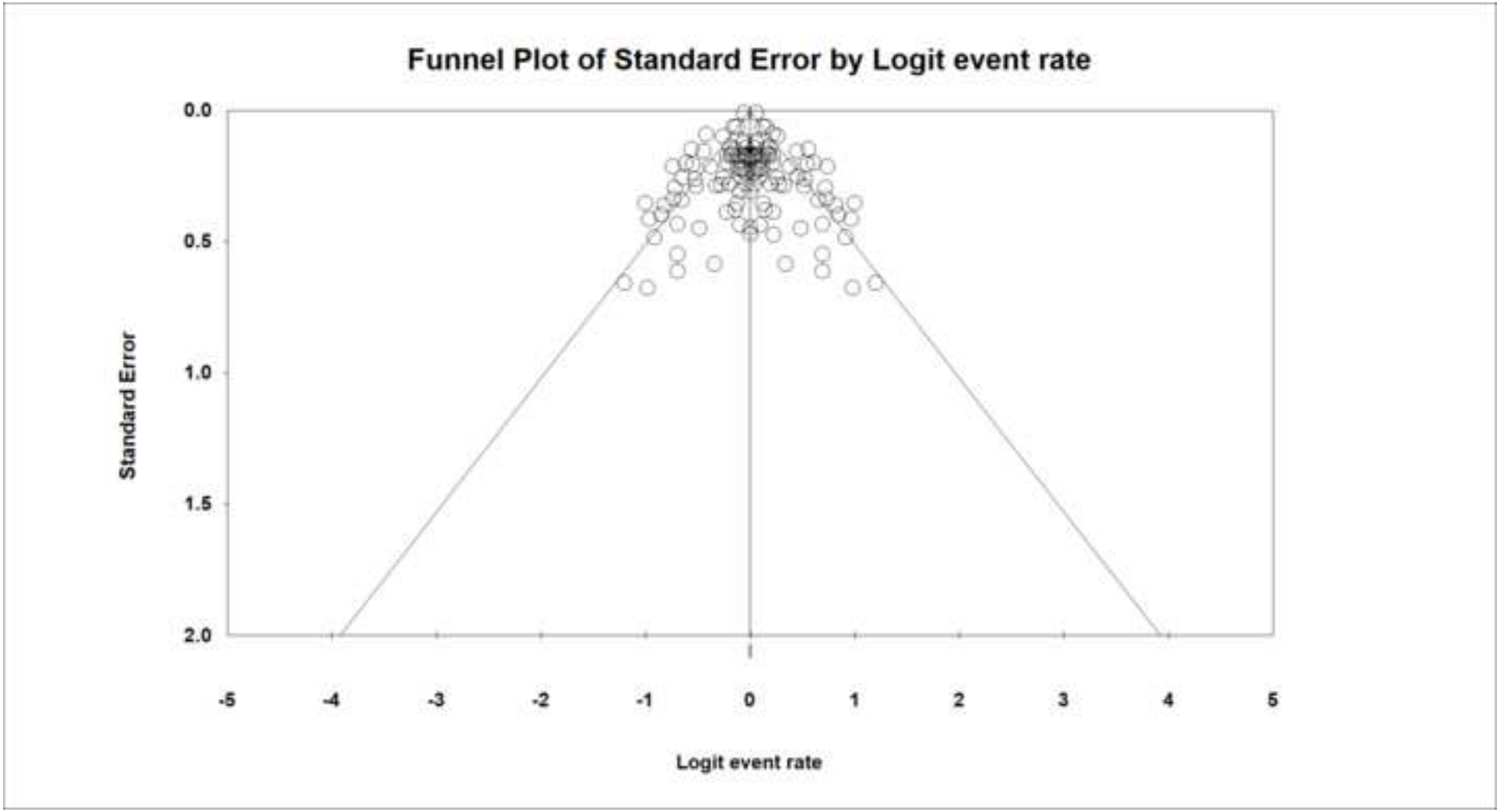

S1 File. PRISMA Checklist

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S2 File. The review protocol which has been registered in PROSPERO International Prospective Register of Systematic

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S4 File. Data characteristics (Full details) (MS Excel).

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