Prevalence of comorbidities in deceased patients with COVID-19
A systematic review

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Methods: This was a systematic review of the literature for observational studies published between December 2019 and September 2020. The protocol for this systematic review was registered in the International prospective register of systematic reviews (PROSPERO) under the number CRD42020176249.

Results: In the 31 studies analyzed, a total of 421,872 (100%) patients were infected with COVID-19, and, of these, 45,399 (10.8%) died. The 3 most prevalent comorbidities were hypertension, diabetes mellitus, and respiratory diseases, respectively. The cure/recovery rate was 89.2% (376,473).

Conclusion: This review revealed a high percentage of comorbidities in the patients with COVID-19, especially those who died.

Abbreviations: ACE = angiotensin converting enzyme, Ang II = angiotensin II, AT1R = angiotensin type 1 receptor, CD = cardiovascular disease, COVID-19 = Corona Virus Disease 2019, DM = diabetes mellitus, ICAM = intercellular adhesion molecule, ICU = intensive care unit, LILACS = Literatura Latino-americana e do Caribe em Ciências da Saúde, NOS = Newcastle-Ottawa, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PROSPERO = International prospective register of systematic reviews, SAH = systemic arterial hypertension, SARS-CoV-2 = Severe Acute Respiratory Syndrome Coronavirus 2, USA = United States of America, VCAM = vascular cell adhesion molecule, WHO = World Health Organization.

Keywords: comorbidities, COVID-19, hospitalization, mortality.

1. Introduction
In December 2019, the outbreak of coronavirus disease (COVID-19) put several countries on a state of alert. Initially, infection by COVID-19, formerly known as 2019-nCoV°, was shown to be not only from exotic animals in Wuhan, in the province of Central China, but also from community transmission.

This disease is an acute disease with a proportion of cases resulting in death due to massive alveolar damage and progressive respiratory failure. In addition, it has been shown to be highly infectious, and the ongoing outbreak has been declared by the World Health Organization - WHO (2020) a global public health emergency, affecting 197 countries worldwide.²,³

According to the WHO (2020), by the end of the first week of October, the disease had already infected 35,659,007 people worldwide. Of these, 1,044,269 died, amounting to approximately 3% of the total. The region with the highest number of infections and deaths is the Americas, and Southeast Asia is second in the number infected, followed by Europe. However, regarding deaths, Europe shows the highest number, being in second place.⁴

The United States of America (USA) leads the ranking with 7,380,326 cases of infection and 208,787 deaths from COVID-19. Brazil remained in second place for a long time, but there has
been a significant increase in the number of cases in India, which has risen to second place with 6,757,131 infected, followed by Brazil with 4,927,235 infected. In terms of deaths, Brazil comes in second with 146,675 deaths, followed by India with 104,555.[4]

Once infected by the virus, the patient may experience a worsening of the disease, leading to hospitalization in an intensive care unit (ICU) and possible death. Thus, several factors may be related to a higher risk of mortality in patients with COVID-19, such as gender, age, and chronic diseases.

Many aspects and factors that contribute to the disease are still unknown and need to be studied in depth. A systematic review is required to investigate the association between COVID-19 infections and specified chronic nontransmissible disease in patients who have died.

2. Methods

Systematic literature review of observational studies published between December 2019 and September 2020. The study was prepared in accordance with the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), without language restrictions. The protocol for this systematic review is registered in the International prospective register of systematic reviews (PROSPERO) as number CRD42020176249.

2.1. Inclusion criteria

The inclusion criteria were summarized as follows: cross-sectional studies, retrospective cohort studies, and case studies without any language restrictions that addressed the relationship between comorbidities and death in patients with COVID-19 of any age. In addition, studies published between December 1, 2019, and September 1, 2020, were considered. We excluded review articles and articles that did not present data on the characteristics of comorbidities in patients with COVID-19 who died.

2.2. Search strategy

The virtual search was performed on PubMed, EMBASE, Scopus, and LILACS databases on September 1, 2020, using a search strategy involving combinations of the descriptors and synonyms shown in Table 1.

2.3. Screening and selection of studies

Two researchers (DJ and KC), independently, conducted the screening and selection of studies. Initially, the screening of the records identified through the database search was performed by reading the title and the abstract. Then, the full text of each article was analyzed.

2.4. Data extraction

The data were extracted according to a spreadsheet previously prepared and standardized that contained fields for the collection of the following data: authors’ names, year of publication, country, study design, age of participants, sex and comorbidities among infected people, deaths, recoveries, and the main results.

2.5. Methodological quality

The methodological quality of the studies was evaluated using the Newcastle-Ottawa (NOS) scale, which is designed for cohort studies and includes 8 items related to selection, comparison, and results. Items related to selection and results can receive a star. For comparison, 2 stars can be assigned. Thus, each study can receive a total score of up to 9 points (stars). Studies with scores ≥6 have been classified as having good methodological quality.[5]

2.6. Database search result

The virtual database search recovered 2110 studies. After evaluation by title and abstract reading, 149 studies were left for eligibility evaluation via full-text reading. Of these, 28 were duplicated, and 90 did not meet the eligibility criteria; ultimately, 31 studies were included in the systematic review as shown in Figure 1.

2.7. Quality of studies

All studies included in the review were of good quality. In this sense, 18 studies received 9 stars, and 13 studies received 8 stars. Table 2 presents the methodological quality of the studies included in the review.

2.8. Ethics and dissemination

The information obtained for the purpose of this study was of a secondary character and was obtained through studies published in the literature; hence, it was not necessary to use personal data, and appreciation of the Research Ethics Committee was not required.

### Table 1

Search strategy used in databases.

| Databases | Combinations | Descriptors |
|-----------|--------------|-------------|
| PubMed, EMBASE, Scopus, and LILACS | (#1 OR #2 OR #3 OR #4) AND (#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12) AND (#13 OR #14 OR #15)) | #1 COVID-19 #2 COVID19 #3 2019-nCoV disease #4 coronavirus disease 2019 #5 comorbidity #6 Chronic Disease #7 Chronic Diseases #8 Chronic Illness #9 Chronic Illnesses #10 Illness #11 Illnesses #12 Chronic #13 mortality #14 Mortalities #15 Death |
2.9. Characteristics of the studies

The selected studies were carried out between December 1, 2019, and September 1, 2020. Regarding the type of studies included in the review, 29 were retrospective, and 1 was prospective. Regarding the research site, 16 studies were conducted in China (Mingli et al, 2020; Zhou et al, 2020; Deng et al, 2020; Chen T et al, 2020; Zhang et al, 2020; Rong-Hui et al, 2020; Tao et al, 2020; Yang et al, 2020; Chen L et al, 2020; Li et al, 2020; Gao et al, 2020; Yang et al, 2020; Asfahan et al, 2020; Liu et al, 2020; Tu et al, 2020; Wang et al, 2020), the first country to record cases of COVID-19, 2 were conducted in Italy (Ciardullo et al., 2020; Zanella et al, 2020), 3 in the United States (Smith et al, 2020; Chilimuri et al, 2020; Gerwen et al, 2020), 3 in Iran (Nikpouraghdam et al, 2020; Zandkarimi et al, 2020; Rastad et al, 2020), 1 in South Africa (Boule et al, 2020), 2 in Spain (Pérez et al, 2020; Borobia et al, 2020), 1 in Georgia (Shan et al, 2020), 1 in South Korea (Hwang et al, 2020), 1 in Brazil (Soares et al, 2020), and 1 in Mexico (Parra-Bracamonte et al, 2020). Chart 1 presents the main characteristics of the studies.

Regarding the study variables, the age group was 0 (Asfahan et al, 2020) to 91 years (Chen T et al, 2020). Considering gender, 21 of the 31 studies included more men than women (Zhou et al, 2020; Chen et al, 2020; Rong-Hui et al, 2020; Tao et al, 2020; Nikpouraghdam et al, 2020; Yang et al, 2020; Zandkarimi et al, 2020; Chen et al, 2020; Ciardullo et al, 2020; Smith et al, 2020; Chilimuri et al, 2020; Gerwen et al, 2020; Pérez et al, 2020; Li et al, 2020; Asfahan et al, 2020; Liu et al, 2020; Rastad et al, 2020; Parra-Bracamonte et al, 2020; Soares et al, 2020; Zanella et al, 2020), as shown in Chart 1.

Chart 2 shows that the samples ranged from 27 (Mingli Y et al, 2020) to 331,298 participants (Parra-Bracamonte et al, 2020). The percentage of deaths ranged from 2% (Asfahan S et al, 2020) to 61% (Yang X et al, 2020), and comorbidities in deaths ranged between 23.2% (Rastad H et al, 2020) and 100% (Gao S et al, 2020).

3.0. Characteristics of participants who died from SARS-CoV-2: association between infected and deaths

In the 31 studies analyzed, a total of 421,872 (100%) patients were infected with COVID-19, and, of these, 45,399 (10.8%) died. This reveals a cure/recovery rate of 376,473 (89.2%). Death rates varied broadly, ranging from higher values of 48% (Zanella A et al, 2020) and 61% (Yang X et al, 2020) to lower values of 2% (Asfahan S et al, 2020), 3% (Boulle A et al, 2020), and 8% (Nikpouraghdam, M et al, 2020, and Zandkarimi E et al, 2020).

For those infected and having at least one comorbidity, death rates of 79% (Borobia AM et al, 2020), 77% (Chilimuri S et al, 2020) and 76% (Li J et al, 2020 and Gao S et al, 2020) were observed. The lower percentages of infected and having at least one comorbidity reported were 25% (Rastad H et al, 2020) and 37% (Zhang J et al, 2020 and Liu J et al, 2020).

The panel of comorbidities among those infected by COVID-19 comprised 421,872 patients, of whom 45,399 died and were represented by the following conditions ordered by numbers of deaths: systematic hypertension (19,619); diabetes mellitus (16,276); respiratory disease (3327); renal disease (3126); cardiovascular disease (1672); and malignancy (477). Regarding the association of age and comorbidities in patients who died from SARS-CoV-2, mention was made in 27 studies (Mingli Y et al, 2020; Zhou F et al 2020; Deng Y et al, 2020; Chen T et al, 2020; Zhang J et al, 2020; Rong Hui Du et al, 2020).
In the 16 studies conducted in China (Mingli Yuan et al, 2020; Zhou F et al, 2020; Deng Y et al, 2020; Chen T et al, 2020; Zhang J et al, 2020; Rong-Hui Du et al, 2020; Tao Chen et al, 2020; Chen L et al, 2020; Li J et al, 2020; Gao S et al, 2020; Yang Q et al, 2020; Asfahan S et al, 2020; Liu J et al, 2020; Tu WJ et al, 2020; Wang L et al, 2020), the lowest average age among studies was 64.6 years (Yang X et al, 2020), while the highest was 76 years (Wang L et al, 2020). It should also be noted that the minimum age was 15 years, and the maximum age was 90 years.

In connection with gender, there were 5 studies in which females were in higher proportion (Mingli Yuan et al, 2020; Zhang J et al, 2020; Gao S et al, 2020; Tu WJ et al, 2020; Wang L et al, 2020), and one study had 50% male and 50% female (Yang Q et al, 2020). Regarding the comorbidities of the studies in China, the following aggravations panorama was perceived: systemic hypertension (433); cardiovascular disease (289); respiratory disease (114); diabetes mellitus (74); renal disease (26); malignancy (44).

In the US studies (Smith AA et al, 2020; Chilimuri S et al, 2020; Gerwen MV et al, 2020), the mean ages observed in patients who died were 73, 68, and 73.5 years, respectively. The minimum age observed was 60, and the maximum was 75. However, the highest mean age among the infected was 67 years. All studies presented a preponderance of men both among the infected and those who died.

Regarding comorbidities in American studies, the following distribution was observed: systemic hypertension (795); diabetes mellitus (446); cardiovascular disease (289); respiratory disease (198); renal disease (72); malignancy (44).

The 2 analyses from Spain (Pérez FM et al, 2020; Borobia AM et al, 2020) reported average ages of 67 and 83 years for deaths, respectively. The minimum age was 66 years, while the maximum was 87 years. For those infected, recorded age did

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**Table 2**

Methodological quality of the studies.

| Study | Selection | Comparability | Exhibition | Total |
|-------|-----------|---------------|------------|-------|
| 1. Mingli Yuan, et al. (2020) | *** | ** | *** | 8 |
| 2. Zhou F, et al. (2020) | *** | ** | *** | 8 |
| 3. Deng Y, et al. (2020) | **** | ** | *** | 9 |
| 4. Chen T et al. (2020) | *** | ** | *** | 8 |
| 5. Zhang J et al (2020) | *** | ** | *** | 8 |
| 6. Rong-Hui Du et al (2020) | *** | ** | *** | 8 |
| 7. Tao Chen, et al (2020) | **** | ** | *** | 9 |
| 8. Nikpouraghdam M et al. (2020) | **** | ** | *** | 9 |
| 9. Yang X. et al (2020) | *** | ** | *** | 8 |
| 10. Zandkarimi E. et al (2020) | **** | * | *** | 8 |
| 11. Boule A et al (2020) | **** | ** | *** | 9 |
| 12. Chen L et al. (2020) | **** | * | *** | 8 |
| 13. Ciardullo S et al (2020) | **** | ** | *** | 9 |
| 14. Smith AA et al (2020) | **** | ** | *** | 9 |
| 15. Chilimuri S et al (2020) | **** | ** | *** | 9 |
| 16. Gerwen MV et al (2020) | **** | ** | *** | 9 |
| 17. Pérez FM et al (2020) | *** | ** | *** | 8 |
| 18. Li J. et al (2020) | **** | ** | *** | 9 |
| 19. Gao S et al (2020) | **** | ** | *** | 9 |
| 20. Yang Q et al (2020) | **** | ** | *** | 9 |
| 21. Shah P et al (2020) | **** | ** | *** | 9 |
| 22. Borobia AM et al (2020) | **** | ** | *** | 9 |
| 23. Asfahan S et al (2020) | **** | * | *** | 9 |
| 24. Liu J et al (2020) | **** | * | *** | 9 |
| 25. Hwang JM et al (2020) | **** | * | *** | 9 |
| 26. Rastad H et al (2020) | **** | * | *** | 9 |
| 27. Tu WJ et al (2020) | **** | * | *** | 9 |
| 28. Wang Let al (2020) | **** | * | *** | 9 |
| 29. Parra-Bracamonte et al (2020) | **** | * | *** | 9 |
| 30. Soares RCM et al (2020) | **** | * | *** | 9 |
| 31. Zanella A et al (2020) | **** | * | *** | 9 |

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al, 2020, Tao Chen et al, 2020; Nikpouraghdam M et al, 2020; Yang X et al, 2020; Zandkarimi E et al, 2020; Boule A et al., 2020; Chen L et al, 2020; Ciardullo S et al, 2020; Smith AA et al, 2020; Chilimuri S et al, 2020; Gerwen MV et al, 2020; Pérez FM et al, 2020; Li J et al, 2020; Yog S et al, 2020; Yang Q et al, 2020; Shah P et al, 2020; Borobia AM et al, 2020; Liu J et al, 2020; Hwang JM et al, 2020; Rastad H et al, 2020; Tu WJ et al, 2020; Wang L et al, 2020). In this respect, the lowest average age of patients who died from COVID-19 was 53 years (Rastad H et al, 2020), while the highest average was 83 years (Borobia AM et al, 2020).

Upon analyzing for association between sex and comorbidities in deaths, men (26,754) were found to represent 63.5% of the total, markedly exceeding the 34.5% proportion for women (15,654). A study from China (Chen T et al, 2020) obtained a percentage of 84.2% for men who died from COVID-19, while another study from China (Mingli Yuan et al, 2020) indicated a percentage of 40.0% for men who died.

Yet, 13 studies (Mingli Yuan, et al, 2020; Zhou F, et al, 2020; Chen T et al, 2020; Zhang J et al, 2020; Tao Chen, et al, 2020; Yang X et al, 2020; Chilimuri S et al, 2020; Pérez FM et al, 2020; Li J et al, 2020; Gao S et al, 2020; Borobia AM et al, 2020; Liu J et al, 2020; Rastad, H et al, 2020) reported the number of infected who had at least 1 comorbidity. It was observed that out of 8390 infected patients, 4041 had at least one comorbidity, representing 48%.

Regarding the number of deaths, 14 studies (Mingli Yuan, et al, 2020; Zhou F, et al, 2020; Deng Y et al, 2020; Chen T et al, 2020; Tao Chen, et al, 2020; Yang X et al, 2020; Chilimuri S et al, 2020; Pérez FM et al., 2020; Li J et al, 2020; Gao S et al, 2020; Borobia AM et al, 2020; Asfahan S et al, 2020; Liu J et al, 2020; Rastad, H et al, 2020) showed that of 2504 deaths, 2096 had at least 1 comorbidity, accounting for 83.7%.

In the US studies (Smith AA et al, 2020; Chilimuri S et al, 2020; Gerwen MV et al, 2020), the mean ages observed in patients who died were 73, 68, and 73.5 years, respectively. The minimum age observed was 60, and the maximum was 75. However, the highest mean age among the infected was 67 years. All studies presented a preponderance of men both among the infected and those who died.

Regarding comorbidities in American studies, the following distribution was observed: systemic hypertension (795); diabetes mellitus (446); cardiovascular disease (289); respiratory disease (198); renal disease (72); malignancy (44).

The 2 analyses from Spain (Pérez FM et al, 2020; Borobia AM et al, 2020) reported average ages of 67 and 83 years for deaths, respectively. The minimum age was 66 years, while the maximum was 87 years. For those infected, recorded age did
### Chart 1
Characteristics of the studies included in the systematic review (n=31).

| Study ID | Type of study/country | Characteristics of the study | Characteristics of participants |
|----------|-----------------------|------------------------------|-------------------------------|
| 1. Mingli Yuan et al (2020)[5] | Retrospective cohort/Wuhan, China | Infected youngest 60 (47–69) Man 12 (45) | Age oldest 55 (35–60) Man 8 (47) |
| 2. Zhou F et al (2020)[6] | Retrospective cohort/Wuhan, China | Infected youngest 56 (46–67) Man 119 (62) | Survivors oldest 52 (45–58) Man 81 (59) |
| 3. Deng Y et al (2020) | Retrospective cohort/China | Infected youngest 33–74 Man 124 (55) | Survivors oldest 40 (33–57) Man 51 (44) |
| 4. Chen T et al (2020) | Retrospective/China | Infected youngest 54 (20–91) Man 108 (53) | Survivors oldest 72 (68–73) Man 18 (68) |
| 5. Zhang J et al (2020) | Retrospective/China | Infected youngest 55.6 (33–74) Man 321 (45) | Survivors oldest 69 (42–65) Man 306 (48) |
| 6. Rong-Hui Du et al (2020) | Prospective coorte/China | Infected youngest 57.6 ± 13.7 Man 97 (54) | Survivors oldest 56.0 ± 13.5 Man 87 (55) |
| 7. Tao Chen et al (2020) | Retrospective case series/China | Infected youngest 62.0 (44.0–70.0) Man 171 (62) | Survivors oldest 51.0 (37.0–66.0) Man 88 (55) |
| 8. Nikpouraghdam M et al (2020) | Retrospective/Irã | Infected youngest 56(46–65) Man 1955 (66) | Survivors oldest 57 (46–65) Man 210 (66) |
| 9. Yang X et al (2020) | Retrospective/China | Infected youngest 59.7 (13.3) Man 35 (67) | Survivors oldest 51.9 (12.9) Woman - |
| 10. Zandkarimi E et al (2020) | Retrospective/Irã | Infected youngest 52.74 ± 22.16 Man 1019 (56) | Survivors oldest 50.70 ± 21.43 Man - |
| 11. Boulle A et al (2020) | Retrospective/Africa do Sul | Infected youngest ≥20 Man 7052 (32) | Survivors oldest ≥20 Man 6767 (31) |
| 12. Chen L et al (2020) | Retrospective/China | Infected youngest 55 (36–68) Man 432 (55) | Survivors oldest 52 (34–65) Man 398 (55) |
| 13. Ciardullo S et al (2020) | Retrospective/Italy | Infected youngest 72 ± 14 Man 244 (65) | Survivors oldest 68 ± 14 Man 146 (63) |
| 14. Smith AA et al (2020) | Retrospective/EUA | Infected youngest 67 Man 194 (56) | Survivors oldest 612 (44) Man 126 (55) |
| 15. Chilimuri S. et al (2020) | Retrospective/EUA | Infected youngest 63.0 (52.0–72.0) Man 236 (63) | Survivors oldest 58.0 (48.0–68.0) Man 124 (58) |
| 16. Gerwen MV et al (2020) | Retrospective/EUA | Infected youngest 64.5 (± 16.4) Man 1181 (59) | Survivors oldest 61.0 (± 16.4) Man 799 (57) |
| 17. Pérez FM et al (2020) | Retrospective/Spain | Infected youngest 63 Man 63 (66) | Survivors oldest 63 Man 30 (63) |
| 18. Li J. et al (2020) | Retrospective/China | Infected youngest 66 (55–72) Man 44 (60) | Survivors oldest 62 (53–70) Man 33 (65) |
| 19. Gao S et al (2020) | Retrospective/China | Infected youngest 71 (67–77) Man - | Survivors oldest 70 (67–74) Man - |

(Continued)
| Study ID | Type of study/country | Characteristics of participants | Characteristics of the study |
|----------|-----------------------|---------------------------------|-----------------------------|
| 20. Yang Q et al (2020) | Retrospective/China | N/D | 20. Yang Q et al (2020) |
| 21. Shah P et al (2020) | Retrospective/Georgia | 63 (50–72) Man - 113 (50) Woman - 113 (50) | 21. Shah P et al (2020) |
| 22. Borobia AM et al (2020) | Coorte/Spain | 61 (46–78) Man - 1074 (51) Woman - 1152 (52) | 22. Borobia AM et al (2020) |
| 23. Asfahan S et al (2020) | Retrospective/China | 0–80 Man - 2281 (51) Woman - 21691 (49) | 23. Asfahan S et al (2020) |
| 24. Liu J et al (2020) | Retrospective/China | 57 (46 - 67) Man - 635 (53,4) Woman - 555 (46,6) | 24. Liu J et al (2020) |
| 25. Hwang JM et al (2020) | Retrospective/South Korea | 67.6 ± 15.32 Man - 52 (50) Woman - 51 (50) | 25. Hwang JM et al (2020) |
| 26. Rastad H et al (2020) | Retrospective/Iran | Median 54,8 Man - 1589 (54) Woman - 1368 (46) | 26. Rastad H et al (2020) |
| 27. Tu WJ et al (2020) | Retrospective/China | N/D | 27. Tu WJ et al (2020) |
| 28. Wang L et al (2020) | Retrospective/China | 69 (65–76) Man - 166 (49) Woman - 173 (51) | 28. Wang L et al (2020) |
| 29. Parra-Bracamonte et al (2020) | Multivariate logistic regression model/Mexico | 44 (33–56) Man - 178,152 (54) Woman - 153,143 (46) | 29. Parra-Bracamonte et al (2020) |
| 30. Soares RCM et al (2020) | Coorte/Brazil | N/D | 30. Soares RCM et al (2020) |
| 31. Zanella A et al (2020) | Retrospective/Italy | N/D | 31. Zanella A et al (2020) |
### Chart 2
Characteristics of the infected with respect to the presence of comorbidities.

| Study ID | Study period | Study ID | Study period |
|----------|--------------|----------|--------------|
| 1. Mingli Yuan et al (2020)[5] | January 1st to January 25, 2020 | 2. Zhou F et al (2020)[6] | December 19, 2019 to January 31, 2020 |
| 3. Deng Y et al (2020) | January 1, 2020 to February 21, 2020 | 4. Chen T et al (2020) | January 1, 2020, to February 10, 2020 |

| Infected | Survivors | Deaths |
|----------|-----------|--------|
| **Comorbidities** | **Types of Comorbidities n (%)** | **Comorbidities** | **Types of Comorbidities n (%)** | **Comorbidities** | **Types of Comorbidities n (%)** |
| **n** | **n (%)** | **n** | **n (%)** | **n** | **n (%)** |
| 27 (100) | 13 (48) | 17 (70) | 5 (29) | 10 (37) | 8 (80) |
| 191 (100) | 91 (48) | 137 (22) | 55 (40) | 54 (28) | 36 (67) |
| 225 | ND | 116 | 48 (41) | 109 (48) | 79 (72) |
| 55 | 37 (67) | 36 | 17 (47) | 19 (34) | 18 (95) |

| **Comorbidities** | **Types of Comorbidities n (%)** | **Comorbidities** | **Types of Comorbidities n (%)** | **Comorbidities** | **Types of Comorbidities n (%)** |
|----------|-----------|----------|-----------|----------|-----------|
| Hypertension 5 (19) | Diabetes 6 (22) | Cardiac disease 3 (11) | ARDS 11 (41) | Chronic gastritis 1 (4) | Cerebral infarction 1 (4) |
| Hypertension 58 (30) | Diabetes 36 (19) | Coronary heart disease 15 (8) | Chronic obstructive lung disease 6 (3) | Carcinoma 2 (1) | Chronic kidney disease 2 (1) Other (12) |
| Hypertension 5 (19) | Diabetes 36 (19) | Coronary heart disease 2 (1) | Chronic obstructive lung disease 2 (1) | Carcinoma 2 (1) | Chronic kidney disease 0 Other (11) (8) |
| Hypertension 18 (16) | Lung Disease 3 (3) | Diabetes 9 (8) | Heart Disease 4 (3) | Malignancy 2 (2) | Others 15 (13) |
| Hypertension 21 (38) | Diabetes 12 (22) | Cardiovascular Disease 11 (20) | Cardiac disease 8 (15) | Chronic liver disease 2 (4) | Chronic renal disease 3 (6) |
| Cardiovascular Disease 5 (14) | Malignancy 4 (11) | Chronic liver disease 1 (3) | Chronic renal disease 1 (3) | COPD 6 (17) | Tuberculosis 0 (0) |
| Cardiovascular Disease 5 (14) | Malignancy 4 (11) | Chronic liver disease 1 (3) | Chronic renal disease 1 (3) | COPD 6 (17) | Tuberculosis 0 (0) |

**P values:**
- Hypertension: .31
- Diabetes: .73
- Cardiovascular Disease: .12
- Malignancy: .47
- Chronic liver disease: 1.0
- Chronic renal disease: .35

*(Continued)*
### Characteristics of the study

| Study ID          | Study period       | Infected n (%) | Survivors n (%) | Deaths n (%) | Comorbidities |
|-------------------|--------------------|----------------|-----------------|--------------|---------------|
| 5. Zhang J et al  | January 11 to 6, 2020 | 663 (247 (37)) | N/D (51 (8))    | N/D (46 (7)) | Respiratory disease (51 (8)) |
|                   |                    |                |                 |              | Cardiovascular disease (164 (25)) |
|                   |                    |                |                 |              | Gastrointestinal disease (31 (5)) |
|                   |                    |                |                 |              | Endocrine system disease (67 (10)) |
|                   |                    |                |                 |              | Urinary system disease (21 (3)) |
|                   |                    |                |                 |              | Inflammatory disease (6 (1)) |
|                   |                    |                |                 |              | Malignant tumor (14 (2)) |
| 6. Rong-Hui Du et al (2020) | December 25 to 2019 | 179 N/D (58 (32)) | 158 N/D (45 (29)) | 21 (11) N/D | Hypertension (58 (32)) |
|                   |                    |                |                 |              | Cardiovascular or cerebrovascular Diseases (17 (11)) |
|                   |                    |                |                 |              | Diabetes (27 (17)) |
|                   |                    |                |                 |              | Chronic digestive disorders (17 (11)) |
|                   |                    |                |                 |              | Tuberculosis (8 (5)) |
|                   |                    |                |                 |              | Chronic hepatic or renal insufficiency (4 (2)) |
|                   |                    |                |                 |              | Peripheral vascular disease (4 (2)) |
|                   |                    |                |                 |              | Malignancy (4 (2)) |
| 7. Tao Chen et al (2020) | January 13 to 2019 | 274 (133 (49)) | 161 (62 (39)) | 113 (41) (71 (63)) | Hypertension (93 (34)) |
|                   |                    |                |                 |              | Diabetes (47 (17)) |
|                   |                    |                |                 |              | Cardiovascular disease (23 (8)) |
|                   |                    |                |                 |              | Chronic heart failure (1 (<1)) |
|                   |                    |                |                 |              | Chronic lung diseases (18 (7)) |
|                   |                    |                |                 |              | Malignancy (7 (3)) |
|                   |                    |                |                 |              | Hepatitis B virus surface (11 (4)) |
|                   |                    |                |                 |              | Cerebrovascular disease (4 (1)) |
|                   |                    |                |                 |              | Chronic kidney disease (4 (1)) |
|                   |                    |                |                 |              | Gastrointestinal diseases (3 (1)) |
|                   |                    |                |                 |              | Metabolic arthritis (4 (1)) |
|                   |                    |                |                 |              | Autoimmune disease (2 (1)) |

(Continued)
## Chart 2
(Continued)

### Characteristics of the study

| Study ID       | Study period   | Infected n | Survivors n | Deaths n | Comorbidities | Types of Comorbidities n (%) | Comorbidities | Types of Comorbidities n (%) | Comorbidities | Types of Comorbidities n (%) |
|----------------|----------------|------------|-------------|----------|---------------|--------------------------------|---------------|--------------------------------|---------------|--------------------------------|
| 8. Nikpouraghdam M et al (2020) | February 19 to April 15, 2020 | 2964 N/D | 239 (8) N/D | Diabetes 113 (4) | Chronic respiratory disease 60 (2) | Cardiovascular disease 37 (1) | Chronic Kidney disease 18 (<1) | Cancer (any) 17 (<1) | Others 19 (<1) |
| 9. Yang X et al (2020) | December 26, 2019 to January 26, 2020 | 52 21 (40) | 32 (61) 16 (50) | Chronic cardiac disease 5 (10) | Chronic pulmonary Disease 4 (8) | Cerebrovascular Disease 7 (14) | Diabetes 9 (17) | Malignancy 2 (4) | Dementia 1 (2) | Malnutrition 1 (2) | Smoking 2 (4) |
| 10. Zandkarimi E. et al (2020) | February 22 to May 18, 2020 | 1831 (100) | 142 (8) N/D | Diabetes 170 (9) | Weak immune system 8 (0) | Coronary heart disease 371 (20) | Chronic lung disease 110 (6) | Chronic kidney disease 48 (3) | Cancer 32 (2) |
| 11. Boule A et al (2020) | March 1 to June 9, 2020 | 22.308 (100) | 21.683 (97) | Diabetes 3474 (16) | Hypertension 5272 (24) | Chronic pulmonary disease 605 (5) | Chronic pulmonary disease/asthma 1661 (7) | Tuberculosis 343 (2) | HIV 3978 (7) |
| 12. Chen L et al (2020) | 15 January to 26 March, 2020 | 792 (100) | 724 (91) N/D | Hypertension 215 (27) | Diabetes 142 (18) | Chronic obstructive pulmonary disease 19 (2) | Chronic kidney disease 26 (3) |

Continued
### Characteristics of the study

| Study ID | Study period | Infected | Survivors | Deaths |
|----------|--------------|----------|-----------|--------|
|          |              | Comorbidities | Types of Comorbidities n (%) | Comorbidities | Types of Comorbidities n (%) | Comorbidities | Types of Comorbidities n (%) | Comorbidities | Types of Comorbidities n (%) |
| 13. Ciardullo S et al (2020) | February 22 to May 15, 2020 | 373 (100) | N/D | Diabetes 69 (19) | Hypertension 237 (65) | Chronic kidney disease 48 (13) | Cardiovascular diseases 140 (38) | Chronic obstructive pulmonary disease 39 (11) | Diabetes 36 (16) | Hypertension 130 (57) | Chronic kidney disease 22 (10) | Cardiovascular diseases 75 (33) | Chronic obstructive pulmonary disease 15 (7) | Diabetes 33 (23) | Hypertension 107 (78) | Chronic kidney disease 26 (18) | Cardiovascular diseases 65 (46) | Chronic obstructive pulmonary disease 24 (17) | Diabetes 71 (52) | Hypertension 94 (51) | Chronic kidney disease 21 (16) | Cardiovascular diseases 67 (40) | Chronic obstructive pulmonary disease 25 (17) | Diabetes 33 (23) | Hypertension 107 (78) | Chronic kidney disease 26 (18) | Cardiovascular diseases 65 (46) | Chronic obstructive pulmonary disease 24 (17) | Diabetes - 0.064 | Hypertension - < 0.001 | Chronic kidney disease - 0.014 | Tumors - 0.320 | Cardiovascular diseases - 0.007 | Chronic obstructive pulmonary disease - 0.001 | Diabetes - 0.004 | Hypertension - 0.0037 | Chronic kidney disease - 0.012 | Neurological disease - 0.373 | Chronic kidney disease - 0.016 | Chronic obstructive lung disease - 0.001 | Diabetes - 0.004 | Hypertension - 0.128 | Chronic kidney disease - 0.0001 | Tumors - 0.4854 | Cardiovascular diseases - 0.0018 | Chronic kidney disease - 0.0060 | HIV/AIDS - 0.469 | Chronic liver disease - 1.420 |
| 14. Smith AA et al (2020) | March 1 to April 22, 2020 | 346 (100) | N/D | Hypertension 241 (70) | Hyperlipidemia 167 (48) | Diabetes 163 (47) | Cardiovascular disease 162 (47) | Neurological disease 95 (28) | Chronic kidney disease 82 (24) | Chronic obstructive lung disease 58 (17) | Cancer 51 (15) | Asthma 47 (14) | Hypothyroid 45 (13) | Diabetes 95 (42) | Cardiovascular disease 96 (42) | Neurological disease 96 (26) | Chronic kidney disease 45 (20) | Chronic obstructive lung disease 27 (12) | Cancer 27 (12) | Asthma 35 (15) | Hypothyroid 25 (11) | Diabetes 150 (66) | Cardiovascular disease 107 (47) | Neurological disease 96 (26) | Chronic kidney disease 45 (20) | Chronic obstructive lung disease 27 (12) | Diabetes 115 (65) | Cardiovascular disease 107 (47) | Neurological disease 96 (26) | Chronic kidney disease 45 (20) | Chronic obstructive lung disease 27 (12) | Diabetes 90 (60) | Cardiovascular disease 66 (56) | Neurological disease 36 (31) | Chronic kidney disease 37 (32) | Chronic obstructive lung disease 37 (27) | Diabetes 90 (60) | Cardiovascular disease 61 (56) | Neurological disease 32 (26) | Chronic kidney disease 31 (19) | Chronic obstructive lung disease 22 (12) | Diabetes 33 (19) | Cardiovascular disease 61 (56) | Neurological disease 32 (26) | Chronic kidney disease 31 (19) | Chronic obstructive lung disease 22 (12) | Diabetes 33 (19) | Cardiovascular disease 61 (56) | Neurological disease 32 (26) | Chronic kidney disease 31 (19) | Chronic obstructive lung disease 22 (12) | Diabetes 33 (19) | Cardiovascular disease 61 (56) | Neurological disease 32 (26) | Chronic kidney disease 31 (19) | Chronic obstructive lung disease 22 (12) | Diabetes 33 (19) | Cardiovascular disease 61 (56) | Neurological disease 32 (26) | Chronic kidney disease 31 (19) | Chronic obstructive lung disease 22 (12) | Diabetes 33 (19) | Cardiovascular disease 61 (56) | Neurological disease 32 (26) | Chronic kidney disease 31 (19) | Chronic obstructive lung disease 22 (12) | Diabetes 33 (19) | Cardiovascular disease 61 (56) | Neurological disease 32 (26) | Chronic kidney disease 31 (19) | Chronic obstructive lung disease 22 (12) | Diabetes - 0.037 | Hypertension - 0.037 | Chronic kidney disease - 0.001 | Tumors - 0.320 | Cardiovascular diseases - 0.007 | Chronic obstructive pulmonary disease - 0.001 | Diabetes - 0.004 | Hypertension - 0.0037 | Chronic kidney disease - 0.012 | Neurological disease - 0.373 | Chronic kidney disease - 0.016 | Chronic obstructive lung disease - 0.001 | Diabetes - 0.004 | Hypertension - 0.128 | Chronic kidney disease - 0.0001 | Tumors - 0.4854 | Cardiovascular diseases - 0.0018 | Chronic kidney disease - 0.0060 | HIV/AIDS - 0.469 | Chronic liver disease - 1.420 |
| 15. Chilimuri S et al (2020) | March 9 to April 9, 2020 | 375 (100) | 287 (77) | Hypertension 225 (60) | Diabetes 175 (47) | Cardiovascular disease 62 (17) | Obstructive airway disease 62 (17) | Chronic kidney disease 51 (14) | HIV/AIDS 22 (6), chronic liver disease 18 (5) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes 115 (51) | Cardiovascular disease 24 (11) | Obstructive airway disease 33 (15) | Chronic kidney disease 20 (9) | HIV/AIDS 8 (4) | Chronic liver disease 7 (3) | Diabetes - 0.064 | Hypertension - < 0.001 | Chronic kidney disease - 0.014 | Tumors - 0.320 | Cardiovascular diseases - 0.007 | Chronic obstructive pulmonary disease - 0.001 | Diabetes - 0.004 | Hypertension - 0.128 | Chronic kidney disease - 0.0001 | Tumors - 0.4854 | Cardiovascular diseases - 0.0018 | Chronic kidney disease - 0.0060 | HIV/AIDS - 0.469 | Chronic liver disease - 1.420 | (Continued)
### Characteristics of the study

| Study ID | Study period       | Infected | Survivors | Deaths |
|----------|--------------------|----------|-----------|--------|
|          |                    | n (%)    | n (%)     | n (%)  |
| 16. Gerwen MV et al (2020) | March 1 to April 1, 2020 | 2015 (100) | 1309 (69) | 616 (31) |
|          |                    | Hypertension 1181 (59) | Hypertension 757 (54) | Hypertension 424 (59) |
|          |                    | Coronary artery disease 372 (19) | Coronary artery disease 220 (16) | Coronary artery disease 153 (25) |
|          |                    | Atrial fibrillation 258 (13) | Atrial fibrillation 147 (11) | Atrial fibrillation 111 (18) |
|          |                    | Congestive heart failure 250 (12) | Congestive heart failure 135 (10) | Congestive heart failure 115 (19) |
|          |                    | Peripheral vascular disease 112 (6) | Peripheral vascular disease 66 (5) | Peripheral vascular disease 46 (6) |
|          |                    | Cerebrovascular accident / transient ischemic attack 109 (6) | Cerebrovascular accident / transient ischemic attack 78 (13) | Cerebrovascular accident / transient ischemic attack 78 (13) |
|          |                    | Dementia 84 (6) | Dementia 67 (13) | Dementia 67 (13) |
|          |                    | Diabetes 795 (40) | Diabetes 502 (36) | Diabetes 502 (36) |
|          |                    | Hypothyroidism 171 (9) | Hypothyroidism 111 (8) | Hypothyroidism 111 (8) |
|          |                    | Chronic kidney disease 293 (15) | Chronic kidney disease 176 (13) | Chronic kidney disease 176 (13) |
|          |                    | Malignancy 228 (11) | Malignancy 147 (11) | Malignancy 147 (11) |
|          |                    | Asthma 232 (12) | Asthma 171 (12) | Asthma 171 (12) |
|          |                    | Chronic obstructive pulmonary disease 145 (7) | Chronic obstructive pulmonary disease 85 (6) | Chronic obstructive pulmonary disease 85 (6) |
|          |                    | Prior venous thromboembolism 89 (4) | Prior venous thromboembolism 63 (5) | Prior venous thromboembolism 63 (5) |
|          |                    | **P value** | | Hypertension - <.001 |
|          |                    | Hypertension - <.001 | Coronary artery disease - < .001 | Hypertension - <.001 |
|          |                    | Atrial fibrillation - <.001 | Atrial fibrillation - <.001 | Atrial fibrillation - <.001 |
|          |                    | Congestive heart failure - < .001 | Congestive heart failure - < .001 | Congestive heart failure - < .001 |
|          |                    | Peripheral vascular disease - <.001 | Peripheral vascular disease - <.001 | Peripheral vascular disease - <.001 |
|          |                    | Cerebrovascular accident / transient ischemic attack - <.001 | Cerebrovascular accident / transient ischemic attack - <.001 | Cerebrovascular accident / transient ischemic attack - <.001 |
| 17. Pérez FM et al (2020) | February 26 to April 29, 2020 | 96 (100) | 60 (62) | 79 (82) |
|          |                    | Hypertension 38 (40) | Hypertension 26 (33) | Hypertension 12 (71) |
|          |                    | Diabetes 15 (16) | Diabetes 13 (17) | Diabetes 2 (13) |
|          |                    | Heart disease 13 (14) | Heart disease 5 (6), asthma 10 (13) | Heart disease 8 (47) |
|          |                    | Asthma 11 (12) | Asthma 1 (6) | Asthma 1 (6) |
|          |                    | Chronic obstructive pulmonary disease 6 (6) | Chronic obstructive pulmonary disease 5 (5) | Chronic obstructive pulmonary disease 2 (12) |
|          |                    | Obstructive sleep apnea syndrome 4 (4) | Obstructive sleep apnea syndrome 3 (4) | Obstructive sleep apnea syndrome 1 (6) |
|          |                    | Cerebrovascular disease 6 (6) | Cerebrovascular disease 2 (3) | Cerebrovascular disease 4 (24) |
|          |                    | Chronic kidney disease 6 (9) | Chronic kidney disease 3 (4) | Chronic kidney disease 3 (19) |
|          |                    | Cancer 3 (5) | Cancer 2 (3) | Cancer 1 (6) |
| 18. Li J et al (2020) | January 25 to February 26, 2020 | 74 (100) | 56 (76) | 60 (81) |
|          |                    | Hypertension 35 (47) | Hypertension 25 (42) | Hypertension 10 (71) |
|          |                    | Diabetes 14 (19) | Diabetes 11 (18) | Diabetes 3 (21) |
|          |                    | Coronary disease 6 (8) | Coronary disease 2 (3) | Coronary disease 4 (29) |
|          |                    | Tuberculosis 6 (8) | Tuberculosis 5 (8) | Tuberculosis 1 (7) |
|          |                    | Chronic liver disease 2 (3) | Chronic liver disease 2 (3) | Chronic liver disease 0 (0) |
|          |                    | Malignancy 2 (3) | Malignancy 2 (3) | Malignancy 0 (0) |
|          |                    | **P value** | | Chronic kidney disease - .058 |
|          |                    | Hypertension - .045 | Diabetes - .516 | Hypertension - .006 |
|          |                    | Heart disease - < .001 | Heart disease - < .001 | Hypertension - .006 |
|          |                    | Asthma - .683 | Asthma - .683 | Diabetes - .516 |
|          |                    | Chronic obstructive pulmonary disease - .287 | Chronic obstructive pulmonary disease - .287 | Chronic obstructive pulmonary disease - .287 |
|          |                    | Obstructive sleep apnea syndrome - .548 | Obstructive sleep apnea syndrome - .548 | Obstructive sleep apnea syndrome - .548 |
|          |                    | Cerebrovascular disease - .008 | Cerebrovascular disease - .008 | Cerebrovascular disease - .008 |
|          |                    | Chronic kidney disease - .447 | Chronic kidney disease - .447 | Chronic kidney disease - .447 |
|          |                    | Cancer - .790 | Cancer - .790 | Cancer - .790 |
|          |                    | Chronic liver disease - .489 | Chronic liver disease - .489 | Chronic liver disease - .489 |
| Study ID | Study period | Study period | n | Comorbidities n (%) | Types of Comorbidities n (%) | Comorbidities n (%) | Types of Comorbidities n (%) | Comorbidities n (%) | Types of Comorbidities n (%) | Comorbidities (P value) |
|----------|--------------|--------------|---|---------------------|-----------------------------|---------------------|-----------------------------|---------------------|-----------------------------|------------------------|
| 19. Gao S et al (2020) | January 23 to February 29, 2020 | 210 (100) | 159 (76) | Hypertension 115 (55) Diabetes 38 (18) Cardiovascular disease 52 (25) Chronic obstructive pulmonary disease 3 (1) Respiratory disease 38 (18) Cerebrovascular disease 13 (6) Chronic liver disease 18 (9) Digestive diseases 21 (10) Chronic kidney disease 18 (9) Cancer 6 (3) | 175 (83) | Hypertension 97 (55) Diabetes 29 (17) Cardiovascular disease 35 (20) Chronic obstructive pulmonary disease 2 (1) Respiratory disease 20 (11) Cerebrovascular disease 6 (3) Chronic liver disease 12 (7) Digestive diseases 15 (9) Chronic kidney disease 8 (5) Cancer 3 (2) | 35 (17) | Hypertension 18 (51) Diabetes 9 (26) Cardiovascular disease 17 (49) Chronic obstructive pulmonary disease 1 (3) Respiratory disease 18 (51) Cerebrovascular disease 7 (20) Chronic liver disease 6 (17) Digestive diseases 17 (6) Chronic kidney disease 10 (29) Cancer 3 (9) | Hypertension - .664 Diabetes - .200 Cardiovascular disease - .001 Chronic obstructive pulmonary disease - .435 Respiratory disease - <.001 Cerebrovascular disease - .047 Chronic liver disease - .123 Chronic kidney disease - <.001 Cancer - .026 Hypertension - <.001 Diabetes - .008 Coronary heart disease - .010 Chronic obstructive pulmonary disease - .124 N/D |
| 2. Yang Q et al (2020) | January 1 to February 29, 2020 | 226 (100) | N/D | N/D | N/D | N/D | N/D | N/D | N/D |
| 21. Shuh P et al (2020) | March 2 to May 6, 2020 | 522 (100) | N/D | Hypertension 416 (80), Diabetes 221 (42), Coronary artery disease 48 (9), Congestive heart failure 70 (13), Chronic obstructive pulmonary disease 47 (9), Asthma 681 (13), Chronic kidney disease 78 (15), End stage renal disease 30 (6), Obesity 347 (67), Morbid obesity 134 (26), Cancer 48 (9), Immunosuppression 29 (6), Chronic liver disease 6 (1) | 430 (82) | Hypertension 330 (77), Diabetes 169 (39), Coronary artery disease 35 (8), Congestive heart failure 50 (12), Chronic obstructive pulmonary disease 34 (8), Asthma 57 (13), Chronic kidney disease 58 (14), End stage renal disease 23 (5), Obesity 290 (67), Morbid obesity 111 (26), Cancer 39 (9), Immunosuppression 17 (4), Chronic liver disease 4 (1) | 92 (18) | Hypertension 86 (94), Diabetes 52 (57), Coronary artery disease 13 (14), Congestive heart failure 20 (22), Chronic obstructive pulmonary disease 13 (14), Asthma 11 (12), Chronic kidney disease 20 (22), End stage renal disease 7 (8), Obesity 52 (62), Morbid obesity 23 (25), Cancer 9 (10), Immunosuppression 12 (13), Chronic liver disease 2 (2) | N/D |
| Study ID | Study period | n | Comorbidities | Types of Comorbidities |
|----------|--------------|---|---------------|-----------------------|
| 22. Borobia AM et al (2020) | February 25 to April 19, 2020 | 2226 | Hypertension 920 (41), Chronic heart disease 429 (19), Diabetes 381 (17), Rheumatological disease 268 (12), Solid malignant disease 252 (11), Obesity 242 (11), Chronic kidney disease 174 (8), Chronic obstructive pulmonary disease 153 (7), Other chronic lung diseases 143 (6), Hematological malignant disease 133 (6), Asthma 115 (5), Liver disease 89 (4), HIV 13 (1) | |
| 23. Asfahan S et al (2020) | | 44672 | 43649 | Hypertension 2522 (12), diabetes 1022 (5), cardiovascular disease 781 (4), chronic respiratory disease 479 (2), cancer 101 (0.5) | |
| 24. Liu J et al (2020) | December 23, 2019 to February 28, 2020 | 1190 | Chronic obstructive pulmonary disease 22 (1.9), Diabetes 144 (12.2), Hypertension 308 (26.1), Chronic cardiac disease 86 (7.3), Chronic kidney disease 30 (2.6), Chronic liver disease 40 (3.4), Stroke 39 (3.3), Malignancy 34 (2.9), Immunosuppression 24 (2.0), Tuberculosis 15 (1.3) | 1033 (87) | Chronic obstructive pulmonary disease 14 (1.4), Diabetes 105 (10.2), Hypertension 244 (23.8), Chronic cardiac disease 61 (6.0), Chronic kidney disease 24 (2.4), Chronic liver disease 32 (3.1), Stroke 28 (2.7), Malignancy 26 (2.5), Immunosuppression 15 (1.5), Tuberculosis 10 (1.4) | 1023 (2) | Chronic obstructive pulmonary disease 8 (5.3), Diabetes 39 (25.5), Hypertension 64 (41.8), Chronic cardiac disease 25 (16.3), Chronic kidney disease 6 (3.9), Chronic liver disease 8 (5.2), Stroke 11 (7.2), Malignancy 8 (5.2), Immunosuppression 9 (5.9), Tuberculosis 5 (3.3) | 504 (49) | Chronic obstructive pulmonary disease - 1, Diabetes - <.001, Hypertension - <.0001, Chronic cardiac disease - <.0001, Chronic kidney disease - <.001, Chronic liver disease - <.001, Stroke - 0.041, Malignancy 1.115, Immunosuppression 0.0009, Tuberculosis - 0.0475 |
| Study ID | Study period          | Infected n | Comorbidities (%) | Types of Comorbidities | survivor n | Types of Comorbidities | Deaths n | Types of Comorbidities | Comorbidities (P value) |
|----------|-----------------------|------------|-------------------|------------------------|------------|------------------------|----------|------------------------|------------------------|
| 25. Hwang, J-M et al (2020) | February 1 to March 25, 2020 | 103 N/D | Hypertension 57 (55) | Diabetes mellitus 35 (34) | 77 (75) | Hypertension 40 (62) | 26 (25) | N/D | Hypertension 17 (65) | Diabetes mellitus - 0.13 | Chronic kidney disease - 0.30 |
|          |                       |            | Chronic kidney disease 17 (17) | Dyslipidemia 13 (13) |            | Chronic kidney disease 14 (18) |            |            | Hypertension - 0.13 | Diabetes mellitus - 0.84 |
|          |                       |            | Chronic lung disease 7 (7) | Carcinoma 9 (9) |            | Dormia 10 (13) |            |            | Chronic lung disease - 0.84 | Diabetes mellitus - 0.16 | Chronic kidney disease - 0.16 |
|          |                       |            | Cardiovascular disease 12 (12) | Dementia 11 (11) |            | Cardiovascular disease 6 (8) |            |            | Chronic lung disease - 0.75 | Diabetes mellitus - 0.036 | Chronic kidney disease - 0.036 |
|          |                       |            | Parkinson 138 | Disease 2 (2) |            | Parkinson disease 1 (1) |            |            | Dementia - 0.001 | Diabetes mellitus - 0.016 | Chronic kidney disease - 0.016 |
|          |                       |            | Stroke 4 (4) | Taking NSAIDs 5 (5) |            | Taking NSAIDs 3 (4) |            |            | Stroke - 0.019 | Diabetes mellitus - 0.036 | Chronic kidney disease - 0.036 |
|          |                       |            | Taking ARB or ACE 13 (13) | Diabetes mellitus 138 (47) |            | Diabetes mellitus 115 (43) |            |            | Taking NSAIDs - 0.436 | Diabetes mellitus - 0.436 | Chronic kidney disease - 0.436 |
|          |                       |            | Cardiovascular Disease 168 (57) | Cardiovascular Disease 68 (57) |            | Cardiovascular Disease 141 (53) |            |            | Taking ARB or ACE - 0.338 | Diabetes mellitus - 0.338 | Chronic kidney disease - 0.338 |
| 26. Rastad H et al (2020) | February 20 to March 25, 2020 | 2957 749 (25) | Hypertension 138 (47) | Diabetes mellitus 138 (47) | 2656 | Hypertension 115 (43) | 301 (10) | Diabetes mellitus 23 (76) | Cardiovascular Disease 27 (9) |
|          |                       |            | Cardiovascular Disease 168 (57) | Cardiovascular Disease 68 (57) |            | Cardiovascular Disease 141 (53) |            |            | N/D | Cardiovascular Disease 27 (9) |
| 27. Tu W-J et al (2020) | January 3 to February 24, 2020 | 149 N/D | Hypertension 25 (16) | Diabetes 11 (7.4) | 149 | Hypertension 25 (16.8) | N/D | Hypertension 12 (48) | Diabetes 6 (24) |
|          |                       |            | Cardiovascular- cerebrovascular diseases 8 (7.4) | Respiratory diseases 8 (7.4) |            | Cardiovascular- cerebrovascular diseases 8 (22) |            |            | Cardiovascular- cerebrovascular disease - <.001 | Diabetes - <.001 |
| 28. Wang L et al (2020) | January 1 to February 6, 2020 | 339 N/D | Hypertension 138 (40.8) | Diabetes 43 (15.8) | 274 | Hypertension 106 (38.9) | 65 (19) | Hypertension 32 (50) | Diabetes 11 (17.2) |
|          |                       |            | Cardiovascular disease 53 (15.7) | Cerebrovascular disease 21 (6.2) |            | Cardiovascular disease 32 (11.7) |            |            | Cardiovascular disease <.001 | Diabetes <.001 |
|          |                       |            | Chronic kidney disease 13 (3.8) | Chronic liver disease 2 (0.6) |            | Chronic kidney disease 11 (4.9) |            |            | Cardiovascular disease <.001 | Diabetes <.001 |
|          |                       |            | Chronic obstructive pulmonary disease 21 (6.2) | Malignancy 15 (4.4) |            | Chronic obstructive pulmonary disease 10 (3.7) |            |            | Chronic kidney disease <.001 | Diabetes <.001 |
|          |                       |            | Autoimmune disease 5 (1.5) | |            | Autoimmune disease 4 (1.5) |            |            | Chronic kidney disease <.001 | Diabetes <.001 |
|          |                       |            | | |            | |            | | | | | | | |
### Characteristics of the study

| Study ID | Study period | Infected | Survivors | Deaths |
|----------|--------------|----------|-----------|--------|
|          | n            | Comorbidities n (%) | Types of Comorbidities n (%) | n            | Comorbidities n (%) | Types of Comorbidities n (%) | n            | Comorbidities n (%) | Types of Comorbidities n (%) |
| 29. Parra-Bracamonte et al (2020) | January 13 to July 17, 2020 | 331.298 | N/D | 292.988 | N/D | 38.310 | N/D | 30. Soares RCM et al (2020) | February 29 to June 11, 2020 | 1152 | N/D | 696 | N/D | 456 | N/D | Cardiovascular diseases - <.001 |
|          |               | Hypertension 66.170 (20) | Obesity 63.459 (19,2) | Diabetes 53.712 (16,2) | Cardiopathy 7351 (2,2) | Chronic obstructive pulmonary disease 5458 (1,6) | Asthma 8983 (2,7) | Immunosuppressed 4196 (1,3) | Chronic kidney disease 6895 (2,1) | Other complication 8901 (2,7) |
|          |               | Hypertension 49.761 (17) | Obesity 53.955 (18,4) | Diabetes 39.417 (13,5) | Cardiopathy 5314 (1,8) | Chronic obstructive pulmonary disease 3619 (1,2) | Asthma 8206 (2,8) | Immunosuppressed 3135 (1,1) | Chronic kidney disease 4307 (1,5) | Other complication 6944 (2,4) |
|          |               | Hypertension 16.409 (42,8) | Obesity 9504 (24,8) | Diabetes 14.295 (37,3) | Cardiopathy 2037 (5,3) | Chronic obstructive pulmonary disease 1839 (4,8) | Asthma 777 (2,0) | Immunosuppressed 1061 (2,8) | Chronic kidney disease 2588 (6,8) | Other complication 1957 (5,1) |
| 30. Soares RCM et al (2020) | February 11, 2020 | 3.988 | N/D | N/D | N/D | 1926 | N/D | Cardiovascular diseases - <.001 |
|          |               | Hypertension 1643 (41) | Hypercholesterolemia 545 (14) | Heart disease 533 (13) | Type 2 diabetes 514 (13) | Malignant neoplasm 331 (8) | Chronic obstructive pulmonary disease 93 (2) | Chronic kidney disease 87 (2) | Liver disease 86 (2) | Other 501(12) |
|          |               | N/D | N/D | N/D | N/D | 456 | N/D | Cardiovascular diseases - <.001 |
|          |               | N/D | N/D | N/D | N/D | 1926 | N/D | Cardiovascular diseases - <.001 |
|          |               | N/D | N/D | N/D | N/D | 456 | N/D | Cardiovascular diseases - <.001 |
|          |               | N/D | N/D | N/D | N/D | 1926 | N/D | Cardiovascular diseases - <.001 |
| 31. Zanella A et al (2020) | February 20 to April 22, 2020 | 3.988 | N/D | N/D | N/D | 1926 | N/D | Cardiovascular diseases - <.001 |
|          |               | Hypertension 1643 (41) | Hypercholesterolemia 545 (14) | Heart disease 533 (13) | Type 2 diabetes 514 (13) | Malignant neoplasm 331 (8) | Chronic obstructive pulmonary disease 93 (2) | Chronic kidney disease 87 (2) | Liver disease 86 (2) | Other 501(12) |
|          |               | N/D | N/D | N/D | N/D | 1926 | N/D | Cardiovascular diseases - <.001 |
|          |               | N/D | N/D | N/D | N/D | 1926 | N/D | Cardiovascular diseases - <.001 |
|          |               | N/D | N/D | N/D | N/D | 1926 | N/D | Cardiovascular diseases - <.001 |

- **Cardiovascular diseases**
- **Diabetes**
- **Kidney diseases**
- **Obesity**
- **Pulmonary diseases**
- **Smoking**
- **Hypertension**
- **Hypercholesterolemia**
- **Heart disease**
- **Type 2 diabetes**
- **Malignant neoplasm**
- **Chronic obstructive pulmonary disease**
- **Chronic kidney disease**
- **Liver disease**
- **Other**

**P values**
- <.001
- .001
- .01
- .05
- N/D
not exceed 63 years, suggesting a discrepancy. In the first study, there was a predominance of males, both in terms of the number of infected and the number of deaths. This was not the case in the second sample, since the female sex was responsible for 58% of the infected people but only 32% of deaths. Regarding possible aggravation by comorbidities in Spain, the following numbers were determined: systemic hypertension (330); cardiovascular disease (203); diabetes mellitus (159); renal disease (97); malignancy (94); respiratory disease (68).

Regarding the studies conducted in Italy (Ciardullo S et al, 2020; Zanella A et al, 2020), only the first study reported the average age, which was 78 years. The average age of those infected was 72 years, an age that decreased to 68 years for those who were recovering. In relation to gender, males were found to be more prevalent in both studies. Italy’s breakdown of comorbidities was as follows: systemic hypertension (1069); cardiovascular disease (407); diabetes mellitus (361); malignancy (224); respiratory disease (91); renal disease (26).

With only one study, South Africa (Boule A et al, 2020) presented a marked difference when average age was analyzed because, for infected and for deaths, it was 20 and 63 years, respectively, with a lowest age of 54 years and a highest of 71 years. Regarding sex, there were more females in both categories: infected (68%) and dead (54%). It should be noted that the cure rate for women was higher than for men since the study reported 15,256 infected women and 14,916 recovered. The apparent order of comorbidities in South Africa was diabetes mellitus (372); systemic hypertension (362); renal disease (111); respiratory disease (84).

The South Korean study reported an average age of 76.5 years among deceased patients (Hwang JM et al, 2020). Among the infected, the sexes were represented equally (50% each), but men comprised the larger proportion of deaths (62%), with women recovering at higher frequency (53%). In order of occurrence, the comorbidities were systemic hypertension (17); diabetes mellitus (14); cardiovascular disease (6); respiratory diseases (5); renal disease (3).

In Iran, the 3 studies analyzed (Nikpouraghdam M et al, 2020; Rastad, H et al, 2020) yielded average ages among the infected of 56, 52.7, and 54.8 years, respectively, and 65, 66.3, 53.3 years for deaths. Moreover, the minimum age reported in deaths was 57 years, while the maximum was 75 years. In all studies, there was a preponderance of males. Comorbidities occurred as follows: cardiovascular disease (84); diabetes mellitus (36); respiratory diseases (21); malignancy (10); hypertension (8); chronic renal disease (8).

Georgia’s study showed deaths for patients aged between 1 and 78 years, with an average age of 70 years (Shah P et al, 2020). Women were represented more strongly among the infected (58%) and recovered (61%), while men comprised the majority in deaths (54%). Comorbidities appeared as follows: hypertension (86); diabetes mellitus (52); cardiovascular disease (33); respiratory disease (24); renal disease (20); malignancy (59).

In Mexico (Parra-Bracamonte et al, 2020), the average age of death was 62 years, with a minimum age of 52 years and a maximum of 71 years. Regarding gender, men were at greater prevalence both among those infected and those who died. The following ranking of comorbidities was found in the Mexican study: hypertension (16,409); diabetes mellitus (14,295); respiratory disease (2616); renal disease (2588).

In the Brazilian study (Soares RCM et al, 2020), the patients were divided into 2 groups: <60 years and >60 years. Of those infected, the majority were <60 years old (78%), while patients over 60 years of age were more prevalent among deaths (35.4%). However, when associations with sex were investigated, in contrast to most other countries, the Brazilian study presented a higher prevalence of females among deaths, while men were in the majority of those infected and recovered. The occurrence of comorbidities in Brazil was ranked as follows: cardiovascular disease (200); diabetes mellitus (142); respiratory disease (58); chronic renal disease (36).

### 3.1. Additional results

The studies of Zhou F et al, Deng Y et al, and Chen T et al showed that the presence of 1 or more comorbidities increased the risk of death. Zhang J et al and Rong-Hui Du et al proposed that risk was greater not only by virtue of comorbidities but also by older age.

Chen T et al reported findings suggesting that smoking was a possible risk factor for death from COVID-19; however, few patients have a history of smoking for at least 30 years. In addition, the study by Shah P et al (2020), presented in Chart 2, showed that 347 (67%) of those infected were obese and 134 (26%) morbidity obese, with 52 (15%) and 23 (17%) died, respectively. Furthermore, in the study by Parra-Bracamonte et al (2020), 63,459 (19.2%) of those infected were obese, of which 9504 (1.4%) died.

Some studies reported that the older the patient and when there were underlying diseases, the evolution to death from infected occurred in a short period, varying between 5 and 13.7 days (Rong-Hui Du et al, Chen T et al).

### 3. Discussion

This review identified a 10.8% proportion of deaths in SARS-CoV-2 infected patients, evidencing the impact of comorbidities on the prognosis of patients with COVID-19. The main comorbidities identified in patients diagnosed with COVID-19 were systemic arterial hypertension (SAH), diabetes mellitus (DM), and cardiovascular disease (CD), as represented in Chart 2. In this context, several factors were identified in the studies as related to the worsening and death of the infected, such as multiple comorbidities, male, and age over 65 years. In addition, all studies refer to dyspnea as the main symptom of aggravation in fatalities.

A related fact of significance is the high prevalence of hypertension in the most diverse regions of the world. Mills et al (2020), estimated that in 2010, 31.1% of the adult population worldwide had SAH, corresponding to 1.39 billion people.

Regarding pathophysiology and cellular function, it is noticeable that hypertension involves failure of vasoconstriction or vasodilation of smooth muscle present in vessel walls. The bronchi possess such musculature; thus, in hypertension, there is the activation of endothelial cells, which induces an increase of inflammatory cytokines (interleukin-8, among others) and molecules of adhesion (P and E-selectin, intercellular adhesion molecule—ICAM, and vascular adhesion molecule—VCAM) that trigger adhesion and migration of leukocytes in the subendothelial space, which is fundamental to beginning and promoting the vascular inflammatory process. This inflammatory mechanism related to hypertension may be one of the contributors to the severe inflammatory condition observed in patients with COVID-19.

In SARS-CoV-2 infection, the immune response occurs with the recruitment of monocytes and macrophages, which act in response to infection through the release of primary B and T lymphocytes and cytokines. In most patients, such a defense mechanism may be sufficient if the infection is controlled. However, in patients with comorbidities that worsen the inflammatory condition, the immune response could be an exacerbated one, which may cause greater difficulty in controlling the disease.

In this sense, macrophages, which are cells of the immune system programmed to respond to microbial stimuli and eliminate pathogens by the production of inflammatory molecules, can play an important role in the worsening of the pro-inflammatory condition in patients with COVID-19.

This is because these cells are a potential source of reactive oxygen species in the inflammatory process, and products
thereof, such as cytokines, can diffuse to adjacent cells of the endothelium and smooth muscle, promoting hyperplasia and vascular hypertrophy. Macrophages also participate in the presentation of antigens to T lymphocytes, which are important in the establishment of the inflammatory process during SAH. In this context, it is believed that infection by SARS-CoV-2 activates angiotensin II, causing an “attack” in the bronchi and generating respiratory difficulties and dyspnea. Thus, if the patient seeks health care after the appearance of several symptoms, including shortness of breath, it may be more difficult to reverse the clinical picture, offering a worse prognosis.

Meng et al. reveal in their findings that patients with SAH that were infected by COVID-19 and who used antihypertensive agents that inhibit the angiotensin II type 1 receptor (ACE/ Ang II/AT1R) system demonstrated moderate symptoms and showed no deaths. This study compared the aforementioned antihypertensive users and nonusers. It implies that lack of control of hypertension may be the real reason for a large number of deaths among hypertensive people in Mexico.

Diabetes mellitus represented the second most common comorbidity, with a high prevalence among patients diagnosed with COVID-19, especially in those who died. The global prevalence of diabetes mellitus as estimated by the Non-Communicable Disease Risk Factor Collaborators in 2014 was 9.0% for men and 7.9% for women, corresponding to 422 million people.

The estimate made by the International Diabetes Federation reveals that diabetes affected 451 million people in 2017 in the age group of 18 to 99 years, a number which is projected to be 693 million in 2045. Furthermore, regarding the cellular scope, in diabetes there is a higher risk of severe pro-inflammatory condition, hypercoagulation, and impairment of the immune system because diabetes is a condition associated with several macrovascular and microvascular complications.

Moreover, inadequate glycemic control in patients with diabetes mellitus can further compromise the immune system’s response capacity. In this sense, proper glycemic control is an important factor in diabetic patients diagnosed with COVID-19.

Regarding cardiovascular diseases, which occupy the third position among comorbidities in patients with COVID-19, they currently represent one of the most serious public health problems because, besides their high prevalence, they are also among the leading causes of mortality worldwide. Joseph et al. found that of the 55,792,000 deaths estimated worldwide in 2015, 17,921,000 were related to cardiovascular diseases.

Several studies have reported a higher risk of disease aggravation and mortality in patients with COVID-19 who present with cardiovascular diseases. The acute cardiac injury, one of the most reported cardiac complications in patients with COVID-19, may contribute to the development of severe clinical conditions due to mechanisms of systemic inflammation, acute coronary events, and direct myocardial injury, as well as generate difficulty in supplying myocardial oxygen demand. The results show that the presence of one or more comorbidities is an aggravating risk factor for complications and death after COVID-19 infection. In this sense, greater occurrence of death was observed in cases with SAH, DM, and cardiovascular disease comorbidities. Although obesity is associated with aggravation of the pro-inflammatory condition, which is observed in patients with COVID-19, only 4 studies presented data on the anthropometric nutritional status.

This evaluation is particularly important because obesity can cause damage to respiratory dynamics through the infiltration of ventilatory structures by adipose tissue that decreases thoracic compliance, resulting in restrictive pneumopathies and inflammatory pneumopathies. Thus, such considerations make obesity one of the factors to be evaluated in patients infected by COVID-19 who died, which, unfortunately, none of the studies addressed.

The limitation of the review was the filtering of studies that fit the purpose proposed in this scope, given the large amount of research on the subject and the constant updating of information on COVID-19.

4. Conclusion

In this study, a high percentage of comorbidities was registered in patients with COVID-19, especially in those who died. The main comorbidities identified in the studies were systemic arterial hypertension, diabetes mellitus, and cardiovascular disease, suggesting that health services need to implement measures directed at patients with chronic noncommunicable diseases in order to reduce their mortality.

Given the results presented, it is conceivable that adopting the right protocols for treating chronic noncommunicable diseases when they interact with acute and severe respiratory infections such as COVID-19 will reduce the mortality rate in this specific population. Each country has had to determine a specific protocol of care for the population, which has contributed to variations in the epidemiological profile of those who died as a result of the new coronavirus.

Author contributions

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