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Prevalence of comorbidities in deceased patients with COVID-19

A systematic review

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Abstract

Background: In December 2019, a new disease, coronavirus disease (COVID-19), emerged, which put several countries on a state of alert. Because it is a novel virus, several aspects and factors that contribute to the evolution of pathogenesis are still unknown and need to be better understood. Therefore, a systematic review is necessary to investigate the association between COVID-19 infection and chronic nontransmissible disease in patients who have died of COVID-19.

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-Analyzes, 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,[1] 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

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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-Analyzes (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

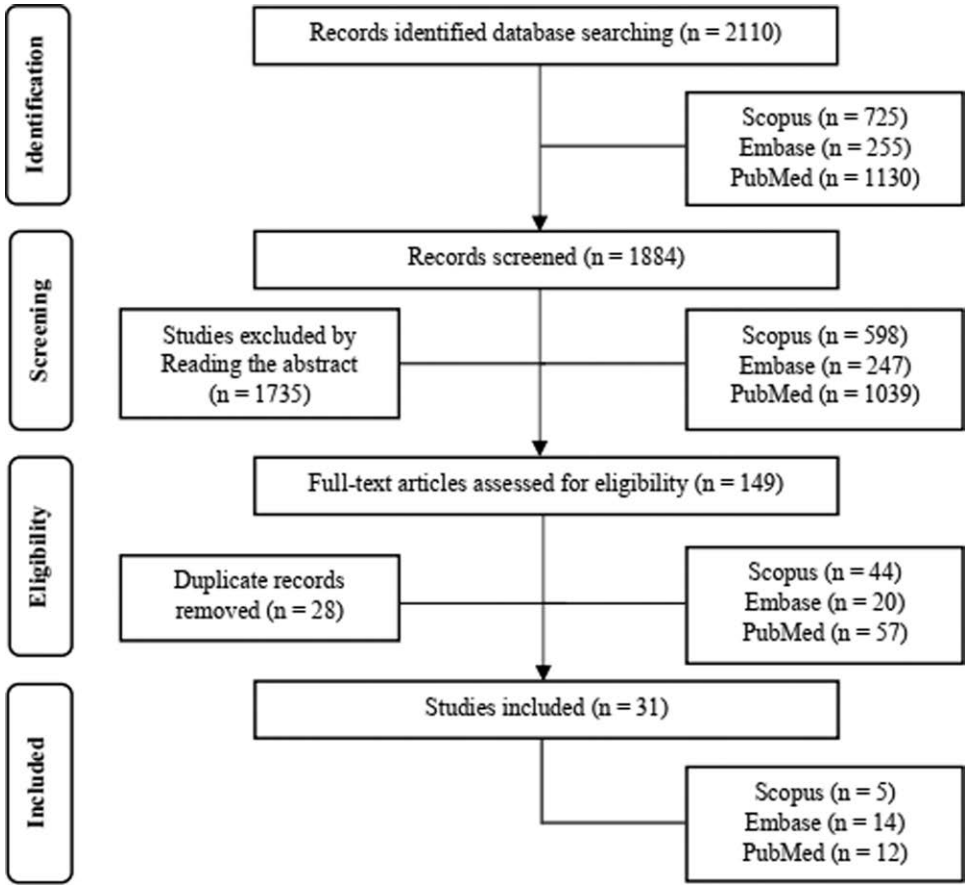

Figure 1. Flowchart of the article selection process.

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 (Boulle 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, 202; 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

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)	****	**	***	9
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)	****	**	***	9
11. Boulle A et al (2020)	****	**	***	9
12. Chen L et al (2020)	****	**	***	9
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)	***	**	***	8
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)	****	*	***	8
24. Liu J et al (2020)	****	**	***	9
25. Hwang JM et al (2020)	***	**	***	8
26. Rastad H et al (2020)	****	**	***	9
27. Tu WJ et al (2020)	***	**	***	8
28. Wang Let al (2020)	****	**	***	9
29. Parra-Bracamonte et al (2020)	****	**	***	9
30. Soares RCM et al (2020)	****	*	***	8
31. Zanella A et al (2020)	****	*	***	8

al, 2020, Tao Chen et al, 2020; Nikpouraghdam M et al, 2020; Yang X et al, 2020; Zandkarimi E et al, 2020; Boulle 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; Gao 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 (29,754) were found to represent 65.5% 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 Y 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 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: systematic 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: systematic 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).

Characteristics of the study		Characteristics of participants					
		Infected		Survivors		Deaths	
Study ID	Type of study/country	Age	Sex	Age	Sex	Age	Sex
1. Mingli Yuan et al (2020)[5]	Retrospective cohort/Wuhan, China	60 (47–69)	Man 12 (45) Woman 15 (55)	55 (35-60)	Man 8 (47)	68 (63–73)	Man (40) Women (60)
2. Zhou F et al (2020)[6]	Retrospective cohort/Wuhan, China	56 (46–67)	Man 119 (62) Woman 72 (38)	52 (45–58)	Man 81 (59) Woman 56 (41)	69 (63–76)	Man 38 (70) Women 16 (30)
3. Deng Y et al (2020)	Retrospective cohort/China	(33–74)	Man 124 (55)	40 (33–57)	Man 51 (44)	69 (62–74)	Man 71 (67)
4. Chen T et al (2020)	Retrospective/China	54 (20–91)	Man 108 (53)	72	Man 18 (50)	Média de 77	Man (84) Woman (16)
5. Zhang J et al (2020)	Retrospective/ China	55.6 (44–69)	Man 321 (48) Woman 342 (52)	59,1 (43–68)	Man 306 (48) Woman 332 (52)	69,3 (34–90)	Man 15 (60) Woman 10 (40)
6. Rong-Hui Du et al (2020)	Prospective coorte/China	57.6 ± 13.7	Man 97 (54) Woman 82 (46)	56.0 ± 13.5	Man 87 (55) Woman 71 (45)	70,2 ± 7,7	Man 10 (48) Woman 11 (52)
7. Tao Chen et al (2020)	Retrospective case series/ China	62.0 (44.0–70.0)	Man 171 (62) Woman 103 (38)	51.0 (37.0-66.0)	Man 88 (55) Woman 73 (45)	68,0 (62,0–77,0)	Man 83 (73) Woman 30 (27)
8. Nikpouraghdam M et al (2020)	Retrospective/Irã	56(46–65)	Man 1955 (66) Woman 1009 (34)	N/D	N/D	65 (57–75)	Man - 167 (70) Woman 72 (30)
9. Yang X et al (2020)	Retrospective/China	59.7 (13.3)	Man 35 (67) Woman 17 (33)	51.9 (12.9)	Woman - 6 (30) Man - 14 (70)	64.6 (11.2)	Man - 21 (66) Woman - 11 (34)
10. Zandkarimi E et al (2020)	Retrospective/Irã	52.74 ± 22.16	Man 1019 (56) Woman 812 (44)	50.70 ± 21.43	Man - 520 (55) Woman - 423 (45)	66.25 ± 15.78	Man - 97 (68) Woman - 45 (32)
11. Boulle A et al (2020)	Retrospective/África do Sul	≥20	Man 7052 (32) Woman 15256 (68)	37 (30–48)	Man - 6767 (31) Woman - 14916 (69)	63 (54–71)	Man - 285 (46) Woman - 340 (54)
12. Chen L et al (2020)	Retrospective/China	55 (36–68)	Man 432 (55) Woman 360 (45)	52 (34–65)	Man - 398 (55) Woman - 326 (45)	70 (68–77)	Man - 34 (50) Woman - 34 (50)
13. Ciardullo S et al (2020)	Retrospective/Italy	72 ± 14	Man 244 (65) Woman 129 (35)	68 ± 14	Man - 146 (63) Woman - 85 (37)	78 ± 10	Man - 98 (69) Woman - 44 (31)
14. Smith AA et al (2020)	Retrospective/EUA	67	Man 194 (56) Woman 152 (44)	Median 64	Man - 126 (55) Woman - 103 (45)	Median 73	Man - 68 (58) Woman - 49 (42)
15. Chilimuri S. et al (2020)	Retrospective/EUA	63,0 (52,0–72,0)	Man 236 (63) Woman 139 (37)	58,0 (48,0–68,0)	Man - 124 (58) Woman - 91 (42)	68,0 (60,0–75,0)	Man - 112 (70) Woman - 48 (30)
16. Gerwen MV et al (2020)	Retrospective/EUA	64.5 (± 16.4)	Man 1181 (59) Woman 834 (41)	61.0 (± 16.4)	Man - 799 (57) Woman - 600 (43)	73.5 (± 13.2)	Man - 382 (62) Woman - 234 (38)
17. Pérez FM et al (2020)	Retrospective/Spain	63	Man 63 (66) Woman 33 (44)	Median 60	Man - 50 (63) Woman - 29 (37)	Median 67	Man - 13 (77) Woman - 4 (23)
18. Li J. et al (2020)	Retrospective/China	66 (55–72)	Man 44 (60) Woman 30 (40)	62 (53–70)	Man - 33 (55) Woman - 27 (45)	71 (69–77)	Man - 11 (79) Woman - 3 (21)
19. Gao S et al (2020)	Retrospective/China	71 (67–77)	Man - 101 (48) Woman - 109 (52)	70 (67–74)	Man - 79 (45) Woman - 96 (55)	74 (70–82)	Man - 22 (63) Woman - 13 (37)

(Continued)

Chart 1

(Continued)

Characteristics of the study		Characteristics of participants					
		Infected		Survivors		Deaths	
Study ID	Type of study/country	Age	Sex	Age	Sex	Age	Sex
20. Yang Q et al (2020)	Retrospective/China	N/D	Man 113 (50) Woman 113 (50)	50 (15,35)	Man - 82 (47) Woman - 94 (53)	68 (15,73)	Man - 31 (62) Woman - 19 (38)
21. Shah P et al (2020)	Retrospective/Georgia	63 (50–72)	Man - 218 (42) Woman - 304 (58)	60 (50–70)	Man - 168 (39) Woman - 262 (61)	70 (1–78)	Man - 50 (54) Woman - 42 (46)
22. Borobia AM et al (2020)	Coorte/Spain	61 (46–78)	Man - 1074 (48) Woman - 1152 (52)	56 (42–71)	Man - 788 (45) Woman - 978 (55)	83 (76–87)	Man - 286 (62) Woman - 174 (38)
23. Asfahan S et al (2020)	Retrospective/China	0–80	Man - 22981 (51) Woman - 21691 (49)	N/D	Man - 22328 (51) Woman - 21321 (49)	N/D	Man - 653 (64) Woman - 370 (36)
24. Liu J et al (2020)	Retrospective/China	57 (46 - 67)	Man - 635 (53,4) Woman - 555 (46,6)	56 (46,65)	Man - 535 (52) Woman - 498 (48)	69 (22,77)	Man - 100 (64) Woman - 57 (36)
25. Hwang JM et al (2020)	Retrospective/South Korea	67.6 ± 15.32	Man - 52 (50) Woman - 51 (50)	64.6 ± 15.8	Man - 36 (47) Woman - 41 (53)	76.5 ± 9.2	Man - 16 (62) Woman - 10 (38)
26. Rastad H et al (2020)	Retrospective/Iran	Median 54,8	Man - 1589 (54) Woman - 1368 (46)	Median 53,3	Man - 1422 (53,5) Woman - 1234 (46,5)	Median 53,3	Man - 167 (55,5) Woman - 134 (44,5)
27. Tu WJ et al (2020)	Retrospective/China	N/D	Man 79 (42) Woman 95 (58)	51 (37–62)	Man - 60 (40,3) Woman - 89 (59,7)	70 (64–80)	Man - 19 (76) Woman - 6 (24)
28. Wang L.et al (2020)	Retrospective/China	69 (65–76)	Man 166 (49) Woman 173 (51)	68 (64–74)	Man - 127 (46,4) Woman - 147 (53,6)	76 (70–83)	Man - 39 (60) Woman - 26 (40)
29. Parra-Bracamonte et al (2020)	Multivariate logistic regression model/Mexico	44 (33–56)	Man 178.152 (54) Woman 153.143 (46)	42 (32–53)	Man- 153.137 (52,3) Woman - 139.851 (47,7)	62 (52–71)	Man - 25.015 (65,3) Woman - 13.292 (34,7)
30. Soares RCM et al (2020)	Coorte/Brazil	N/D	Man 658 (57) Woman 494 (43)	N/D	Man - 407 (61,9) Woman - 289 (58,5)	N/D	Man - 251 (38,1) Woman - 205 (41,5)
31. Zanella A et al (2020)	Retrospective/Italy	N/D	Man 4764 (80) Woman 1146 (20)	N/D	Man - 3188 (80) Woman - 800 (20)	N/D	Man - 1580 (80) Woman - 346 (20)

Chart 2

Characteristics of the infected with respect to the presence of comorbidities.

Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	Comorbidities (*P* value)
1. Mingli Yuan et al (2020)[5]	January 1st to January 25, 2020	27 (100)	13 (48)	Hypertension 5 (19) Diabetes 6 (22) Cardiac disease 3 (11) ARDS 11 (41) Chronic gastritis 1 (4) Cerebral infarction 1 (4) Tumor 1 (4)	17 (70)	5 (29)	Tumor 1 (6) ARDS 1 (6) Chronic gastritis 1 (6)	10 (37)	8 (80)	Hypertension 5 (50) Diabetes 6 (60) Heart disease 3 (30) ARDS 10 (100) Cerebral infarction 1 (10)	Hypertension - .003 Diabetes - .001 Cardiac diseas - 0,041 ARDS -<.0001 Chronic gastritis - 1.000 Cerebral infarction - .370 Tumor - 1.000
2. Zhou F et al (2020)[6]	December 19, 2019 to January 31, 2020	191 (100)	91 (48)	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)	137 (22 72)	55 (40)	Hypertension 32 (23) Diabetes 19 (14) Coronary heart disease 2 (1) Chronic obstructive lung disease 2 (1) Carcinoma 2 (1) Chronic kidney disease 0 Other 11 (8)	54 (28)	36 (67)	Hypertension 26 (48) Diabetes 17 (31) Heart disease 13 (24) Chronic obstructive pulmonary disease 4 (7) Carcinoma 0 (0) Chronic kidney Disease 2 (4) Other 11 (20)	Hypertension - .0008 Diabetes - .0051 Heart disease- < .0001 Chronic obstructive pulmonary disease - .047 Carcinoma - .37 Chronic kidney Disease - .024 Other - .016
3. Deng Y et al (2020)	January 1, 2020 to February 21, 2020	225	N/D	N/D	116	48 (41)	Hypertension 18 (16) Lung Disease 3 (3) Diabetes 9 (8) Heart Disease 4 (3) Malignancy 2 (2) Others 15 (13)	109 (48)	79 (72)	Hypertension 40 (37) Lung disease 22 (20) Diabetes 17 (16) Heart disease 13 (12) Malignancy 6 (6) Others 31 (28)	Hypertension - < .001 Lung disease - < .001 Diabetes - .066 Heart disease - .031 Malignancy - .242 Others - .004
4. Chen T et al (2020)	January 1, 2020, to February 10, 2020	55	37 (67)	Hypertension 21 (38) Diabetes 12 (22) Cardiovascular Disease 11 (20) Cerebrovascular Disease 8 (15) Malignancy 5 (9) Chronic liver disease 2 (4) Chronic renal disease 3 (6) Chronic obstructive pulmonary disease 7 (13) Tuberculosis 1 (2)	36	17 (47)	Hypertension 12 (33) Diabetes 7 (19) Cardiovascular Disease 5 (14) Cerebrovascular Disease 5 (14) Malignancy 4 (11) Chronic liver Disease 1 (3) Chronic renal Disease 1 (3) COPD 6 (17) Tuberculosis 0 (0)	19 (34)	18 (95)	Hypertension 9 (47) Diabetes 5 (26) Cardiovascular Disease 6 (32) Cerebrovascular Disease 3 (16) Malignancy 1 (5) Chronic liver Disease 1 (5) Chronic renal Disease 2 (11) Chronic obstructive pulmonary disease 1 (5) Tuberculosis 1 (5)	Hypertension - .31 Diabetes - .73 Cardiovascular Disease - .12 Cerebrovascular Disease - 1.0 Malignancy - .47 Chronic liver Disease - 1.0 Chronic renal Disease - .27 Chronic obstructive pulmonary disease - .40 Tuberculosis - .35

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Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	Comorbidities (*P* value)
5. Zhang J et al (2020)	January 11 to February 6, 2020	663	247 (37)	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)	N/D	N/D	Respiratory disease 46 (7) Cardiovascular disease 148 (23) Gastrointestinal disease 30 (5) Endocrine system disease 64 (10) Urinary system disease 21 (3) Inflammatory disease 5 (1) Malignant tumor 13 (2)	N/D	N/D	Respiratory disease 5 (20) Cardiovascular disease 16 (64) Gastrointestinal disease 1 (4) Endocrine system disease 3 (12) Urinary system disease 0 (0) Inflammatory disease 1 (4) Malignant tumor 1 (4)	Respiratory disease -.019 Cardiovascular disease - < .001 Gastrointestinal disease - .749 Endocrine system disease - .986 Urinary system disease - 1.000 Inflammatory disease - .556 Malignant tumor - .968
6. Rong-Hui Du et al (2020)	December 25, 2019 and February 7, 2020	179	N/D	Hypertension 58 (32) Cardiovascular or cerebrovascular Diseases 29 (16) Diabetes 33 (18) Chronic digestive disorders 21 (12) Tuberculosis 8 (5) Chronic hepatic or renal insufficiency 4 (2) Peripheral vascular disease 4 (2) Malignancy 4 (2)	158	N/D	Hypertension 45 (29) Cardiovascular or cerebrovascular Diseases 17 (11) Diabetes 27 (17) Chronic digestive disorders 17 (11) Tuberculosis 8 (5) Chronic hepatic or renal insufficiency 2 (1) Peripheral vascular disease 2 (1) Malignancy 3 (2)	21 (11)	N/D	Hypertension 13 (62) Cardiovascular or cerebrovascular Diseases 12 (57) Diabetes 6 (29) Chronic digestive disorders 4 (19) Tuberculosis 0 (0) Chronic hepatic or renal insufficiency 2 (10) Peripheral vascular disease 2 (10) Malignancy 1 (5)	Hypertension - .005 Cardiovascular or cerebrovascular Disease- < .001 Diabetes - .231 Chronic digestive disorders - .279 Tuberculosis - .599 Chronic hepatic or renal insufficiency - .068 Peripheral vascular disease - .068 Malignancy - .396
7. Tao Chen et al (2020)	January 13, 2019 to February, 12, 2020	274	133 (49)	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 antigen positivity 11 (4) Cerebrovascular disease 4 (1) Chronic kidney disease 4 (1) Gastrointestinal diseases 3 (1) Metabolic arthritis 4 (1) Autoimmune disease 2 (1)	161	62 (39)	Hypertension 39 (24) Diabetes 23 (14) Cardiovascular disease 7 (4) Chronic heart failure 0 (0) Chronic lung diseases 7 (4) Malignancy 2 (1) Hepatitis B virus surface antigen positivity 6 (4) Cerebrovascular disease 0 (0) Chronic kidney disease 1 (1) Gastrointestinal diseases 2 (1) Metabolic arthritis 3 (2) Autoimmune disease 1 (1)	113(41)	71 (63)	Hypertension 54 (48) Diabetes 24 (21) Cardiovascular disease 16 (14) Chronic heart failure 1 (<1) Chronic lung diseases 11 (10) Malignancy 5 (4) Hepatitis B virus surface antigen positivity 5 (4) Cerebrovascular disease 4 (4) Chronic kidney disease 4 (4) Gastrointestinal diseases 1 (1) Metabolic arthritis 1 (1) Autoimmune disease 1 (1)	N/D

(Continued)

Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	Comorbidities (*P* value)
8. Nikpouraghdam M et al (2020)	February 19 to April 15, 2020	2964	N/D	Diabetes 113 (4) Chronic respiratory disease 60 (2) Hypertension 59 (2) Cardiovascular disease 37 (1) Chronic Kidney disease 18 (<1) Cancer (any) 17 (<1) Others 19 (<1)	N/D	N/D	N/D	239 (8)	N/D	Diabetes 11 (5) Chronic respiratory diseases 9 (4) Hypertension 8 (3) Cardiovascular diseases 4 (2) Chronic Kidney diseases 3 (1) Cancer 1 (<1) Others 2(<1)	N/D
9. Yang X et al (2020)	December 26, 2019 to January 26, 2020	52	21 (40)	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)	20	5 (25)	Chronic cardiac disease 2 (10) Chronic pulmonary disease 2 (10) Cerebrovascular Disease 0 (0) Diabetes 2 (10) Malignancy 0 (0) Dementia 0 (0) Malnutrition 0 (0) Smoking 2 (10)	32 (61)	16 (50)	Chronic cardiac disease 3 (9) Chronic pulmonary disease 2 (6) Cerebrovascular Disease 7 (22) Diabetes 7 (22) Malignancy 1 (3) Dementia 1 (3) Malnutrition 1 (3) Smoking 0 (0)	N/D
10. Zandkarimi E. et al (2020)	February 22 to May 18, 2020	1831 (100)	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)	943 (52)	N/D	Diabetes 99 (10) Weak immune system 5 (0) Coronary heart disease 171 (18) Chronic lung disease 60 (6) Chronic kidney disease 22 (2) Cancer 15 (2)	142 (8)	N/D	Diabetes 23 (16) Weak immune system 1 (1) Coronary heart disease 53 (37) Chronic lung disease 12 (8) Chronic kidney disease 5 (4) Cancer 9 (6)	Diabetes - <.001 Weak immune system - .634 Coronary heart disease - <.001 Chronic lung disease - .245 Chronic kidney disease - .648 Cancer - <.001
11. Boulle A et al (2020)	March 1 to June 9, 2020	22.308 (100)	N/D	Diabetes 3474 (16) Hypertension 5272 (24) Chronic kidney disease 605(3) Chronic pulmonary disease/ asthma 1661 (7) Tuberculosis 343 (2) HIV 3978 (7)	21.683 (97)	N/D	Diabetes 3.102 (14) Hypertension 4.910 (23) Chronic kidney disease 494 (2) Chronic pulmonary disease/ asthma 1.577 (7) Tuberculosis 317 (1) HIV 3.863 (18)	625 (3)	N/D	Diabetes 372 (60) Hypertension 362 (58) Chronic kidney disease 111 (18) Chronic pulmonary disease/ asthma 84 (13) Tuberculosis 26 (4) HIV 115 (18)	Diabetes - <.001 Hypertension - .004 Chronic kidney disease - <.001 Chronic pulmonary disease/ asthma - .514 Tuberculosis - <.001 HIV - <.001
12. Chen L et al (2020)	15 January to 26 March, 2020	792 (100)	N/D	Hypertension 215 (27) Diabetes 142 (18) Chronic obstructive pulmonary disease 19 (2) Chronic kidney disease 26 (3)	724 (91)	N/D	Hypertension 215 (27) Diabetes 142 (18) Chronic obstructive pulmonary disease 19 (2) Chronic kidney disease 26 (3)	68 (9)	N/D	Hypertension 215 (27) Diabetes 142 (18) Chronic obstructive pulmonary disease 19 (2) Chronic kidney disease 26 (3)	Hypertension - <.001 Diabetes - <.001 Chronic obstructive pulmonary disease - .005 Chronic kidney disease - .049

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Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	Comorbidities (*P* value)
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) Tumors 50 (14) Cardiovascular diseases 140 (38) Chronic obstructive pulmonary disease 39 (11)	231 (62)	N/D	Diabetes 36 (16) Hypertension 130 (57) Chronic kidney disease 22 (10) Tumors 28 (12) Cardiovascular diseases 75 (33) Chronic obstructive pulmonary disease 15 (7)	142 (38)	N/D	Diabetes 33 (23) Hypertension 107 (78) Chronic kidney disease 26 (18) Tumors 22 (16) Cardiovascular diseases 65 (46) Chronic obstructive pulmonary disease 24 (17)	Diabetes - .064 Hypertension - <.001 Chronic kidney disease - .014 Tumors - .320 Cardiovascular diseases - .007 Chronic obstructive pulmonary disease - .001
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)	229 (66)	N/D	Hypertension 151 (66) Hyperlipidemia 107 (47) Diabetes 95 (42) Cardiovascular disease 96 (42) Neurological disease 59 (26) Chronic kidney disease 45 (20) Chronic obstructive lung disease 27 (12) Cancer 27 (12) Asthma 35 (15) Hypothyroid 25 (11)	117 (34)	N/D	Hypertension 90 (77) Hyperlipidemia 60 (51) Diabetes 68 (58) Cardiovascular disease 66 (56) Neurological disease 36 (31) Chronic kidney disease 37 (32) Chronic obstructive lung disease 31 (27) Cancer 24 (21) Asthma 12 (10) Hypothyroid 20 (17)	Hypertension - .037 Hyperlipidemia - .429 Diabetes - .004 Cardiovascular disease - .012 Neurological disease - .373 Chronic kidney disease - .016 Chronic obstructive lung disease - .001 Cancer - .037 Asthma - .246 Hypothyroid - .128
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)	215 (57)	145 (67)	Hypertension 110 (51) Diabetes 85 (40) Cardiovascular disease 24 (11) Obstructive airway disease 33 (15) Chronic kidney disease 20 (9) HIV/AIDS 8 (4) Chronic liver disease 7 (3)	160 (43)	142 (89)	Hypertension 115 (72) Diabetes 90 (56) Cardiovascular disease 38 (24) Obstructive airway disease 29 (18) Chronic kidney disease 31 (19) HIV/AIDS 14 (9) Chronic liver disease 11 (7)	Hypertension - < .0001 Diabetes - .0017 Cardiovascular disease - .0018 Obstructive airway disease - .4854 Chronic kidney disease - .0060 HIV/AIDS - .0469 Chronic liver disease - .1420

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Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	Comorbidities (*P* value)
16. Gerwen MV et al (2020)	March 1 to April 1, 2020	2015 (100)	N/D	Hypertension 1181 (59) Coronary artery disease 373 (19) Atrial fibrillation 258 (13) Congestive heart failure 250 (12) Peripheral vascular disease 112 (6) Cerebrovascular accident / transient ischemic attack 187 (9) Dementia 183 (9) Diabetes 795 (40) Hypothyroidism 171 (9) Chronic kidney disease 293 (15) Malignancy 228 (11) Asthma 232 (12) Chronic obstructive pulmonary disease 145 (7) Prior venous thromboembolism 89 (4)	1399 (69)	N/D	Hypertension 757 (54) Coronary artery disease 220 (16) Atrial fibrillation 147 (11) Congestive heart failure 135 (10) Peripheral vascular disease 66 (5) Cerebrovascular accident / transient ischemic attack 109 (8) Dementia 84 (6) Diabetes 502 (36) Hypothyroidism 111 (8) Chronic kidney disease 176 (13) Malignancy 147 (11) Asthma 171 (12) Chronic obstructive pulmonary disease 85 (6) Prior venous thromboembolism 63 (5)	616 (31)	N/D	Hypertension 424 (69) Coronary artery disease 153 (25) Atrial fibrillation 111 (18) Congestive heart failure 115 (19) Peripheral vascular disease 46 (8) Cerebrovascular accident / transient ischemic attack 78 (13) Dementia 99 (16) Diabetes 293 (48) Hypothyroidism 60 (10) Chronic kidney disease 117 (19) Malignancy 81 (13) Asthma 61 (26) Chronic obstructive pulmonary disease 60 (10) Prior venous thromboembolism 28 (4)	Hypertension - <.001 Coronary artery disease - <.001 Atrial fibrillation - <.001 Congestive heart failure - <.001 Peripheral vascular disease - .013 Cerebrovascular accident / transient ischemic attack - <.001 Dementia - <.001 Diabetes - <.001 Hypothyroidism - .180 Chronic kidney disease - <.001 Malignancy - .085 Asthma - .133 Chronic obstructive pulmonary disease - .003 Prior venous thromboembolism - .776
17. Pérez FM et al (2020)	February 26 to April 29, 2020	96 (100)	60 (62)	Hypertension 38 (40) Diabetes 15 (16) Heart disease 13 (14) Asthma 11 (12) Chronic obstructive pulmonary disease 6 (6) Obstructive sleep apnea syndrome 4 (4) Cerebrovascular disease 6 (6) Chronic kidney disease 6 (6) Cancer 3 (3)	79 (82)	45 (57)	Hypertension 26 (33) Diabetes 13 (17) Heart disease 5 (6), asthma 10 (13) Chronic obstructive pulmonary disease 4 (5) Obstructive sleep apnea syndrome 3 (4) Cerebrovascular disease 2 (3) Chronic kidney disease 3 (4) Cancer 2 (3)	17 (18)	16 (94)	Hypertension 12 (71) Diabetes 2 (13) Heart disease 8 (47) Asthma 1 (6) Chronic obstructive pulmonary disease 2 (12) Obstructive sleep apnea syndrome 1 (6) Cerebrovascular disease 4 (24) Chronic kidney disease 3 (19) Cancer 1 (6)	Hypertension - .006 Diabetes - .516 Heart disease - < .001 Asthma - .683 Chronic obstructive pulmonary disease - .287 Obstructive sleep apnea syndrome - .548 Cerebrovascular disease - .008 Chronic kidney disease - .058 Cancer - .447
18. Li J et al (2020)	January 25 to February 26, 2020	74 (100)	56 (76)	Hypertension 35 (47) Diabetes 14 (19) Coronary disease 6 (8) Tuberculosis 6 (8) Chronic liver disease 2 (3) Malignancy 2 (3)115	60 (81)	44 (73)	Hypertension 25 (42) Diabetes 11 (18) Coronary disease 2 (3) Tuberculosis 5 (8) Chronic liver disease 2 (3) Malignancy 2 (3)	7 (19)	12 (86)	Hypertension 10 (71) Diabetes 3 (21) Coronary disease 4 (29) Tuberculosis 1 (7) Chronic liver disease 0 (0) Malignancy 0 (0)	Hypertension - .045 Diabetes - .790 Coronary disease - .002 Tuberculosis - .883 Chronic liver disease - .489 Malignancy - .489

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Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	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 diseases 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)	124 (71)	Hypertension 97 (55) Diabetes 29 (17) Cardiovascular disease 35 (20) Chronic obstructive pulmonary diseases 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)	135 (100)	Hypertension 18 (51) Diabetes 9 (26) Cardiovascular disease 17 (49) Chronic obstructive pulmonary diseases 1 (3) Respiratory disease 18 (51) Cerebrovascular disease 7 (20) Chronic liver disease 6 (17) Digestive diseases 6 (17) Chronic kidney disease 10 (29) Cancer 3 (9)	Hypertension - .664 Diabetes - .200 Cardiovascular disease - <.001 Chronic obstructive pulmonary diseases - .435 Respiratory disease - <.001 Cerebrovascular disease - <.001 Chronic liver disease - .047 Digestive diseases - .123 Chronic kidney disease - <.001 Cancer - .026
2. Yang Q et al (2020)	January 1 to February 29, 2020	226 (100)	N/D	N/D	176 (78)	N/D	Hypertension 47 (27) Diabetes 28 (16) Coronary heart disease 6 (3) Chronic obstructive pulmonary disease 3 (2)	50 (22)	N/D	Hypertension 37 (74) Diabetes 17 (34) Coronary heart disease 7 (14) Chronic obstructive pulmonary disease 3 (6)	Hypertension - < .001 Diabetes - .008 Coronary heart disease - .010 Chronic obstructive pulmonary disease - .124
21. Shah 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 6811 (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)	N/D	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)	N/D	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

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Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	Comorbidities (*P* value)
22. Borobia AM et al (2020)	February 25 to April 19, 2020	2226 (100)	1747 (79)	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)	1766 (78)	1299 (74)	Hypertension 602 (34), Chronic heart disease 234 (13), Diabetes 224 (13), Rheumatological disease 188 (11), Solid malignant disease 159 (9), Obesity 176 (10), Chronic kidney disease 80 (5), Chronic obstructive Pulmonary disease 88 (5), Other chronic lung diseases 94 (5), Hematological malignant Disease 87 (5), Asthma 98 (6), Liver disease 66 (4), HIV 9 (1)	460 (22)	448 (97)	Hypertension 318 (69), Chronic heart Disease 195 (42), Diabetes 157 (34), Rheumatological Disease 80 (17), Solid malignant Disease 93 (20), Obesity 66 (14), Chronic kidney Disease 94 (20), Chronic obstructive Pulmonary disease 65 (14), Other chronic lung Diseases 49 (11), Hematological Malignant disease 46 (10), Asthma 17 (4), Liver disease 23 (5), HIV 4 (1)	Hypertension - <.001 Chronic heart disease - <.001 Diabetes - <.001 Rheumatological disease - <.001 Solid malignant disease - <.001 Obesity - .009 Chronic kidney disease - <.001 Chronic obstructive pulmonary disease <.001 Other chronic lung diseases - <.001 Hematological malignant disease <.001 Asthma - .138 Liver disease - .272 HIV - .318
23. Asfahan S et al (2020)	N/D	44672	N/D	N/D	43649	20308	Hypertension 2522 (12), diabetes 1022 (5), cardiovascular disease 781 (4), chronic respiratory disease 479 (2), cancer 101 (0.5)	1023 (2)	504 (49)	Hypertension 161 (40) Diabetes 80 (20) Cardiovascular disease 92 (23) Chronic respiratory disease 32 (8) Cancer 6 (2)	N/D
24. Liu J et al (2020)	December 29, 2019 to February 28, 2020	1190	441 (37)	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) Immunosupression 24 (2,0) Tuberculosis 15 (1,3)	1033 (87)	345 (33,4)	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) Immunosupression 15 (1,5) Tuberculosis 10 (1,4)	157 (13)	96 (61)	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) Immunosupression 9 (5,9) Tuberculosis 5 (3,3)	Chronic obstructive pulmonary disease - 1 Diabetes - <.0001 Hypertension - <.0001 Chronic cardiac disease- <.0001 Chronic kidney disease- .38 Chronic liver disease- .01779 Stroke - .0041 Malignancy .1115 Immunosupression - .0009 Tuberculosis - .0475

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Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	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) Chronic kidney disease 17 (17) Dyslipidemia 13 (13) Chronic lung disease 7 (7) Carcinoma 9 (9) Cardiovascular disease 12 (12) Dementia 11 (11) Parkinson 138 Disease 2 (2) Stroke 4 (4) Taking NSAIDs 5 (5) Taking ARB or ACEi 13 (13)	77 (75)	N/D	Hypertension 40 (52) Diabetes mellitus 21 (27) Chronic kidney disease 14 (18) Dyslipidemia 10 (13) Chronic lung disease 2 (3) Carcinoma 5 (6) Cardiovascular disease 6 (8) Dementia 3 (4) Parkinson disease 1 (1) Stroke 1 (1) Taking NSAIDs 3 (4) Taking ARB or ACEi 8 (10)	26 (25)	N/D	Hypertension 17 (65) Diabetes mellitus 14 (54) Chronic kidney disease 3 (12) Dyslipidemia 3 (12) Chronic lung disease 5 (19) Carcinoma 4 (15) Cardiovascular disease 6 (23) Dementia 8 (31) Parkinson disease 1 (4) Stroke 3 (12) Taking NSAIDs 2 (8) Taking ARB or ACEi 5 (19)	Hypertension - Diabetes mellitus - .013 Chronic kidney disease - .430 Dyslipidemia - .848 Chronic lung disease - .004 Carcinoma - .165 Cardiovascular disease - .036 Dementia - .000 Parkinson disease - .416 Stroke - .019 Taking NSAIDs - .436 Taking ARB or ACEi - .338
26. Rastad H et al (2020)	February 20 to Mach 25, 2020	2957	749 (25)	Diabetes mellitus 138 (4,7) Cardiovascular Disease 168 (5,7)	2656	615 (23,2)	Diabetes mellitus 115 (4,3) Cardiovascular Disease 141 (5,3)	301 (10)	615 (23,2)	Diabetes mellitus 23 (7,6) Cardiovascular Disease 27 (9)	N/D
27.Tu W-J et al (2020)	January 3 to February 24, 2020	149	N/D	N/D	149	36 (24,2)	Hypertension 25 (16,8) Diabetes 11 (7,4) Cardiovascular- cerebrovascular diseases 8 (7,4) Respiratory diseases 8 (7,4)	N/D	N/D	Hypertension 12 (48) Diabetes 6 (24) Cardiovascular- cerebrovascular diseases 8 (32) Respiratory diseases 4 (16)	Hypertension - <.001 Diabetes - .010 Cardiovascular- cerebrovascular disease - <.001 Respiratory diseases - .130
28. Wang L et al (2020)	January 1 to February 6, 2020	339	N/D	Hypertension 138 (40,8) Diabetes 54 (16,0) Cardiovascular disease 53 (15,7) Cerebrovascular disease 21 (6,2) Chronic kidney disease 13 (3,8) Chronic liver disease 2 (0,6) Chronic obstructive pulmonary disease 21 (6,2) Malignancy 15 (4,4) Autoimmune disease 5 (1,5)	274	N/D	Hypertension 106 (38,8) Diabetes 43 (15,8) Cardiovascular disease 32 (11,7) Cerebrovascular disease 11 (4,0) Chronic kidney disease 9 (3,3) Chronic liver disease 1 (0,4) Chronic obstructive pulmonary disease 10 (3,7) Malignancy 12 (4,4) Autoimmune disease 4 (1,5)	65 (19)	N/D	Hypertension 32 (50) Diabetes 11 (17.2) Cardiovascular disease 21 (32.8) Cerebrovascular disease 10 (15.6) Chronic kidney disease 4 (6.3) Chronic liver disease 1 (1.6) Chronic obstructive pulmonary disease 11 (17.2) Malignancy 3 (4.7) Autoimmune disease 1 (1,6)	Hypertension - .031 Diabetes - .116 Cardiovascular disease - <.001 Cerebrovascular disease - <.001 Chronic kidney disease - .066 Chronic liver disease - .065 Chronic obstructive pulmonary disease - <.001 Malignancy - .12 Autoimmune disease - .121

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Chart 2

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Characteristics of the study		Resulted									
		Infected			Survivors			Deaths			
Study ID	Study period	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	n	Comorbidities n (%)	Types of Comorbidities n (%)	Comorbidities (*P* value)
29. Parra-Bracamonte et al (2020)	January 13 to July 17, 2020	331.298	N/D	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)	292.988	N/D	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)	38.310 (12)	N/D	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)	N/D
30. Soares RCM et al (2020)	February 29 to june 11, 2020	1152	N/D	N/D	696 (60,4)	N/D	Cardiovascular diseases 270 (39) Diabetes 135 (19) Kidney diseases 23 (3) Obesity 63(9) Pulmonary diseases 53 (8) Smoking 38 (5)	456 (40)	N/D	Cardiovascular diseases 200 (44) Diabetes 142 (31) Kidney diseases 36 (8) Obesity 50 (11) Pulmonary diseases 58 (13) Smoking 39 (8)	Cardiovascular diseases - <.001 Diabetes - <.001 Kidney diseases - .001 Obesity - .334 Pulmonary diseases - .006
31. Zanella A et al (2020)	February 20 to April 22, 2020	3.988	N/D	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	1926 (48)	N/D	Hypertension 962 (50) Hypercholesterolemia 376 (19) Heart disease 342 (18) Type 2 diabetes 328 (17) Malignant neoplasm 202 (10) Chronic obstructive pulmonary disease 67 (3) Chronic kidney disease 71 (4) Liver disease 42 (2) Other 274 (14)	Hypertension - <.001 Hypercholesterolemia - <.001 Heart disease - <.001 Type 2 diabetes - <.001 Malignant neoplasm - <.001 Chronic obstructive - <.001 pulmonary disease - <.001 Chronic kidney disease - <.001 Liver disease - .87 Other - .01

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: systematic 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: systematic hypertension (1069); cardiovascular disease (407); diabetes mellitus (361); malignancy (224); respiratory disease (91); renal disease (26).

With only one study, South Africa (Boulle 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 systematic 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; Zandkarimi E 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 (09).

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 71years. 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 (14,295respiratory 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 (55.4%). 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%) morbidly 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[6] 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 this same 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 leucocytes 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.[7]

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.[8]

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.[8]

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 installation 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.[7] 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[9] 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.[10] The global prevalence of diabetes mellitus as estimated by the Non-Communicable Diseases Risk Factor Collaboration in 2014 was 9.0% for men and 7.9% for women, corresponding to 422 million people.[11]

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.[12–14] 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.[10]

Moreover, inadequate glycemic control in patients with diabetes mellitus can further compromise the immune system's response capacity.[15] In this sense, proper glycemic control is an important factor in diabetic patients diagnosed with COVID-19.[13]

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.[16] Joseph et al[17] 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.[18–20] 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.[20]

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.[21]

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

Conceptualization: DCPJ.
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Formal analysis: DCPJ, KTSC and TNBM.
Investigation: DCPJ, KTSC and TNBM.
Methodology: DCPJ, KTSC and TNBM.
Writing – original draft: DCPJ, DFOS, KTSC and TNBM.
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