

## Prevalence of comorbidities in patients and mortality cases affected by SARS-CoV2: a systematic review and meta-analysis

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### ABSTRACT

The new coronavirus, COVID-19 was declared a pandemic by the World Health Organization on March 11, 2020. Risk factors associated with this disease are age, sex, and the presence of comorbidities, the most common being hypertension, diabetes, and heart disease. The aim of this meta-analysis was to calculate the prevalence and geographical distribution of comorbidities in all patients admitted to intensive care units (ICUs), and the mortality rate of COVID-19. We selected studies based upon epidemiological and clinical descriptions of the patients and mortality from the disease to determine the pooled prevalence of comorbidities in all patients and in mortality cases due to COVID-19. The pooled prevalence was estimated using the random effects model, and odds ratios were used to measure the probability of death for a patient with a comorbidity. The total prevalence of comorbidities in patients with COVID-19 was 42% (95% CI: 25-60), 61% (95% CI: 42-80) in those admitted to the ICU, and 77% (95% CI: 68-86) among death cases; males were the most affected. Hypertension was the most prevalent comorbidity in all three groups studied, accounting for 32%, 26%, and 35%, respectively. The odds ratio of death for a patient with a comorbidity compared to one with no comorbidity was 2.4 ( $P < 0.0001$ ). The higher the prevalence of comorbidities the higher the odds that the COVID-19 patient will need intensive care or will die, especially if the pre-existing disease is hypertension, heart disease, or diabetes.

**KEYWORDS:** COVID-19. SARS-CoV2. Prevalence. Comorbidity. Mortality. Meta-analysis.

### INTRODUCTION

The 2019 pandemic coronavirus (COVID-19) has affected more than three million people in 211 countries, causing more than two hundred thousand deaths as of the end of April 2020<sup>1</sup>. The etiologic agent of this disease is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), which is transmitted through contact with infected persons or contaminated fluids<sup>2,3</sup>.

Several risk factors are associated with this disease. In a multicenter cohort study, advanced age was found to be significantly correlated with overall COVID-19 prevalence, which is consistent with the higher incidence observed in older adults<sup>4</sup>. The sex is another risk factor as a higher prevalence has been seen in men than women<sup>4</sup>. Other studies have shown that the presence of any comorbidity increases the chances of COVID-19 infection causing respiratory failure and death in patients<sup>5</sup>. Another study reports that patients admitted to the intensive care unit (ICU) had a higher number of comorbidities (72.2%) than those not admitted to

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Received: 12 June 2020

Accepted: 12 June 2020

the ICU (37.3%)<sup>6</sup>. Hence, comorbidities are considered a risk factor for fatality, and data from other reports show up to a 90% prevalence of comorbidities in fatal cases<sup>7</sup>, with cardiovascular diseases, diabetes, hypertension, chronic obstructive pulmonary disease being the most prevalent known comorbidities in COVID-19 cases<sup>8</sup>.

Currently, several published studies describe the epidemiological and clinical characteristics of patients and mortality cases affected by COVID-19 in different parts of the world. For this reason, the aim of this meta-analysis was to estimate the prevalence and geographical distribution of comorbidities in all patients, in those admitted to the ICU, and in mortality cases affected by COVID-19 using the previously published data.

## METHODS

The protocol for this systematic review was published in the International Prospective Registry of Systematic Reviews (PROSPERO 2020: CRD42020182479) before its implementation. The protocol and the final report were developed based on the Cochrane Manual of Systematic Reviews of Interventions<sup>9</sup>.

### Review question

What is the prevalence of comorbidities in all patients, patients admitted to the ICU, and in fatal cases affected by the new coronavirus (COVID-19)?

### Inclusion criteria

This review considered studies that conducted epidemiological and clinical descriptions in patients and in fatal cases from different parts of the world, in order to determine the prevalence and geographic distribution of comorbidities in patients affected by COVID-19.

### Search strategy

An initial search limited to MEDLINE was performed using MeSH index terms and related keywords. This search was followed by an analysis of the words in the text of the title, abstract, and index terms used to describe the articles. A second search using all the identified keywords and index terms was conducted on May 15, 2020 using the following databases: Latin American and Caribbean Health Sciences Literature (LILACS), the bibliographic database of the US National of Medicine (Medline), the Elsevier database (EMBASE), Web of Science and SCOPUS. The MeSH Index Term search included COVID-19, SARS-CoV2,

prevalence, and comorbidity. As COVID-19 is a recent topic, thesis and dissertation papers have not yet been published and were not evaluated.

## Methodological quality assessment

The articles selected for data recovery were analyzed by two independent reviewers who assessed the methodological validity of each text before their inclusion in this review. The quality of the publications included were evaluated based on the criteria derived from the Grading of Recommendations Assessment, Development and Evaluation method (GRADE). Points were awarded to the studies if they did not present limitations in study design or execution (risk of bias), inconsistency of results, evidence based on indirect data, imprecision, and publication bias. A score of four to five points was considered as high quality, three points as moderate quality, and zero to two points as low quality.

### Data extraction

The data were added to the Review Manager (RevMan 5.3) for analysis. A data extraction table was created to assess the quality of demographic data, study location, sample size, number of cases, number of positives and the diagnostic test.

### Data synthesis

The random-effect model meta-analysis method was used to analyze the pooled prevalence of comorbidities in patients and in fatal cases affected by COVID-19 in different parts of the world. The heterogeneity among the studies was analyzed using the Higgins test ( $I^2$ ) that shows the percentage of variation among studies. These analyses were compiled by using the STATA software, version 12 (StataCorp LLC, Texas, USA). The Odds Ratio test, with a 95% Confidence Interval (95% CI), was calculated to measure the likelihood of death for a patient with a comorbidity compared to a patient without comorbidities.

## RESULTS

Our search resulted in 1,150 manuscripts related to the search strategies used. The search strategy used for each database was: BVS (Comorbidades OR Comorbidities OR Comorbilidades) AND (“Infecções por Coronavírus” OR “Coronavirus Infections” OR “Infecciones por Coronavirus”) OR (Betacoronavirus OR Betacoronavirus OR Betacoronavirus) OR (COVID-19) OR (SARS-CoV2); PUBMED (Comorbidity OR Comorbidities) AND

("Coronavirus Infections" OR Betacoronavirus OR COVID-19 OR SARS-CoV2); CINAHL (Comorbidity OR Comorbidities) AND ("Coronavirus Infections" OR Betacoronavirus OR COVID-19 OR SARS-CoV2); EMBASE 2 ('comorbidity'/exp OR comorbidity OR 'comorbidities'/exp OR comorbidities) AND ('coronavirus infection'/exp OR 'coronavirus infection' OR 'betacoronavirus'/exp OR betacoronavirus OR 'COVID 19'/exp OR ' COVID 19' OR 'sars cov2'); WEB OF SCIENCE (Comorbidit\* AND ("Coronavirus Infections" OR Betacoronavirus OR COVID-19 OR SARS-CoV2); SCOPUS (Comorbidit\* AND ("Coronavirus Infections" OR Betacoronavirus OR COVID-19 OR SARS-CoV2).

After applying the eligibility exclusion criteria (duplicate texts, articles related to other topics, text excluded by the review criteria or method quality), 42 studies were considered for analyses<sup>5-7,10-48</sup>. Of them, 39 were used to calculate the total prevalence of comorbidities in patients affected by COVID-19, six were used to calculate the prevalence of comorbidities in patients admitted to the ICU, and 11 were used to calculate the comorbidity prevalence in fatal cases. The characteristics of the studies included in this meta-analysis are shown in Table 1. The results of the search strategy are shown in a PRISMA flow chart (Figure 1). The data extracted from the final selection are shown in the Supplementary Table S1.

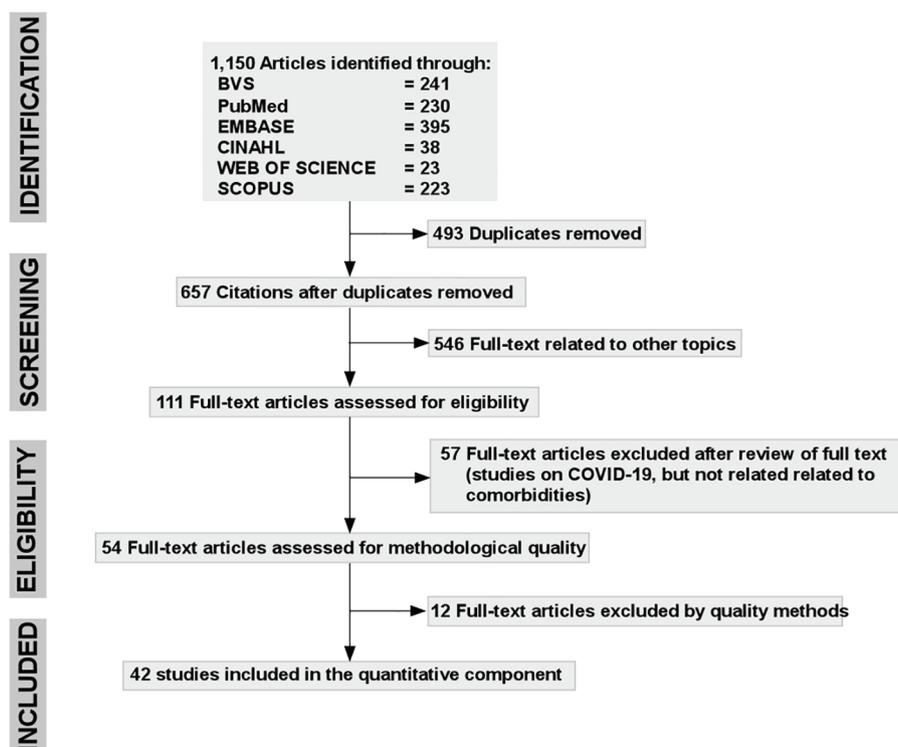
According to the criteria applied based on GRADE, the studies that met the selection criteria presented high

methodological quality with a score of five. The  $I^2$  test indicated a low heterogeneity among the studies. Publication bias was not evaluated because the currently available methods are not considered useful for studies on proportions. The summaries of methodological quality and bias risk and applicability for each study and among the included studies are shown in the Supplementary Figures S1 and S2.

### Overall prevalence of comorbidities

In the 39 studies used to calculate the pooled prevalence of comorbidities, 89,238 patients affected by COVID-19 were analyzed; 11,341 (12.7%) presented one or more comorbidities, 2,172 (2.4%) were admitted to the ICU, and 3,532 (4 %) patients died. The patients age range was 41 to 70 years. Among these studies, only one was conducted in the USA<sup>43</sup>, and included a large number of patients (74,439) but did not segregate patients according to sex. In the other 38 studies, 14,844 patients were registered with a total of 8,518 (57.4%) males and 6,413 (42.6%) females. The reported comorbidities included hypertension, heart disease, diabetes, cancer, chronic obstructive pulmonary disease, asthma, chronic diseases of the liver, kidneys, digestive system, autoimmune disorders, immunodeficiencies, stroke, and others. Only one study specified which diseases were included in the category "Others".

Regarding the geographical distribution of the studied patients, 80,139 (88.7%) were in the USA and 9,051



**Figure 1** - A flowchart of the steps performed in the systematic review.

**Table 1** - A summary of the included studies.

Study	Country	Total	ICU	Death	M	F	Co %	H %	CV %	D %	COPD %
<i>Chen et al.</i> <sup>5</sup>	China	99	N.S.	11	67	32	50.5	0.0	+40	0.0	1.0
<i>Wang et al.</i> <sup>6</sup>	China	138	36	6	75	63	46.4	31.2	14.5	10.1	2.9
CDC Korea <sup>7</sup>	Korea	54	N.S.	54	33	21	90.7	0.0	59.3	29.6	13.0
<i>Cheng et al.</i> <sup>10</sup>	China	698	138	113	367	331	42.6	33.4	0.0	14.3	1.9
<i>Huang et al.</i> <sup>11</sup>	China	41	13	N.S.	30	11	31.7	15.0	6.0	8.0	1.0
<i>Liu et al.</i> <sup>12</sup>	China	137	13	16	61	76	19.7	9.5	7.3	10.2	17.5
<i>Liu et al.</i> <sup>13</sup>	China	12	6	N.S.	7	5	58.3	25.0	33.3	16.6	8.3
<i>Guan et al.</i> <sup>14</sup>	China	1099	33	15	640	459	23.7	15.0	2.5	7.4	1.1
<i>Du et al.</i> <sup>15</sup>	China	109	51	72	74	35	78.0	59.6	+33.9	31.2	15.6
<i>Guan et al.</i> <sup>16</sup>	China	1590	99	50	904	686	25.0	20.3	3.8	9.0	1.5
<i>Xu et al.</i> <sup>17</sup>	China	63	1	0	36	27	31.7	8.0	0.0	2.0	2.0
<i>Chen et al.</i> <sup>18</sup>	China	203	N.S.	26	108	95	43.3	12.9	3.4	2.7	3.9
<i>Liang et al.</i> <sup>19</sup>	China	1590	90	50	904	674	25.1	16.9	3.7	8.2	1.5
<i>Wang et al.</i> <sup>20</sup>	China	399	N.S.	65	226	173	60.7	40.8	17.7	16.0	6.2
<i>Cao et al.</i> <sup>21</sup>	China	102	N.S.	17	53	49	46.1	27.5	4.9	10.8	9.8
<i>Zhou et al.</i> <sup>22</sup>	China	191	50	54	119	72	47.6	30.0	8.0	19.0	3.0
<i>Zhang et al.</i> <sup>23</sup>	China	120	N.S.	7	43	77	26.7	16.0	8.0	6.0	3.0
<i>Chen et al.</i> <sup>24</sup>	China	274	N.S.	113	171	103	48.5	34.0	8.0	17	7.0
<i>Zhang et al.</i> <sup>25</sup>	China	140	N.S.	N.S.	71	69	64.3	30.0	5.0	12.1	1.4
<i>Wang et al.</i> <sup>26</sup>	China	69	N.S.	5	32	37	36.2	13.0	12.0	10.0	6.0
<i>Yang et al.</i> <sup>27</sup>	China	52	37	32	35	17	40.4	0.0	10.0	17.0	8.0
<i>Wu et al.</i> <sup>28</sup>	China	201	53	44	128	73	32.8	19.4	4.0	10.9	2.5
<i>Huang et al.</i> <sup>29</sup>	China	34	8	N.S.	20	14	47.1	23.5	17.6	11.8	2.9
<i>Li et al.</i> <sup>30</sup>	China	83	6	N.S.	44	39	18.1	6.0	1.2	7.8	6.0
<i>Xu et al.</i> <sup>31</sup>	China	90	N.S.	N.S.	39	51	50.0	19.0	3.0	6.0	1.0
<i>Wu et al.</i> <sup>32</sup>	China	80	0	0	39	41	47.5	0.0	+31.2	6.2	1.2
<i>Yang et al.</i> <sup>33</sup>	China	149	0	0	81	68	34.9	0.0	+18.7	6.0	0.7
<i>Liu et al.</i> <sup>34</sup>	China	3	N.S.	N.S.	2	1	33.3	0.0	0.0	33.3	33.3
<i>Lei et al.</i> <sup>35</sup>	China	34	15	7	14	20	58.8	58.8	20.6	23.5	2.9
<i>Feng et al.</i> <sup>36</sup>	China	476	N.S.	38	271	205	43.1	0.0	8.0	10.3	4.6
<i>Yuan et al.</i> <sup>37</sup>	China	27	N.S.	10	12	15	48.1	19.0	11.0	22.0	0.0
<i>Mo et al.</i> <sup>38</sup>	China	155	N.S.	N.S.	86	69	45.8	23.9	9.7	9.7	3.2
<i>Wang et al.</i> <sup>39</sup>	China	116	11	7	67	49	44.0	37.1	0.0	15.5	0
<i>Zhang et al.</i> <sup>40</sup>	China	221	23	12	108	113	35.3	24.4	10	10	2.7
<i>Guo et al.</i> <sup>41</sup>	China	256	45	43	91	165	73.0	32.6	11.2	15.0	2.1
<i>Richardson et al.</i> <sup>42</sup>	USA	5700	373	553	3437	2263	93.9	56.6	11.1	33.8	5.4
<i>Chow et al.</i> <sup>43</sup>	USA	74439	1069	2112	N.S.	N.S.	3.6	0.0	9.0	10.9	9.2
<i>Young et al.</i> <sup>44</sup>	Singapore	18	2	0	9	9	27.8	N.S.	N.S.	N.S.	N.S.
<i>Gupta et al.</i> <sup>45</sup>	India	21	N.S.	N.S.	14	7	28.6	23.8	0.00	14.2	0.0
<i>Grasselli et al.</i> <sup>46</sup>	Italy	1591	1591	N.S.	1304	287	65.5	49.0	21.0	17.0	4.0
<i>Du et al.</i> <sup>47</sup>	China	85	N.S.	85	23	62	68.2	37.6	11.8	22.4	2.5
CDC Korea <sup>48</sup>	Korea	7755	N.S.	66	37	29	96.8	47.6	15.9	36.5	17.5

ICU = Intensive Care Unit; M = Male; F = Female; Co. % = Percentage of patients with comorbidities; H % = Percentage of Chronic Heart Disease; CV % = Percentage of Cardiovascular Disease; D % = Percentage of Diabetes; COPD % = Percentage of Chronic Obstructive Pulmonary Disease; CDC = Center for Disease Control and Prevention; + = Cardiovascular and Cerebrovascular Disease; N.S. = Not Specified

(10.1%) in China. This study also included 21 cases from India, 54 from South Korea, and 18 from Singapore, representing less than 1% of the total patients included.

The analysis of the general population affected by COVID-19 indicated a 42% pooled prevalence of comorbidities (95% CI: 25-60; weight 100%). In China, the geographical distribution analysis showed a 43% prevalence of comorbidities (95% CI: 37-48; weight 89.4%), followed by the USA with 8% (95% CI: 7-8; weight 5.34%), India 29% (95% CI: 14-50; weight 2.59%), and Singapore 28% (95% CI: 12 -51; weight 2.58%) (Figure 2).

Among those who had one or more previous diseases, there was a total of 16,222 comorbidities. Hypertension was the most prevalent in 32% (95% CI: 31-33; weight 6.54%), followed by diabetes 22% (95% CI: 21-23; weight 6.57%), heart disease 13% (95% CI: 13-14; weight 6.62%), and Chronic Obstructive Pulmonary Disease (COPD) 8%

(95% CI: 7-8; weight 6.65%). In addition to these, other comorbidities were also assessed, such as kidney disease (5%), cancer (3%), asthma (3%), liver disease (2%), stroke (2%), immunodeficiencies (2%), and others (8%). The pooled prevalence with 95% CI values for each disease are shown in Table 2.

Prevalence of comorbidities in ICU patients

Of the six studies that conducted descriptions of the epidemiological and clinical profiles in patients admitted to the ICU, five divided the data according by sex. In these five studies, 1,661 patients were described<sup>6,11,13,36,48</sup>. Among these patients, 1,345 (81%) were male, 316 (19%) were female, and the age range was 46 to 63 years. The clinical characteristics of 2,730 patients were also described, indicating that 1,449 (53%) had one or more comorbidities.

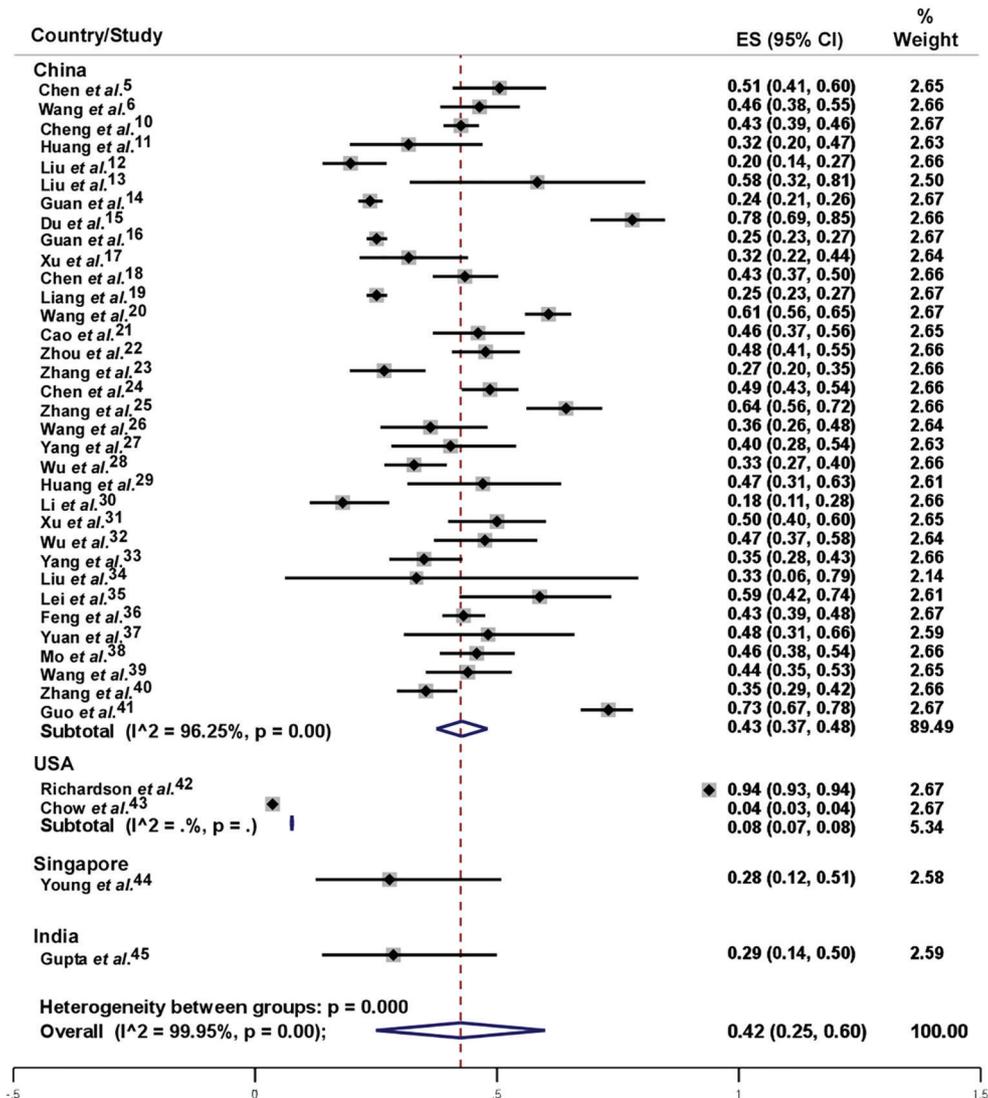


Figure 2 - Forest plot for a random-effect meta-analysis of comorbidities in all the patients affected by COVID-19.

**Table 2** - Overall prevalence of comorbidities, in the group admitted to the ICU and in the fatal cases by COVID-19.

Comorbidity	Overall Prevalence			ICUs Patients			Fatal Cases		
	PP	95% CI	W %	PP	95% CI	W %	PP	95% CI	W %
Hypertension	32	31 - 33	6.54	27	25 - 29	6.86	35	31- 38	8.10
Chronic Heart Disease	13	13 - 14	6.62	18	18 - 19	7.15	17	14 - 20	8.61
Diabetes	22	21 - 23	6.57	17	15 -19	7.17	19	16 - 22	8.53
Malignancy	3	3 - 4	6.68	5	4 - 6	7.81	5	4 -7	9.22
COPD	8	7 - 8	6.65	7	6 - 8	7.67	9	7 -11	9.03
Asthma	3	3 - 3	6.69	0	0 - 0	0.00	0	0 - 0	0.00
Chronic Kidney Disease	5	5 - 5	6.67	5	6 - 8	7.81	4	3 - 6	9.29
Chronic Liver Disease	2	1 - 2	6.7	2	4 - 6	8.01	3	2 - 4	9.42
Cerebrovascular Accident	2	1 - 3	6.7	1	1 - 2	8.05	6	5 - 9	9.15
Immunodeficiency	2	2 - 3	6.69	2	1 - 3	7.97	0	0 - 0	0.00
Autoimmune Disease	0	0 - 0	6.71	0	0 - 0	8.12	0	0 - 1	9.57
Cardiovascular and Cerebrovascular Accident	1	1 - 1	6.71	0	0 - 0	0.00	0	0 - 0	0.00
Digestive Disease	0	0 - 0	6.71	0	0 - 1	8.11	0	0 - 1	9.60
Peripheral Vascular Disease	0	1 - 0	6.71	0	0 - 0	8.12	0	0 - 0	0.00
Other	8	7 - 8	6.65	18	16 - 19	7.15	2	1 - 3	9.48
<b>Overall</b>	<b>7</b>	<b>5 - 8</b>	<b>100</b>	<b>7</b>	<b>6 - 8</b>	<b>100</b>	<b>9</b>	<b>6 - 11</b>	<b>100</b>

ICU = Intensive Care Unit; PP = Pooled Prevalence; W = Weight; COPD = Chronic Obstructive Pulmonary Disease; CI = Confidence Interval.

In total, there were 2,050 comorbidities among patients admitted to the ICU.

The pooled prevalence of comorbidities in ICU patients was 61% (95% CI: 42-80; weight 100%). The geographical distribution analysis showed a 69% prevalence of comorbidities (95% CI: 52-86; weight 61.09%) in China, followed by Italy, with 66% (95% CI: 63-68; weight 19.47%), and the USA, with 33% (95% CI: 31-36; weight 19.44%). The forest plot for a random-effect meta-analysis of comorbidities in patients admitted to ICUs by COVID-19, are shown in the [Supplementary Figure S3](#).

The most prevalent comorbidities in the ICU population were hypertension 26% (95% CI: 25-29; weight 6.86%), heart disease 18% (95% CI: 16-19; weight 7.15%), diabetes 17% (95% CI: 16-19; weight 7.17%), and others 17% (95% CI: 16-19; weight 7.15%). In addition to these diseases, patients with COPD (7%), cancer (5%), kidney disease (5%), liver disease (2%), and stroke (1%) were also evaluated. The pooled prevalence with the 95% CI values for each disease is shown in [Table 2](#).

#### Prevalence of comorbidities among mortality cases

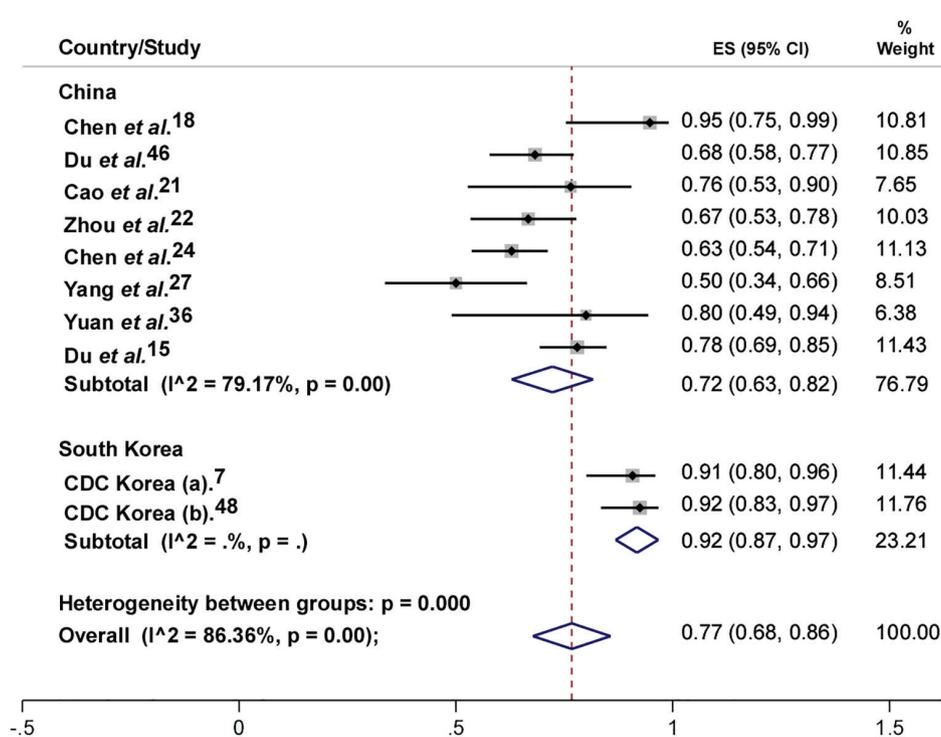
Eleven studies included descriptions of the epidemiological and clinical profiles of a total of 624 cases

of mortality. In these studies, 394 patients were males and 218 females, with an age range between 64 and 70 years. Among the 624 fatal cases, 415 of the patients had one or more previous diseases, totaling 751 comorbidities. The pooled prevalence of comorbidities among the fatal cases was 77% (95% CI: 68-86; weight 100%). Only two countries were analyzed in the geographical distribution: China, with 71% (95% CI: 63-82; weight 76.79%) and Korea, with 92% (95% CI: 87-97; weight 23.21%) ([Figure 3](#)).

The most prevalent comorbidities in this population were hypertension 35% (95% CI: 25-29; weight 8.10%), diabetes 19% (95% CI: 16-22; weight 8.53%), heart disease 17% (95% CI: 14-20; weight 8.61%), and COPD 9% (95% CI: 7-11; weight 9.22%). In addition to these diseases, patients with cerebrovascular accident (6%), cancer (5%), kidney disease (4%), liver disease (3%), and other (2%) were also evaluated. The pooled prevalence with 95% CI values for each disease is shown in [Table 2](#).

#### Odds ratio

The probability of a patient with comorbidity of dying from COVID-19, and the significance of this associations using the Fisher's exact test, were calculated. The number of patients with comorbidities who died and those who



**Figure 3** - Forest plot for a random-effect meta-analysis of comorbidities in fatal cases of COVID-19.

survived, in addition to the patients without comorbidities who died and who survived, were used to calculate an odds ratio of 2.4 with 95% CI 1.7-3.3 and in the Fisher's exact test the value of  $P < 0.0001$ .

## DISCUSSION

This meta-analysis was based on 42 studies, including a large number of descriptions from China and the United States. Studies conducted in India, Italy, the United Kingdom, South Korea, and Singapore were also analyzed. A higher prevalence of male patients infected with COVID-19 was observed compared to females. This predisposition of the male sex was also observed in the diseases MERS-CoV and SARS-Co, which are also caused by viruses of the coronavirus family<sup>49,50</sup>.

The pooled prevalence of comorbidities in the general population of patients affected by the new coronavirus (COVID-19) was 42% (95% CI: 26–59). China was the country with the highest prevalence, although there were also more studies analyzed from this country. However, it is important to highlight that two studies from the United States resulted in contrasting prevalence values (4% and 94%). Since the United States is the country that leads the statistics so far with the highest number of confirmed cases (more than one million) and deaths from coronavirus (more than seventy thousand), on May 8, 2020, it is of utmost importance to publish

more data on the clinical characteristics of the disease in this country.

The results of this study confirm that the prevalence of comorbidities increases as the patient's clinical conditions worsens. In the general population affected by COVID-19, the prevalence of comorbidities was 42%, 61% among patients admitted to the ICU, and 77% among fatal cases. Males were the most affected in the three groups. On the other hand, the mean age also increases when we compare the group of patients in general with the group of fatal cases, as previously described among risk factors such as age, sex, and comorbidities<sup>4-7</sup>.

Regarding comorbidities, in the three groups analyzed (general population, admission to ICU, and fatal cases), hypertension was the most prevalent comorbidity, accounting for 32%, 26%, and 35%, respectively. In the general population, diabetes was the second-most prevalent (22%) comorbidity, followed by heart disease (13%) and COPD (8%). However, in patients admitted to the ICU, diabetes (17%) and heart disease (18%) showed similar values. The same phenomenon was observed in fatal cases, with diabetes (19%), and heart disease (17%) showing similar values. Considering that type 1 diabetes mellitus usually manifests during childhood or adolescence, type 2 diabetes frequently manifests in adults, and heart diseases are more prevalent in older patients, one may think that the earlier onset of diabetes may account for it to rank second among the comorbidities in the general population affected

by COVID-19. On the other hand, the group of fatal cases is composed of predominantly older adults, a population in which hypertension, diabetes, and heart disease are prevalent.

The odds ratio for any comorbidity was 2.4 with 95% CI 1.7-3.3 with a statistical significance of  $P < 0.0001$ . In other words, a patient with a comorbidity has 2.4 times the chance of dying from COVID-19 compared to a patient without a comorbidity. This may explain the high prevalence of comorbidities among fatal cases,

In developing this study, we encountered several limitations. Firstly, not all studies segregated epidemiological and clinical data (age, sex, percentage of comorbidity, and patients hospitalized in the ICU). Secondly, some studies classified comorbidities in the "Other" category, but only one study described which diseases were comprised in this category. Thirdly, since China is the primary focus of the rise of the pandemic, most of the studies included were from this country. No studies from Africa, Oceania, or Latin America were found. Finally, in meta-analyses, it is recommended that publication bias are always assessed by statistical methods. However, currently available methods, such as the funnel plot and the Egger regression test, are not considered useful tools in studies on proportions<sup>51</sup>.

One can conclude that the existence of comorbidities increases the probability of dying from COVID-19 by 2.4 times compared to those who do not have pre-existing conditions. The most relevant comorbidities were shown to be hypertension, heart disease, and diabetes. Thus, comorbidities are more prevalent in the group of mortality cases when compared to the general population group. However, these conclusions are based on the evidence obtained, mostly from studies conducted in China. For this reason, studies describing the epidemiological and clinical profiles of COVID-19 cases in Africa, Oceania, and Latin America are recommended to clarify the behavior of this disease in these regions, and, thus, be able to apply effective measures aimed at safeguarding populations at risk.

## AUTHORS' CONTRIBUTIONS

OAE and ASZ contributed to create and design the study, analyze, and interpret the data, and write the first and final version of the manuscript; EFA, FGL, TAM and PFB contributed to analyze data and wrote the first version of the manuscript. All authors approved the final version of the manuscript and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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## SUPPLEMENTARY MATERIAL

**Table S1** - PRISMA Checklist.

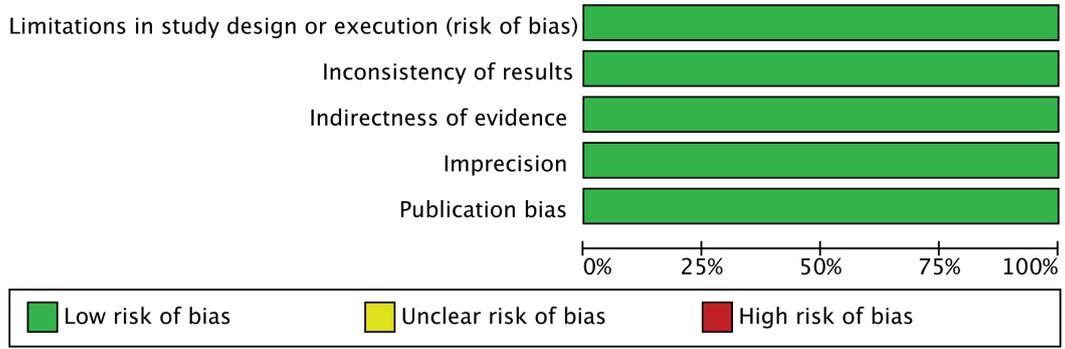
Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction and Methods: Review Question.
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Methods
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Methods: Inclusion Criteria
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Methods: Search Strategy

**Table S1** - PRISMA Checklist (cont.).

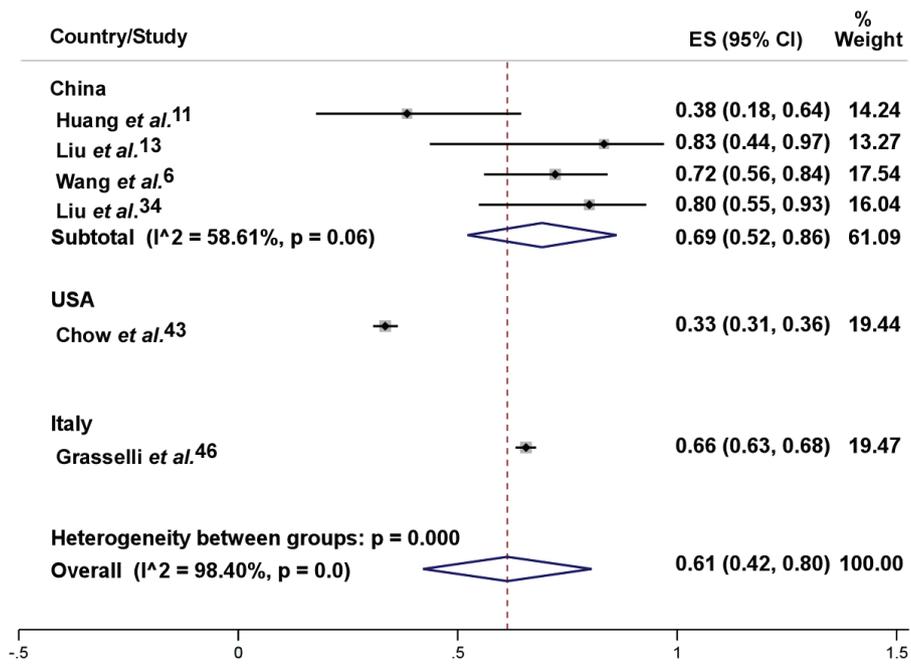
Section/topic	#	Checklist item	Reported on page #
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Methods: Search Strategy
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Methods: Study Strategy
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Methods: Data extraction
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Methods: Data extraction/Quality assessment
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Additional File. Figure S1.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Methods: Data Synthesis
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	Methods: Data Synthesis
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Additional File. Figure S2.
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Methods: Data Synthesis
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Results (Figure 1)
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Results (Table 1)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Additional File. Figure S2 and Figure S1.
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Results. Figure 2, 3 and 4.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Results (Figures 2, 3 and 4)
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Additional File. Figure S2.
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Results (Odds Ratio)
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Discussion
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Conclusion
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA

	Limitations in study design or execution (risk of bias)	Inconsistency of results	Indirectness of evidence	Imprecision	Publication bias
Cao <i>et al.</i> <sup>21</sup>	+	+	+	+	+
CDC Korea (a) <sup>7</sup>	+	+	+	+	+
CDC Korea (b) <sup>48</sup>	+	+	+	+	+
Chen <i>et al.</i> <sup>5</sup>	+	+	+	+	+
Chen <i>et al.</i> <sup>18</sup>	+	+	+	+	+
Chen <i>et al.</i> <sup>24</sup>	+	+	+	+	+
Cheng <i>et al.</i> <sup>10</sup>	+	+	+	+	+
Chow <i>et al.</i> <sup>43</sup>	+	+	+	+	+
Du <i>et al.</i> <sup>15</sup>	+	+	+	+	+
Du <i>et al.</i> <sup>47</sup>	+	+	+	+	+
Feng <i>et al.</i> <sup>36</sup>	+	+	+	+	+
Grasselli <i>et al.</i> <sup>46</sup>	+	+	+	+	+
Guan <i>et al.</i> <sup>14</sup>	+	+	+	+	+
Guan <i>et al.</i> <sup>16</sup>	+	+	+	+	+
Guo <i>et al.</i> <sup>41</sup>	+	+	+	+	+
Gupta <i>et al.</i> <sup>45</sup>	+	+	+	+	+
Huang <i>et al.</i> <sup>11</sup>	+	+	+	+	+
Huang <i>et al.</i> <sup>29</sup>	+	+	+	+	+
Lei <i>et al.</i> <sup>35</sup>	+	+	+	+	+
Liang <i>et al.</i> <sup>19</sup>	+	+	+	+	+
Li <i>et al.</i> <sup>30</sup>	+	+	+	+	+
Liu <i>et al.</i> <sup>12</sup>	+	+	+	+	+
Liu <i>et al.</i> <sup>13</sup>	+	+	+	+	+
Liu <i>et al.</i> <sup>34</sup>	+	+	+	+	+
Mo <i>et al.</i> <sup>38</sup>	+	+	+	+	+
Richardson <i>et al.</i> <sup>42</sup>	+	+	+	+	+
Wang <i>et al.</i> <sup>6</sup>	+	+	+	+	+
Wang <i>et al.</i> <sup>20</sup>	+	+	+	+	+
Wang <i>et al.</i> <sup>26</sup>	+	+	+	+	+
Wang <i>et al.</i> <sup>39</sup>	+	+	+	+	+
Wu <i>et al.</i> <sup>28</sup>	+	+	+	+	+
Wu <i>et al.</i> <sup>32</sup>	+	+	+	+	+
Xu <i>et al.</i> <sup>17</sup>	+	+	+	+	+
Xu <i>et al.</i> <sup>31</sup>	+	+	+	+	+
Yang <i>et al.</i> <sup>27</sup>	+	+	+	+	+
Yang <i>et al.</i> <sup>33</sup>	+	+	+	+	+
Young <i>et al.</i> <sup>44</sup>	+	+	+	+	+
Yuan <i>et al.</i> <sup>37</sup>	+	+	+	+	+
Zhang <i>et al.</i> <sup>23</sup>	+	+	+	+	+
Zhang <i>et al.</i> <sup>25</sup>	+	+	+	+	+
Zhang <i>et al.</i> <sup>40</sup>	+	+	+	+	+
Zhou <i>et al.</i> <sup>22</sup>	+	+	+	+	+

**Figure S1** - The methodological quality summary bias risk concern and applicability for each study.



**Figure S2** - The methodological quality summary bias risk concern and applicability for across the included studies.



**Figure S3** - The forest plot for a random-effect meta-analysis of comorbidities in patients admitted in ICUs.