Clinical Features of COVID-19 Patients in the First Year of Pandemic: A Systematic Review and Meta-Analysis.

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Clinical Features of COVID-19 Patients in the First Year of Pandemic: A Systematic Review and Meta-Analysis

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The new coronavirus disease (COVID-19) carries a high risk of infection and has spread rapidly around the world. However, there are limited data about the clinical symptoms globally. The purpose of this systematic review and meta-analysis is to identify the prevalence of the clinical symptoms of patient with COVID-19.

A systematic review and meta-analysis were carried out. The following databases were searched: PubMed, CINAHL, MEDLINE, EMBASE, PsycINFO, medRxiv, and Google Scholar, from December 1st, 2019 to January 1st, 2021. Prevalence rates were pooled with meta-analysis using a random-effects model. Heterogeneity was tested using I-squared (I

A total of 215 studies, involving 132,647 COVID-19 patients, met the inclusion criteria. The pooled prevalence of the four most common symptoms were fever 76.2% (

This meta-analysis found the most prevalent symptoms of COVID-19 patients were fever, coughing, fatigue, and dyspnea. This knowledge might be beneficial for the effective treatment and control of the COVID-19 outbreak. Additional studies are required to distinguish between symptoms during and after, in patients with COVID-19.

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At the end of December 2019, a new coronavirus disease (COVID-19) emerged in Wuhan City, Hubei province, China, and subsequently spread worldwide (

World Health Organization, 2020

A large number of studies have been published aiming to identify the clinical features of COVID-19. Several systematic reviews and meta-analyses have been published which have assessed the prevalence of baseline clinical characteristic and associated factors (

Rodriguez-Morales et al., 2020

This systematic review and meta-analysis were undertaken according to the PRISMA standards.

A systematic literature search for the period between December 1st, 2019 and January 1st, 2021, was conducted using the following databases: PubMed, CINAHL, MEDLINE, EMBASE, PsycINFO, medRxiv, and Google Scholar. Search terms used both free text words and medical subject headings, that is, MeSH terms, to search for papers to be included in the review; that is, (MH ‘COVID-19’) OR (MH ‘coronavirus disease 2019’) OR (MH ‘severe acute respiratory syndrome coronavirus 2’) OR (MH ‘SARS-CoV-2’) OR (MH ‘2019 novel coronavirus’) OR (MH ‘2019-nCoV’) OR (MH ‘coronavirus’) OR (MH ‘corona virus’) OR ‘Wuhan pneumonia’ OR ‘COVID’ OR ‘Betacoronavirus’ OR ‘Alphacoronavirus’ OR ‘coronavir*’ AND (MH ‘clinical characteristics’) OR (MH ‘symptomatology’) OR (MH ‘Features’) OR (MH ‘Symptom*’) OR ‘signs’. In addition, the reference lists of the retrieved studies and review articles were screened to identify any further studies.

Two investigators (MM; SM) performed the search, scrutinizing all titles and abstracts for eligibility against the inclusion and exclusion criteria. Any disagreements were resolved by discussion with a third investigator (KB). Studies were included in the review based on the following inclusion criteria: (1) diagnosed with COVID-19; (2) reported prevalence of clinical symptoms; (3) subjects aged 15 or older; (4) all types of settings; (5) cross-sectional or cohort surveys (only the baseline data were extracted);

and (6) sample size greater than 40 to avoid selection bias from small studies. The exclusion criteria were the following: (1) protocol papers, and conference abstracts; and (2) case reports and studies with a sample size of less than 40. For any additional information, the study authors were contacted.

Upon retrieval of the applicable studies, quality assessment was completed using the Newcastle-Ottawa Scale (NOS;

Li & Katikireddi, 2019

The mean point of prevalence, the odds ratio (OR) with a 95% Confidence Interval (CI), was calculated as the effect size by using a random-effects model. Heterogeneity was tested using I-squared (I

Patsopoulos et al., 2008

Publication bias was estimated using Egger's linear regression test (

Neyeloff et al., 2012

The database search identified 4365 papers. Of these, 4018 papers were excluded during the title and abstract screening process. A further 132 papers were excluded during full text review for the following reasons: 34 papers were not conducted during the COVID-19 period; 9 did not give data about symptoms; 39 were duplicated papers; 50 were commentary, editorial or letter papers. As such, 215 studies were identified as being eligible for meta-analysis (

General Characteristics

Two hundred and fifteen studies, involving 132,647 COVID-19 patients, were included in this meta-analysis. All studies were conducted between January 2020 and June 2020: 7 in January, 112 in February, 50 in March, 28 in April, 15 in May, and 3 in June. Seventeen preprint studies (

One hundred and fifty-one studies originated from China, 16 from the USA, 6 from Spain, 5 from Iran, 4 each from Italy, Korea, and the UK, 3 each from Belgium, France, the Kingdom of Saudi Arabia and Kuwait, 2 from Jordan, and 1 from each of the following: Bangladesh, Bulgaria, Canada, Germany, Japan, the Netherlands, Pakistan, Poland, Singapore, Somalia, and Turkey (see Supplementary Table 1 for the general characteristics of the studies).

The studies were assessed using the NOS checklist. Thirty-nine studies were classified as having a low risk of bias, and 166 as moderate risk. The detailed results of the quality assessment of the studies included in this meta-analysis are listed in

Supplementary Table 2

Demographic and Comorbidity Characteristics

The mean age of patients among 191 studies was 54.26 years (95% CI 52.64–55.87). All meta-analyses of prevalence estimate that in terms of the gender distribution of COVID-19, male patients accounted for 53.1% (71,194/132,546 participants, 95% CI 51.9–54.2). One hundred and ninety-three studies provided information about comorbidities. The most frequent comorbidities among patient were hypertension 26.8% (32,925/93,909 participants, 95% CI 24.7–29.1), followed by diabetes with 13.4% (18,372/124,199, 95% CI 12.4–14.4).

Fever was estimated to occur in 214 studies. The overall pooled point estimates of prevalence for fever varied between 7.5% and 99.1%. All meta-analyses of prevalence estimates of fever reported by the 214 studies yielded a summary prevalence of 76.2% (84,823/132,436 participants, 95% CI 73.9–78.5) (

Forest plot of the prevalence of symptoms among COVID-19 patients.

Prevalence of Symptoms.

Subgroups Analyses and Meta-Regression.

Coughing was identified in 215 studies. The overall pooled point estimates of the prevalence of coughing varied between 16% and 93.3%. All meta-analyses of prevalence estimates of coughing reported by the 215 studies yielded a summary prevalence of 60.4% (73,778/132,647 participants, 95% CI 58.6–62.1). A subgroups analysis by continent showed a coughing prevalence of 57.7% for North America, 54.7% for Asia, and 49% for Europe.

Fatigue was estimated in 175 studies. The overall pooled point estimates of prevalence for fatigue varied between 3.4% and 90.6%. All meta-analyses of prevalence estimates of fatigue reported by the 175 studies yielded a summary prevalence of 33.6% (28,306/78,973 participants, 95% CI 31.2–36.1). The pooled prevalence rates with regard to fatigue were 45.7% for Europe, 36.7% for North America, and 31.7% for Asia.

Dyspnea was estimated in 195 studies. The overall pooled point estimates of prevalence for dyspnea varied between 1% and 99%. All meta-analyses of the prevalence estimates of dyspnea reported by the 195 studies yielded a summary prevalence of 26.2% (46,681/127,715 participants, 95% CI 24.1–28.5). In the subgroup analyses by continent, the pooled prevalence of dyspnea was 42.4% for Europe, 41.6% for North America, and 22.5% for Asia. The pooled prevalence of dyspnea was highest in May (34.6%). In meta-regression analyses, the mean age and patients with respiratory disease were significantly associated with the dyspnea prevalence rate (

Expectorant was estimated in 102 studies. The overall pooled point estimates of prevalence for expectorant varied between 2.2% and 56.5%. All meta-analyses of prevalence estimates of expectorant reported by the 102 studies yielded a summary prevalence of 22.2% (14,159/65,275 participants, 95% CI 20.1–24.4). A subgroups analysis by continent showed the expectorant prevalence of 29.8% for Asia and 17.5% for Europe.

Anorexia was estimated in 63 studies. The overall pooled point estimates of prevalence for anorexia varied between 3% and 86%. All meta-analyses of prevalence estimates of anorexia reported by the 63

studies yielded a summary prevalence of 21.6% (4126/19,004 participants, 95% CI 18–25.8). In the subgroup analyses, the prevalence of anorexia was reported in 39.5% of the studies conducted in Europe compared to 20% of the studies conducted in Asia. The male gender, hypertension, and liver disease patients were significantly associated with the anorexia symptoms prevalence rate (

Myalgias were estimated in 130 studies. The overall pooled point estimates of prevalence for myalgias varied between 0.8% and 65.3%. All meta-analyses of prevalence estimates of myalgias reported by the 130 studies yielded a summary prevalence of 17.5% (16,762/91,491 participants, 95% CI 15.3–19.8). In the subgroup analyses, the prevalence of myalgias was similarly reported by studies from Europe (36.7%) and North America (26.6%), whereas it was lower in Asia (15.4%). The pooled prevalence of myalgia was highest in April (30.6%).

Chills were estimated in 45 studies. The overall pooled point estimates of prevalence for chills varied between 1.6% and 53.3%. All meta-analyses of the prevalence estimates of chills reported by the 45 studies yielded a summary prevalence of 15% (2728/17,303 participants, 95% CI 11.9–18.6).

Sore throat was estimated in 80 studies. The overall pooled point estimates of prevalence for sore throat varied between 1.2% and 57.4%. All meta-analyses of prevalence estimates of sore throat reported by the 80 studies yielded a summary prevalence of 14.1% (5389/41,810 participants, 95% CI 11.6–16.9). In the subgroup analyses, the highest prevalence of sore throat was in Europe (24.1%) and North America (21.6%) compared to studies conducted in Asia (12.3%). Pooled prevalence of sore throat was highest in April (25.4%).

Headache was estimated in 141 studies. The overall pooled point estimates of prevalence for headache varied between 1.5% and 75%. All meta-analyses of prevalence estimates of headache reported by the 141 studies yielded a summary prevalence of 12.1% (9164/63,999 participants, 95% CI 10.3–14.3). A subgroup analysis by continent showed the headache prevalence of 27.1% for Europe, 23.7% for North America, and 10.2% for Asia. The month of April showed the highest prevalence of headache (25.6%).

Diarrhea was estimated in 186 studies. The overall pooled point estimates of prevalence for diarrhea varied between 1% and 50.3%. All meta-analyses of prevalence estimates of diarrhea reported by the 186 studies yielded a summary prevalence of 11.7% (14,008/95,345 participants, 95% CI 10.7–12.8). The prevalence of diarrhea in North America was 18.3%, in Europe 16.8%, and in Asia 16.7%. Male patients were significantly associated with the prevalence of diarrhea symptoms (

Nausea or vomiting was estimated in 95 studies. The overall pooled point estimates of prevalence for nausea or vomiting varied between 1% and 96.3%. All meta-analyses of prevalence estimates of nausea or vomiting reported by the 95 studies yielded a summary prevalence of 8.7% (4093/41,319 participants, 95% CI 7.1–10.5). A subgroups analysis by continent showed that nausea or vomiting prevalence was highest North America (20.1%), compared to Europe (13.3%) and Asia (7.1%). In meta-regression analyses, patients with cardiovascular, renal, and cerebrovascular disease were significantly associated with the nausea or vomiting prevalence rate (

Rhinorrhea was estimated in 76 studies. The overall pooled point estimates of prevalence for rhinorrhea varied between 0.2% and 60.1%. All meta-analyses of prevalence estimates of rhinorrhea

reported by the 76 studies yielded a summary prevalence of 8.2% (3452/30,150 participants, 95% CI 6.2–10.6). In the subgroup analyses, the prevalence of rhinorrhea was higher in both North America (28.4%) and Europe (25.1%), whereas in Asia it was reported as 5.9%.

Hemoptysis was estimated in 41 studies. The overall pooled point estimates of prevalence for hemoptysis varied between 0.1% and 41.4%. All meta-analyses of the prevalence estimates of hemoptysis reported by the 41 studies yielded a summary prevalence of 3.3% (12,578/49,942 participants, 95% CI 1.8–6.2).

Sensitivity analysis was conducted with regard to all subgroups by excluding one study each time. This demonstrated that there were no differences in the overall estimation by more or less than 1%.

Publication bias was assessed using Egger's regression test. Evidence of bias was found with regard to the following: Coughing (

COVID-19 is viewed as a major threat to public health due to the incredible damage it is doing to the medical services and the economies of almost all countries across the global (

Wiebers & Feigin, 2020

This meta-analysis found that there was a minor variation in terms of COVID-19 patients between male (53.7%) and female (46.3%). This is consistent with other meta-analyses that have found that there were slightly more male than female patients (

Peckham et al. (2020)

In this meta-analysis, the most frequently reported clinical features of COVID-19 were fever, coughing, fatigue, and dyspnea (76.2%, 60.4%, 33.6%, and 26.2%. respectively). These results are lower by between approximately 5% and 20% compared to other meta-analyses (

Rodriguez-Morales et al., 2020

Rodriguez-Morales et al., 2020

The results of the current meta-analyses are even lower when compared with studies which reported symptoms at onset of fever, coughing, fatigue, and dyspnea for the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) epidemics (

Yin & Wunderink, 2018

The findings of this analysis suggested that four symptoms have slight variations in prevalence between the continents—fever, coughing, fatigue, and diarrhea. However, it is recommended that every country should have its own symptoms list to evaluate patients.

The meta-regression analysis also revealed that male patients were significantly associated with a pooled estimation of anorexia, diarrhea, and nausea or vomiting. In addition, mean age and respiratory disease yielded a higher prevalence of dyspnea. These finding warrant further examination.

The major strength of this meta-analysis is the large sample size of over 132,647 subjects drawn from 215 studies which estimated the symptom onset of patients diagnosed with COVID-19. However, there are several potential limitations to this meta-analysis. First, this review searched medRxiv's preprint studies which, at the time of searching, were not peer reviewed. This might introduce publication bias. Second, there is a possibility that some studies have not been included in this meta-analysis, even though this analysis used different MeSH terms and several databases. In addition, only studies published, unpublished, or translated into English were included in this analysis. Third, around 151 of the studies originated from China, while the other 64 studies originated from 22 countries. Two studies from Spain included 25,615 subjects. Fourth, there were insufficient data available with regard to the demographic and clinical characteristics, so not all information could be eliminated thoroughly. Finally, all findings were derived from retrospective designs, which means that we cannot rule out selection bias.

This is a systematic review and meta-analysis reporting pooled estimates with regard to the prevalence of symptoms associated with COVID-19. Thus, the findings can be used to help healthcare professionals and policy makers identify and monitor patients as part of the early screening process of COVID-19 patients. This might help ensure the appropriate utilization of healthcare resources, which in turn might help to reduce the severity of the impact of COVID-19 and be beneficial when it comes to effective management and treatment.

This meta-analysis has been undertaken to estimate the aggregate prevalence of the clinical signs and symptoms of COVID-19 patients. This meta-analysis found that the most prevalent symptoms with regard to COVID-19 patients were fever, coughing, fatigue, and dyspnea. This knowledge might be beneficial for the effective treatment and control of the COVID-19 pandemic. Additional studies are required to distinguish between symptoms during and after in patients with COVID-19.

Supplemental Material

sj-pdf-1-brn-10.1177_10998004211055866 – Supplemental Material for Clinical Features of COVID-19 Patients in the First Year of Pandemic: A Systematic Review and Meta-Analysis

Click here for additional data file.

Supplemental Material, sj-pdf-1-brn-10.1177_10998004211055866 for Clinical Features of COVID-19 Patients in the First Year of Pandemic: A Systematic Review and Meta-Analysis by Mohammed Al Maqbali, Khalid Al badi, Mohammed Al Sinani, Norah Madkhali and Geoffrey L. Dickens in Biological Research For Nursing

sj-pdf-2-brn-10.1177_10998004211055866 – Supplemental Material for Clinical Features of COVID-19 Patients in the First Year of Pandemic: A Systematic Review and Meta-Analysis

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Declaration of conflicting interests:

Supplementary Material:

https://orcid.org/0000-0003-2023-5627

An assessment on impact of COVID-19 infection in a gender specific manner

Stem Cell Reviews and Reports

10.1007/s12015-020-10048-z

Multifacility outbreak of middle east respiratory syndrome in Taif, Saudi Arabia

Emerging Infectious Diseases

10.3201/eid2201.151370

The middle east respiratory syndrome (MERS)

Infectious Disease Clinics of North America

10.1016/j.idc.2019.08.001

Clinical characteristics and risk factors for fatal outcome in patients with 2019-coronavirus infected disease (COVID-19) in Wuhan, China

[SSRN Scholarly Paper]

Caution: The clinical characteristics of COVID-19 patients at admission are changing

10.1101/2020.03.03.20030833

Clinical characteristics and risk factors for mortality among inpatients with COVID-19 in Wuhan, China

Clinical and Translational Medicine

Severe acute respiratory syndrome (SARS)

[Content truncated for PDF size. Full text available at: https://www.ncbi.nlm.nih.gov/pmc/articles/8968436/]

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