Frequency of underlying diseases, symptoms and mortality rate of COVID-19: a systematic review and meta-analysis

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Coronavirus disease 2019 (COVID-19) is known to be affected by underlying diseases of the respiratory system. In this meta-analysis, the keywords of COVID-19, underlying diseases, symptoms, and mortality were searched in national and international databases to obtain the related studies. The inclusion criteria were as follows: interventional, clinical, descriptive and cross-sectional, and studies focusing on COVID-19. This study was conducted based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol. Eighteen studies were selected to be finally analyzed. The mean percentage of mortality was 14% ($I^2 = 98.9$, $P < 0.001$). The most common symptoms were fever (91%, $I^2 = 88.5$, $P < 0.001$) and cough (71%, $I^2 = 84.5$, $P < 0.001$), and the most frequent underlying diseases were hypertension (41%, $I^2 = 98.9$, $P < 0.001$), diabetes mellitus (18%, $I^2 = 88.7$, $P < 0.001$) and cardiovascular disease (11%, $I^2 = 87.7$, $P < 0.001$). Findings of present study suggest that individuals with underlying diseases have a higher rate of mortality following COVID-19 infection.

Introduction

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China, in December 2019. At first, it was named SARS-CoV-2. Because of the rapid spread at the end of 2019, this virus was named COVID-19. On 30 January 2020, WHO has announced emergency condition [1,2]. Many reports suggested this virus is being spread in 26 countries. Consequently, the statistical and clinical data of affected persons are of high importance for WHO [3].

Based on COVID-19 studies, researchers have found COVID-19 patients were recognized with two clinical presentations: systemic and respiratory symptoms. Systemic symptoms included fever, dry cough, tiredness, sputum production, and headache. On the other hand, the respiratory symptoms comprised of rhinorrhea, sneezing, sore throat, pneumonia, and serious acute respiratory syndrome [4–6].

Based on present reports, this disease is easily spreading from one person to the others and its primary reservoir is not identified definitely. Scientists attempted to discover its genesis and concluded it was originally occurred in animals [6]. Spread from one person to other is mainly through direct contact or droplets, which spread by coughing or sneezing of patients infected with COVID-19 [6].

Consequently, prevention is the best solution. Therefore, people must utilize health and immunity considerations, including avoiding the face touching, putting on the face

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mask, keeping a safe distance with high-risk persons, and less going into crowded and closed-in places not having adequate ventilation. By employing these considerations, we will not be afflicted and the rate of spread is reduced considerably [6,7].

COVID-19 is routinely diagnosed by means of clinical symptoms obtained from computed tomography scan and chest X-ray examinations of suspected patients [4,5]. In regard to the rate of mortality, we could refer to respective studies, which reporting to be 10−35% [8,9]. Two months after its outbreak, 82 000 COVID-19 cases were diagnosed and the number of deceased patients was reported to be more than 2800 persons, mostly in China [1]. Results of another study showed that out of 99 afflicted patients 57 (58%) were hospitalized, 31 (31%) released, and solely 11 (11%) deceased [5].

High-risk persons have been those with compromised immune system as well as those with underlying illness and comorbidities such as renal, heart, and respiratory diseases and senescence [4,5].

The highest rate of this disease was reported in China, subsequently in Iran and then Italy. Iran has close relationships with China and the disease spread by this route. Shortly after its outbreak, a great number of people were being affected, unfortunately, some were deceased, and some others were recuperated and released.

Although there are a number of extensive studies performed by systematic review and meta-analysis methodology, given the complexity and many unknown aspects of the disease, the demand for such studies may be continued. One advantage of these studies is the validity of their results and, therefore, their results could be generalized [10,11]. With regard to various studies and the validity of the obtained data, it seems necessary to conduct a meta-analysis in order to provide a valid and precise scale for researchers and scholars. The present study was conducted by meta-analysis and systematic review methodology to evaluate the frequency of underlying diseases and symptoms in relation to the mortality rate of COVID-19.

Methods

The present systematic review and meta-analysis were conducted based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol during 2019−2020 [12]. This study was performed in five steps in the following order: primary designing, searching data resources, collecting and considering articles in regard to inclusion criteria, assessment of articles, and finally, data statistical analysis. To inhibit publication bias, the searching process was performed by two investigators independently, and the acquired results were combined by this party.

Searching strategy
In order to obtain studies related to the research question, two investigators were independently performed a comprehensive searching in national and international academic sources (Scopus, PubMed, Cochrane, and Web of Science) and Google Scholar search engine. With reference to the research question, the following keywords were utilized to search the relevant articles: coronavirus, COVID-19, mortality, and comorbidity symptoms. At first, these keywords were considered separately. Subsequently, a combination of these keywords was used for searching. Finally, in order to find related articles, all references of obtained articles were also reviewed. Of these references, the pertinent and not-repetitiveness articles were selected and their full text was being prepared and provided by the investigators.

Inclusion criteria
For the meta-analysis, the inclusion criteria were the interventional articles and clinical, descriptive, and cross-sectional trials considering COVID-19.

Exclusion criteria
Articles with irrelevant information regarding the underlying conditions, symptoms, and mortality rate of COVID-19 were excluded from the study.

Assessment tools
Finally, full and comprehensive studies about COVID-19 were assessed.

Data extraction
Considered variables in every article were including corresponding anther, data and location of research, sample volume, COVID-19 mortality, COVID-19 symptoms, COVID-19 clinical symptoms, and recovery from COVID-19. These data were selected from final articles and thereupon introduced into a researcher-made checklist.

Statistical analysis
Considering combined data, publication bias and funnel plot were not implemented (as the number of final studies was less than 10). To calculate heterogeneity, the I^2 index was used. In various studies, this index was calculated for every variable of COVID-19, separately. With respect to lack of essential quality, lack of cohesion to the subject matter, incomplete reporting review paper, case reports, correspondence (letter to editor), and abstracts presented in seminars contained incomplete data.

Selection and assessment of articles quality
To assess the quality of articles, strengthening the reporting of observational studies in epidemiology statement (checklist) was applied [12,13]. Two authors dedicated 0−2 scores to every part, separately. Based on the obtained scores, in regard to quality, articles were divided into three categories: weak, moderate, and strong, with 1−15, 16−30, and 31−44 scores, respectively. Articles with the least 16 score were included in the meta-analysis.

Meaning fullness of heterogeneity of raider ($P < 001.0$), was used in the meta–analysis model with random effects in order to combine results of different studies. Data were analyzed using (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Results

Study characteristics

First, a list of all the titles and abstracts of the articles retrieved from the databases was prepared by the researchers. After hiding the details of the articles including journals' and authors' names, the full texts of the articles were provided to the researchers. The initial search resulted in 100 related articles of which 30 duplicates were excluded. In addition, 40 articles were excluded because of limited and incomplete results. By reviewing the full texts of the articles, 12 related articles were omitted due to the lack of necessary criteria. Finally, 18 articles enrolled for evaluation process (Fig. 1). According to the results of this study, the mean age of patients was 45.44 years. The overall sample size was 2720 rendering an average of 151 subjects per study.
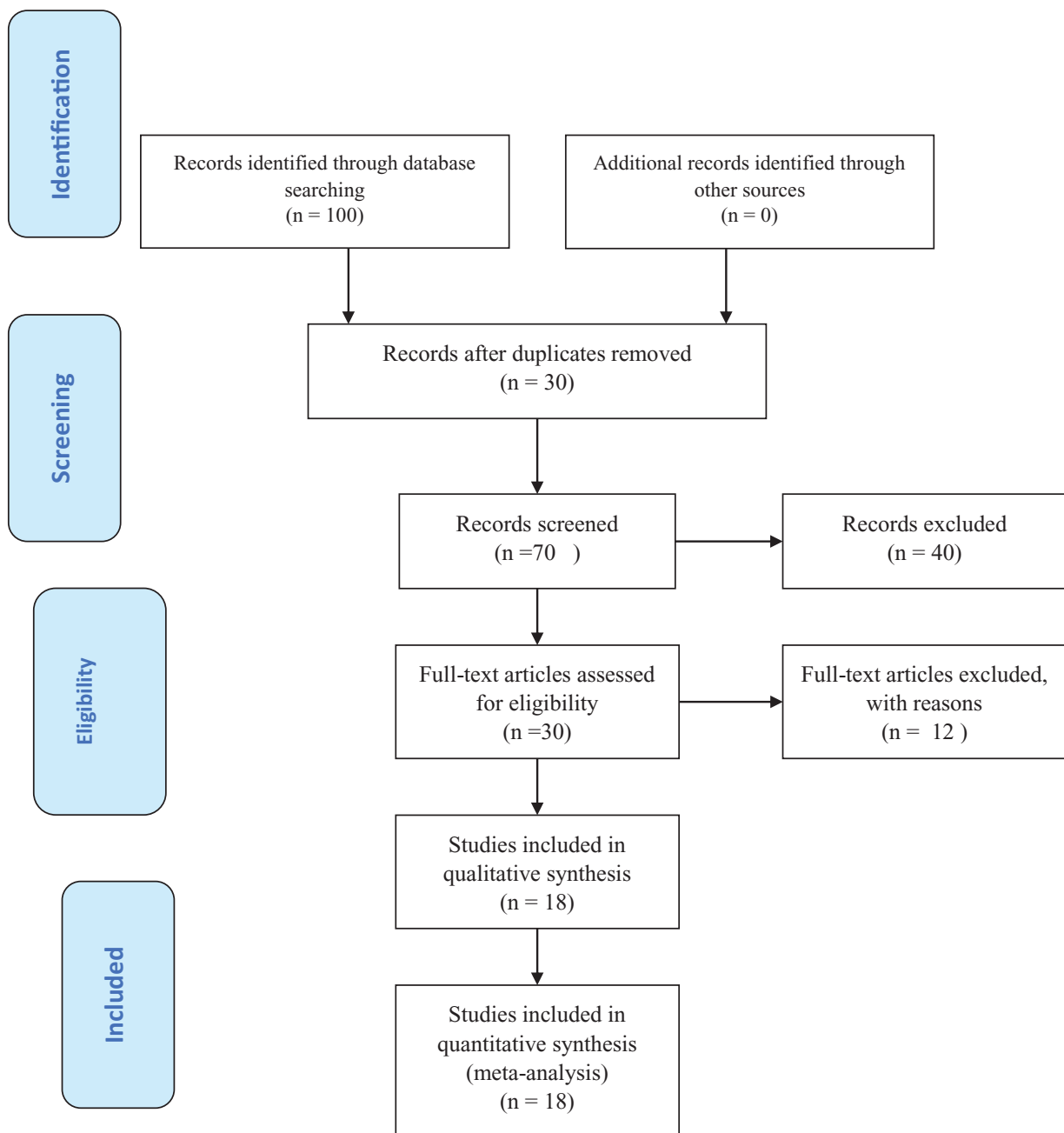

Fig. 1. The flowchart for the inclusion of studies in meta-analysis.

Table 1. The main characteristics of the included studies.

Variables	Subgroup	Articles (N)	%	95% CI	I^2	P value
Mortality	–	4	14	12–16	98.9	<0.001
comorbidities (%)	Hypertension	9	41	19–64	98.9	<0.001
	Diabetic	12	18	12–24	88.7	<0.001
	chronic pulmonary obstructive disease	9	6	3–9	91.3	<0.001
	Cardiovascular	9	11	6–16	87.7	<0.001
	Brain disease	4	17	9–25	66.1	0.031
	Other[a]	6	15	7–22	84	<0.001
Symptoms of the disease	Fever	16	91	87–95	88.5	<0.001
	Cough	16	71	65–77	84.5	<0.001
	Fatigue	10	46	32–60	97.1	<0.001
	Dyspnea	10	44	28–60	97.2	<0.001
	Sputum	8	29	18–39	90.6	<0.001

CI, confidence interval.
[a]Liver disease, digestive disease, kidney disease.

The characteristics of the reviewed articles have been presented in Table 1. The frequencies of underlying diseases, symptoms, and mortality rate of COVID-19 along with the significance levels and I^2 indices have been shown in Table 2.

Figures 2 and 3 show the forest plots of most common underlying diseases (i.e. hypertension and diabetes mellitus), and Figs. 4 and 5 demonstrate the forest plots related to the most frequent symptoms (i.e. fever and cough).

The publication bias in the data obtained here has been depicted in Fig. 6. The circle sizes exhibit the studies weights (larger circles reflect higher sample sizes and smaller ones represent lower sample sizes).

Meta-regression was performed to compare the COVID-19 based on different genders, sample sizes, and years of the studies. Meta-regression was also used to seek the heterogeneity reasons among the studies (Figs. 7 and 8).
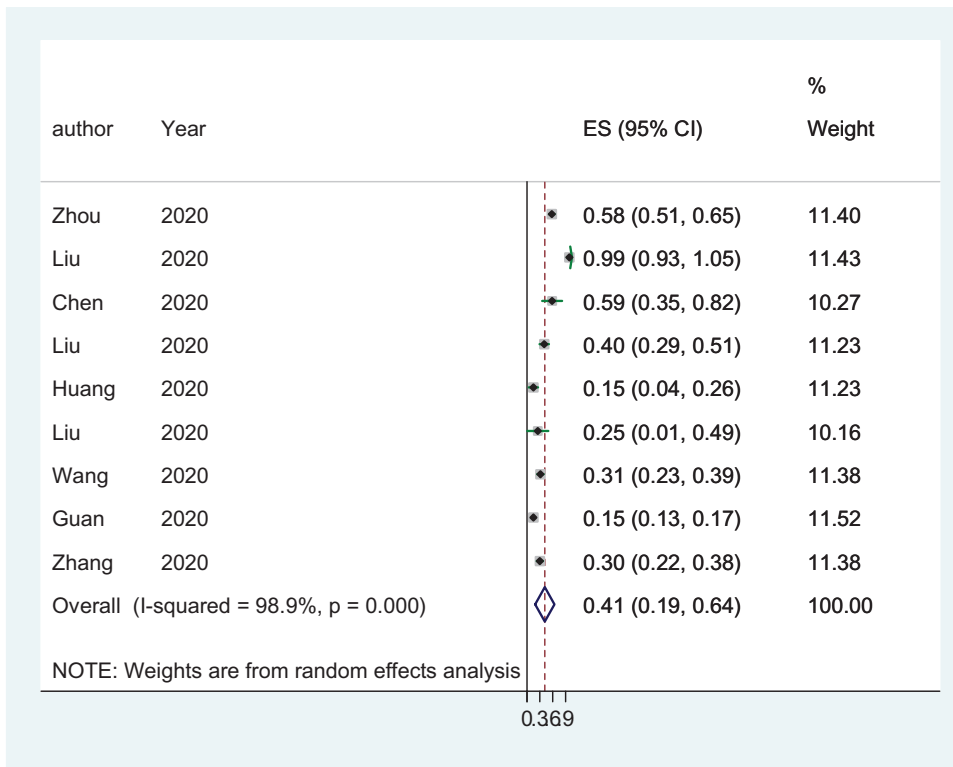
Discussion

The aim of the present study was to evaluate the prevalence of underlying diseases, symptoms, and mortality rate of COVID-19 by a systematic review and meta-analysis. The I^2 heterogeneity index represents a numerical value, which is utilized as a substitute for the odd ratio to estimate the variance of statistically heterogeneous studies. In this regard, $I^2 \leq 25$ shows low heterogeneity, whereas I^2 values of 26–50%, 51–75%, and 76–100% indicate moderate, statistically significant, and high heterogeneities, respectively. In this study, the I^2 index was 96.5%, which shows a high heterogeneity [10,11].
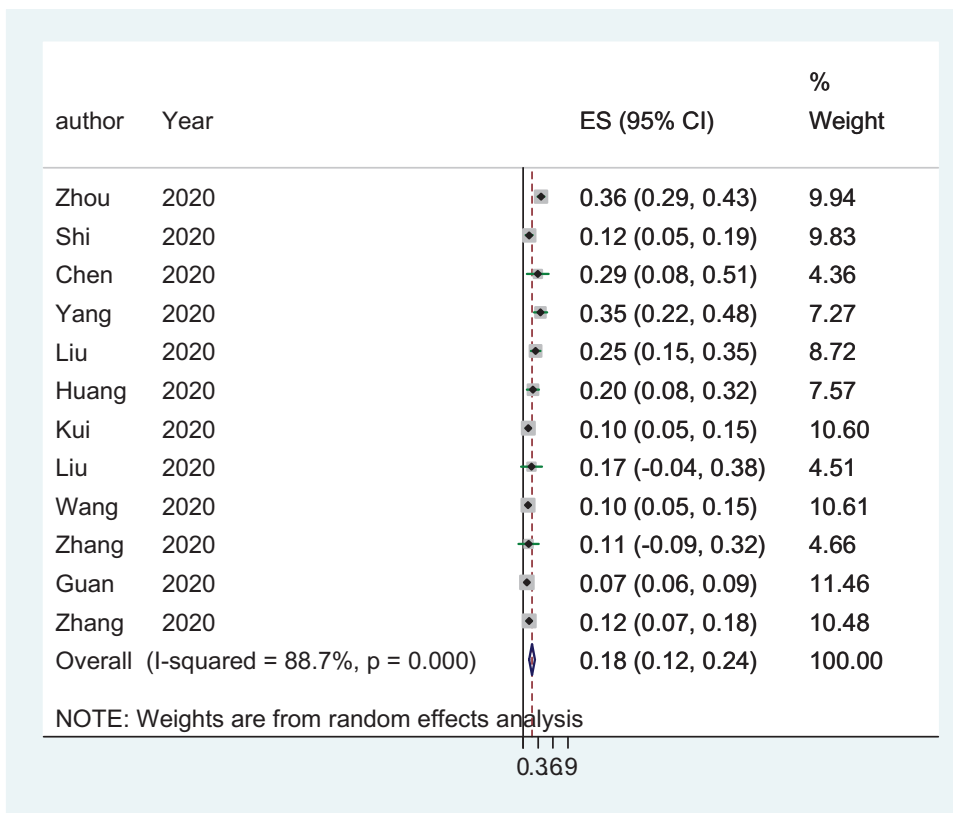
The results of the present study revealed a mortality rate of 14%. Similar studies across the world have reported mortality rates ranging from 10 to 35% [8,9]. In one study on 99 patients with COVID-19 infection, 57 (58%) were hospitalized, 31 (31%) were discharged, and only 11 (11%) died of the infection [5]. These were consistent

Table 2. The prevalence of underlying diseases, symptoms, and mortality rate of COVID-19.

References	Author	Place	Year	Total (N)	Female (N)	Male (N)	Age
[13]	Liu	China	2020	73	32	41	41.6
[14]	Chen	China	2020	9	–	–	32.7
[15]	Zhou	China	2020	191	72	119	–
[16]	Yang	China	2020	149	68	81	–
[17]	Liu	China	2020	10	6	4	42.0
[2]	Shi	China	2020	81	39	42	–
[18]	Hish	Taiwan	2020	2	1	1	–
[19]	Chen	China	2020	17	–	–	62.8
[20]	Yang	China	2020	52	17	35	59.7
[21]	Sun	China	2020	482	201	281	46.0
[22]	Liu	China	2020	78	39	39	–
[23]	Huang	China	2020	41	11	30	49.0
[24]	Kui	China	2020	137	76	61	57.0
[25]	Liu	China	2020	12	4	8	53.0
[26]	Wang	China	2020	138	75	63	56.0
[27]	Zhang	China	2020	9	4	5	35.2
[28]	Guan	China	2020	1099	459	640	47.0
[29]	Zhang	China	2020	140	69	71	57.0

author	Year		ES (95% CI)	% Weight
Zhou	2020		0.58 (0.51, 0.65)	11.40
Liu	2020		0.99 (0.93, 1.05)	11.43
Chen	2020		0.59 (0.35, 0.82)	10.27
Liu	2020		0.40 (0.29, 0.51)	11.23
Huang	2020		0.15 (0.04, 0.26)	11.23
Liu	2020		0.25 (0.01, 0.49)	10.16
Wang	2020		0.31 (0.23, 0.39)	11.38
Guan	2020		0.15 (0.13, 0.17)	11.52
Zhang	2020		0.30 (0.22, 0.38)	11.38
Overall (I-squared = 98.9%, p = 0.000)			0.41 (0.19, 0.64)	100.00

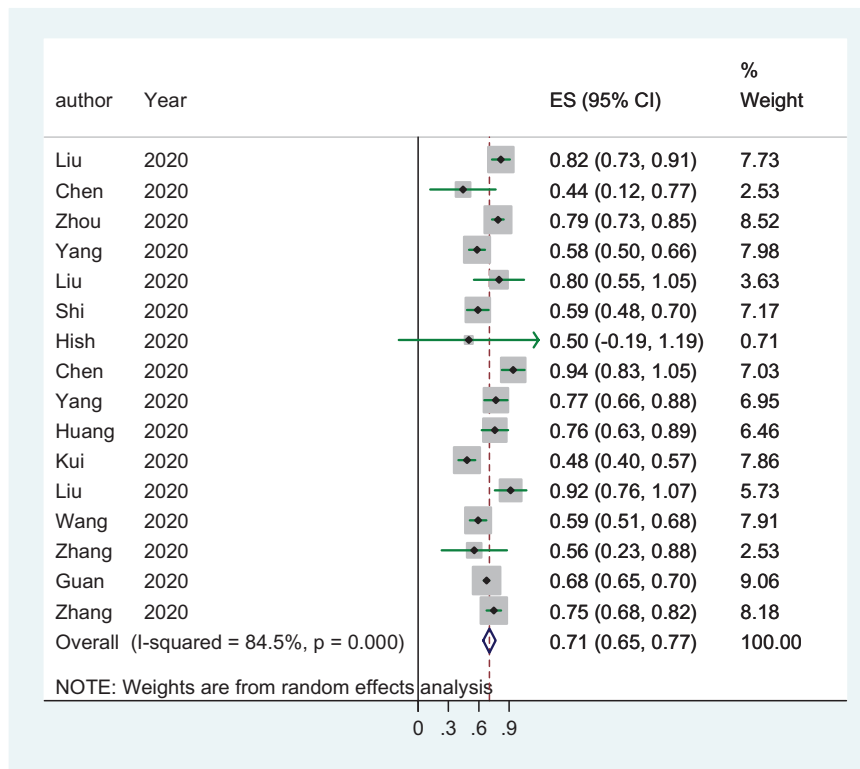NOTE: Weights are from random effects analysis

0.369

Fig. 2. Forest plot of Hypertension percentage with 95% confidence interval. The middle point of each line estimated the percentage of hypertension in individual studies. The diamond shows the total confidence interval of fear of fall in all the studies.

author	Year		ES (95% CI)	% Weight
Zhou	2020		0.36 (0.29, 0.43)	9.94
Shi	2020		0.12 (0.05, 0.19)	9.83
Chen	2020		0.29 (0.08, 0.51)	4.36
Yang	2020		0.35 (0.22, 0.48)	7.27
Liu	2020		0.25 (0.15, 0.35)	8.72
Huang	2020		0.20 (0.08, 0.32)	7.57
Kui	2020		0.10 (0.05, 0.15)	10.60
Liu	2020		0.17 (-0.04, 0.38)	4.51
Wang	2020		0.10 (0.05, 0.15)	10.61
Zhang	2020		0.11 (-0.09, 0.32)	4.66
Guan	2020		0.07 (0.06, 0.09)	11.46
Zhang	2020		0.12 (0.07, 0.18)	10.48
Overall (I-squared = 88.7%, p = 0.000)			0.18 (0.12, 0.24)	100.00

NOTE: Weights are from random effects analysis

0.369

Fig. 3. Forest plot of diabetic percentage with 95% confidence interval. The middle point of each line estimated the percentage of diabetic in individual studies. The diamond shows the total confidence interval of fear of fall in all the studies.

author	Year	ES (95% CI)	% Weight
Liu	2020	0.93 (0.87, 0.99)	7.51
Chen	2020	0.78 (0.51, 1.05)	1.57
Zhou	2020	0.94 (0.91, 0.97)	8.57
Yang	2020	0.76 (0.70, 0.83)	7.05
Liu	2020	0.90 (0.71, 1.09)	2.81
Shi	2020	0.73 (0.63, 0.83)	5.70
Hish	2020	0.99 (0.85, 1.13)	4.09
Chen	2020	0.99 (0.94, 1.04)	8.02
Yang	2020	0.98 (0.94, 1.02)	8.40
Huang	2020	0.98 (0.94, 1.02)	8.21
Kui	2020	0.82 (0.75, 0.88)	7.22
Liu	2020	0.83 (0.62, 1.04)	2.34
Wang	2020	0.99 (0.97, 1.01)	8.98
Zhang	2020	0.89 (0.68, 1.09)	2.44
Guan	2020	0.88 (0.86, 0.90)	8.99
Zhang	2020	0.92 (0.87, 0.96)	8.09
Overall (I-squared = 88.5%, p = 0.000)		0.91 (0.87, 0.95)	100.00

NOTE: Weights are from random effects analysis

0   .3   .6   .9

Fig. 4. Forest plot of fever percentage with 95% confidence interval. The middle point of each line estimated the percentage of fever in individual studies. The diamond shows the total confidence interval of fear of fall in all the studies.

author	Year	ES (95% CI)	% Weight
Liu	2020	0.82 (0.73, 0.91)	7.73
Chen	2020	0.44 (0.12, 0.77)	2.53
Zhou	2020	0.79 (0.73, 0.85)	8.52
Yang	2020	0.58 (0.50, 0.66)	7.98
Liu	2020	0.80 (0.55, 1.05)	3.63
Shi	2020	0.59 (0.48, 0.70)	7.17
Hish	2020	0.50 (-0.19, 1.19)	0.71
Chen	2020	0.94 (0.83, 1.05)	7.03
Yang	2020	0.77 (0.66, 0.88)	6.95
Huang	2020	0.76 (0.63, 0.89)	6.46
Kui	2020	0.48 (0.40, 0.57)	7.86
Liu	2020	0.92 (0.76, 1.07)	5.73
Wang	2020	0.59 (0.51, 0.68)	7.91
Zhang	2020	0.56 (0.23, 0.88)	2.53
Guan	2020	0.68 (0.65, 0.70)	9.06
Zhang	2020	0.75 (0.68, 0.82)	8.18
Overall (I-squared = 84.5%, p = 0.000)		0.71 (0.65, 0.77)	100.00

NOTE: Weights are from random effects analysis

0   .3   .6   .9

Fig. 5. Forest plot of cough percentage with 95% confidence interval. The middle point of each line estimated the percentage of cough in individual studies. The diamond shows the total confidence interval of fear of fall in all the studies.
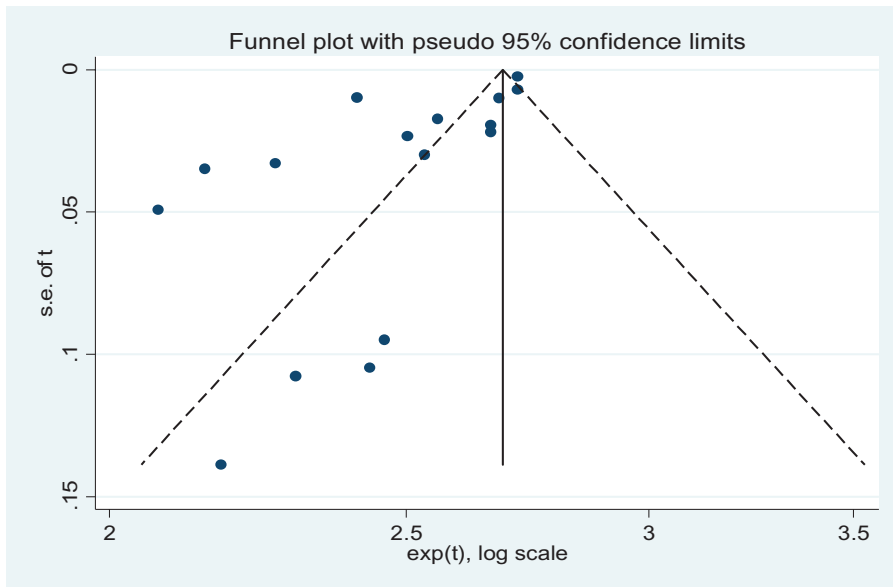
Fig. 6. Publication bias regarding COVID-19.

with the findings of the present study. It has also been highlighted in these studies that the disease is rapidly spreading and easily transmitted between individuals. Therefore, compliance with safety and health principles is of great importance.

Our results showed that hypertension, heart disease, diabetes mellitus, as well as respiratory and cerebral diseases were the most common comorbidities observed in COVID-19 affected patients. Various studies have shown that deceased patients had underlying diseases, such as hypertension, history of angiography, and diabetes mellitus. The presence of these underlying conditions including cardiac and cerebral diseases along with

weakened immune system predisposes to the spread of the virus throughout the body and a higher probability of death [5,30−33]. In conclusion, the role of underlying diseases is important in this condition by increasing the mortality rate of COVID-19.

The results of the present study showed that fever, cough, fatigue, dyspnea, and sputum were the most prevalent symptoms. In similar studies on patients hospitalized with the definitive diagnosis of COVID-19, fever, cough, and dyspnea were more common than other signs and symptoms, which is in line with our results [4,5]. Accordingly, the above-mentioned symptoms can be considered as the main symptoms of COVID-19, and any
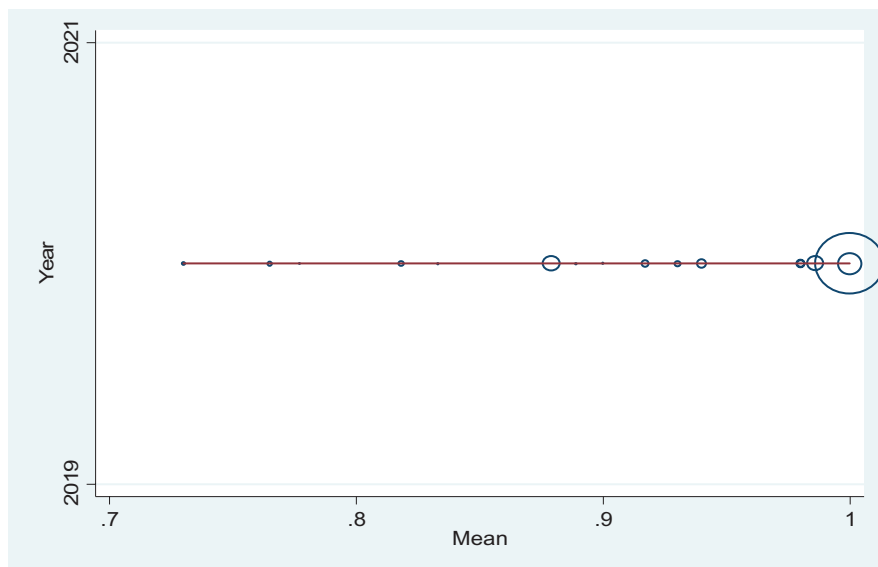
Fig. 7. The meta-regression of COVID-19 on studies years.
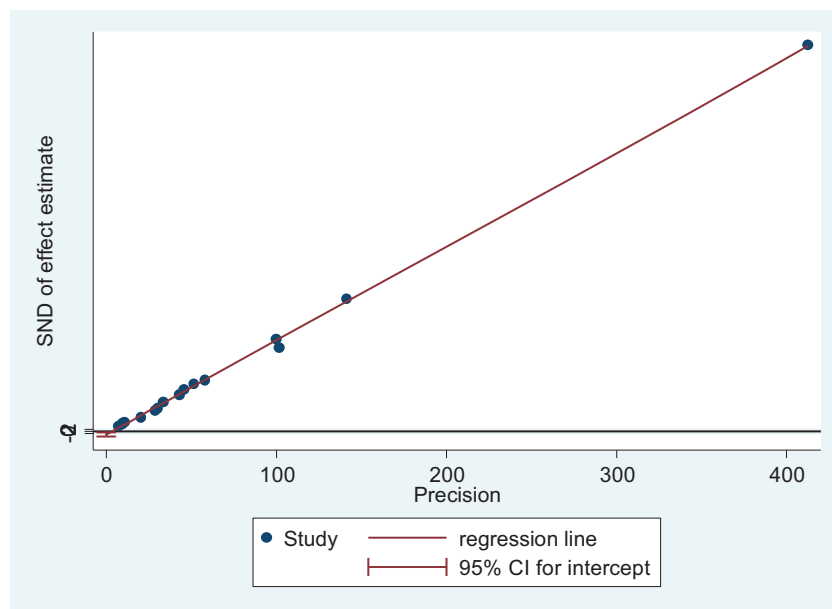
Fig. 8. The meta-regression of COVID-19 on studies sample size.

person with these symptoms should refer to the hospital and health center.

Early results regarding the clinical features of the COVID-19 in Iran also reveal similarities with the results of this meta-analysis. Although the underlying diseases, including cardiovascular diseases, hypertension, diabetes mellitus, malignancy, kidney injury, and chronic lung diseases were the most common risk factor of deceased among Iranian patients with COVID-19 [34,35]. As such, symptoms including dyspnea and cough, fatigue, as well as abnormal chest X-ray were the most reported symptoms in Iranian patients with COVID-19 [34,35].

Limitations

The variables studied in the studies were limited, and we could not properly analyze them. There were no comparisons between men and women, and only general data had been presented in some studies.

Conclusion and recommendations

The results of the present meta–analysis reveal that underlying diseases (hypertension, diabetes mellitus, and cardiovascular disease) are the major risk factors of mortality among the COVID–19 patients, hence, it could be used as a prognostic factor in infected patients. Therefore, such preventive measures, including social distancing, quarantine, and the use of the personal protection equipment (PPE) as well as early detection and treatment should be greater consideration in patients with underlying diseases.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1. Wilder-Smith A, Chiew CJ, Lee VJ. **Can we contain the COVID-19 outbreak with the same measures as for SARS.** *Lancet Infect Dis* 2020; **20**:e102–e107.
2. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, *et al*. **Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study.** *Lancet Infect Dis* 2020; **20**:425–434.
3. Xu B, Kraemer MUG, on behalf of the Open COVID-19 Data Curation Group. **Open access epidemiological data from the COVID-19 outbreak.** *Lancet Infect Dis* 2020; **20**:534. https://doi.org/10.1016/S1473-3099(20)30119-5.
4. Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, *et al*. **A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster.** *Lancet* 2020; **395**:514–523.
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al*. **Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.** *Lancet* 2020; **395**:507–513.

6. Rothan HA, Byrareddy SN. **The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak.** *J Autoimmun* 2020; **109**:102433.

7. P. Wu, X. Hao, E.H.Y. Lau, J.Y. Wong, K.S.M. Leung, J.T. Wu, *et al.*, Real-time tentative assessment of the epidemiological characteristics of novel coronavirus infections in Wuhan, China, as at 22 January 2020, Euro Surveill. 25 (2020).

8. Yin Y, Wunderink RG. **MERS, SARS and other coronaviruses as causes of pneumonia.** *Respirology* 2018; **23**:130–137.

9. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, *et al.* **From SARS to MERS, thrusting coronaviruses into the spotlight.** *Viruses* 2019; **11**:59.

10. Azami M, HafeziAhmadi MR, Sayehmiri K. **Hepatitis B vaccination efficacy in Iranian healthcare workers: a meta-analysis study.** *Hepat Mon* 2017; **17**:e37781. doi: 10.5812/hepatmon.37781.

11. Khalighi E, Tarjoman A, Abdi A, Borji M. **The prevalence of delirium in patients in Iran: a systematic review and meta-analysis.** *Future Neurol* 2019; **14**:378–389.

12. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.** *PLoS Med* 2009; **6**:e1000097.

13. Liu K-C, Xu P, Lv W-F, Qiu X-H, Yao J-L, Wei-Wei J-FG. **CT manifestations of coronavirus disease-2019: a retrospective analysis of 73 cases by disease severity.** *Eur J Radiol* 2020; **126**:108941.

14. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, *et al.* **Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women a retrospective review of medical records.** *Lancet* 2020; **395**:809–815.

15. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al.* **Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study.** *Lancet* 2020; **395**:1054–1062.

16. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, *et al.* **Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multicenter study in Wenzhou city, Zhejiang, Chin.** *J Infect* 2020; **80**:388–393.

17. Liu F, Xu A, Zhang Y, Xuan W, Yan T, Pan K, *et al.* **Patients of COVID-19 may benefit from sustained lopinavir-combined regimen and the increase of eosinophil may predict the outcome of COVID-19 progression.** *Int J Infect Dis* 2020; **95**:188–193.

18. Hsih W-H, Cheng M-Y, Ho M-W, Chou C-H, Lin P-C, Chi C-Y, *et al.* **Featuring COVID-19 cases via screening symptomatic patients with epidemiologic link during flu season in a medical center of central Taiwan**. *J Microbiol Immunol Infect.* 2020;**53**:459–466.

19. Chen J, Hu X, Chen L, *et al.* Clinical study of mesenchymal stem cell treatment for acute respiratory distress syndrome induced by epidemic influenza A (H7N9) infection: a hint for COVID-19 treatment, *Engineering.* 2020; 6:1153–1161.

20. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, *et al.* **Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered retrospective, observational study.** *Lancet Respir Med* 2020; **8**:475–481.

21. Sun K, Chen J, Viboud C. **Early epidemiological analysis of the coronavirus disease [2019outbreak] based on crowdsourced data: a population level observational study.** *Lancet Digital Health* 2020; **2**:201–208.

22. Liu W, Tao Z-W, Wang L, Yuan M-L, Liu K, Zhou L, *et al.* **Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease.** *Chinese Med J* 2020; **133**:1032–1038.

23. Huang] C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* **Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.** *Lancet* 2020; **395**:497–506.

24. Kui L, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, *et al.* **Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province.** *Chine Med J* 2020; **133**:1025–1031.

25. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, *et al.* **Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury.** *Sci China Life Sci* 2020; **63**:364–374.

26. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al.* **Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China.** *JAMA* 2020; **323**:1061–1069.

27. Zhang WJ, *et al.* **Clinical features of 2019 novel coronavirus pneumonia in the early stage from a fever clinic in Beijing.** *ZhonghuaJie He He Hu Xi ZaZhi* 2020; **43**:E013.

28. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al.* **Clinical characteristics of coronavirus disease 2019 in China.** *N Engl J Med* 2020; **382**:1708–1720.

29. Zhang J-J, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, *et al.* **Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China.** *Allergy* 2020; **00**:1–12.

30. Badawi A, Ryoo SG. **Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis.** *Int J Infect Dis* 2016; **49**:129–133.

31. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. **Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection.** *J Immunol* 2017; **198**:4046–4053.

32. Jaillon S, Berthenet K, Garlanda C. **Sexual dimorphism in innate immunity.** *Clin Rev Allergy Immunol* 2019; **56**:308–321.

33. Dryden M, Baguneid M, Eckmann C, Corman S, Stephens J, Solem C, *et al.* **Pathophysiology and burden of infection in patients with diabetes mellitus and peripheral vascular disease: focus on skin and soft-tissue infections.** *Clin Microbiol Infect* 2015; **21 (suppl 2)**:S27–S32.

34. Norooznezhad AH, Najafi F, Riahi P, Moradinazar M, Shakiba E, Mostafaei S. **Primary symptoms, comorbidities, and outcomes of 431 hospitalized patients with confirmative RT-PCR results for COVID-19.** *Am J Trop Med Hyg* 2020; **103**:834–837.

35. Emami A, Javanmardi F, Akbari A, Moghadami M, Bakhtiari H, Falahati F, *et al.* **Characteristics of deceased patients with CoVID-19 after the first peak of the epidemic in Fars province, Iran.** *Infect Ecol Epidemiol* 2020; **10**:1781330.