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COMORBIDITIES AND MORTALITY IN ELDERLY PEOPLE WITH SARS-COV: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

The objective of this study is to review and synthesize findings of the presence of comorbidities and mortality in the elderly after SARS-CoV infection. A systematic review and meta-analysis were conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive systematic search was performed on Pubmed and EMBASE, to find articles published until May 2020. For the prevalence estimates of the included observational studies, a random effects meta-analysis model was used with the Variance Estimator. The data of 64643 patients presented in 15 articles were initially included in this study. According to the linear correlation analysis, in the elderly population investigated as explained comorbidities, approximately 70% ($r^2 = 0.69$) of mortality cases. Meta-analysis revealed that General mortality explained 62% of mortality in the elderly population studied (95% CI, 0.23-0.90; i2 = 100%) and a comorbidity in the elderly population with SARS-CoV 2 was 95% (95% CI, 0.58-1.00; i2 = 100%. In the present study, it is noticed that there is a moderate relation of deaths by SARS-Cov in patients with comorbidities and old age, the main hypothesis is the alteration of hemostasis and the compromised immune response, due to age.

INTRODUCTION

In 2003, a different coronavirus epidemic caused by the SARS-CoV-1 virus had emerged in Guangdong, China and subsequently spread to 26 other countries, on this occasion, human coronaviruses (HCoVs) were reported as pathogens that cause severe symptoms in infections of the respiratory tract (Hung, 2003). Recently, the first case of coronavirus disease 2019 (COVID-19) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in Wuhan, China, it is novel strainishighlytransmittableandseveredisease, responsible for the deaths of more than 25,000 people (Zhu *et al*., 2019). The rapid increase in the number of cases, deaths and subsequent global transmission led the outbreak to be classified as pandemic by WHO (WHO, 2020).

According to most epidemiological data already released, in this pandemic, elderly people and those who have multiple previous diseases are particularly more susceptible to the disease, both in terms of prevalence, as well as in terms of severity and mortality (Wu *et al*., 2020; Sohrabi *et al*., 2020; Wu; McGoogan, 2020; Yang *et al*., 2020; Liu *et al*, 2020; Gao *et al*., 2020; Zhou *et al*., 2020; Cheng *et al*., 2020).

The main complication of COVID-19 is acute respiratory distress syndrome (ARDS). However, previous evidence shows that people over the age of 65 years develop atypical signs of coronavirus infection 19, including mild pneumonia, delirium, postural instability or diarrhea, which can lead to delays or dignified errors, making treatment difficult to

establish (WHO, 2020b; D'Adam, Yoshikawa, & Ouslander, 2020; Abbara *et al*., 2019; Godaert *et al*., 2018).

The greater severity of the disease and the risk of death after infection by the coronavirus 19 increases with age, especially among those who diagnose chronic comorbidities, such as diseases of cardiovascular, hepatic, renal or malignant tumor (Lloyd-Sherlock *et al*., 2020; Jiang, Xia, Ying, & Lu, 2020; Wang *et al*., 2020). Some data already recorded from cases in China and the USA show that elderly people represent half of hospital admissions related to COVID-19, more than half of hospitalizations in intensive care units and account for 80% of fatal cases (CDC, 2020).

Considering the growing interest in the identification of potential risk factors for mortality due to SARS-CoV infections, the main objective of this review was to evaluate the evidence of an association between the presence of comorbidities and mortality of elderly people due to coronavirus infections.

METHODS

Search strategy and Sources of data: We conducted a systematic review and meta-analysis in compliance with the recommendations and criteria described in the preferred reporting items for systematic reviews and metanalyses (PRISMA) and Cochrane Handbook (Higgins, Thomas, Chandler, Cumpston, Page, & Welch, 2019).

Potential studies were identified via a comprehensive strategy. The systematic review wasperformed in the following data bases: Pubmed and EMBASE. The search strategy involved the cross checking of keywords selected based on the Medical Subjects Headings (Mesh) and Health Sciences Descriptors (Decs). There was no languageres triction. For each database, a specific strategy for crossing descriptors or keywords was developed to recover subjects from the scientific literature. At Pubmed, the search strategy with the following syntax was applied: (Mortalities OR Mortality OR "Case Fatality Rate" OR "Case Fatality Rates" OR "ExcessMortalities" OR "ExcessMortality" OR "Mortality Declines" OR "Mortality Decline" OR "Mortality Determinants" OR "Mortality Determinant" OR "Differential Mortalities" OR "Differential Mortality" OR "Age-Specific Death Rate" OR "Age-Specific Death" Rates OR Age Specific Death Rate OR Death Rate OR Death Rates OR Mortality Rate OR Mortality Rates AND (coronavirus OR coronavirus OR "coronavirus infections" OR betacoronavirus OR OR coronaviruses OR "Coronavirus Infection" OR "COVID-19" OR "2019 Novel Coronavirus Infection" OR "2019-nCoV Infection" OR "2019 nCoV Infection" OR "2019-nCoV Infections" OR "Novel Coronavirus Pneumonia" OR "2019 novel coronavirus" OR nCoV OR covid OR "SARS-CoV-2" OR "SARS2"OR "Wuhan coronavirus" OR MERS OR Middle East Respiratory Syndrome)

At EMBASE, a strategy was used:((('veryelderly':ti,ab,kw OR 'institutionalizedelderly':ti,ab,kw OR aged:ti,ab,kw) AND mortality:ti,ab,kw OR 'mortality rate':ti,ab,kw OR 'death rate changes':ti,ab,kw OR 'age specific death rate':ti,ab,kw) AND 'middle east respiratory syndrome coronavirus': ti,ab, kw OR 'coronavirusdisease 2019':ti, ab,kw OR 'sarscoronavirus': ti,ab,kw) AND [article]/lim AND ([aged]/lim OR [veryelderly]/lim) AND [humans]/lim AND [embase]/lim

After the selection of potentially relevant studies, the full-text versions were analyzed for methodological quality by two researchers independently and disagreement between reviewers was resolved by discussion or arbitration by the other researcher.

Inclusion and Exclusion Criteria: The following criteria were adopted for the selection of the studies: Cross-sectional studies; cross-sectional studies that evaluate the elderly and their usefulness for SARS-CoV outbreak. Editorial, letter to the editor, viewpoint, case presentation or brief communication were excluded as it did not contain SARS COV.

Data extraction and analysis: Initial the studies were exported to a Mendeley® file and reported in the PRISMA diagram (Figure 1). The first two screenings (selection by title and abstract) were performed by two independent researchers (ML and RS), who selection of articles potentially to be included in the final compilation. In cases where there were disagreements, a fourth independent researcher (KCC) resolved the discrepancies. Regarding data extraction, the three independent researchers (ML, RS and KCC) used a form which was intended to record: study data (authors, journal name, country and study scenario, year of publication), methodological information (objective of the study, design, size of the total sample, aspect or variable of quality of life, exercise practice and instruments used to evaluate them).

Linear regression analysis was performed to verify the association between the dependent (comorbidities) and independent (mortality) variables in the elderly population investigated in Microsoft Excel (2019 version). To this end, it was Pearson's correlation coefficient (CC) was calculated. This one is a measure of the degree of linear relationship between two variables quantitative. The calculation of the Coefficient of Determination (CD) was also performed, which indicates, in percentage, how much the variable dependent can be explained by the independent variable.

For the prevalence estimates of the included observational studies, a random effects meta-analysis model was used with the Variance Estimator DerSimonian and Laird (1983), assuming that the effect of interest is the same in all studies and that the differences observed between them are due only to sampling errors (variability within the studies). The Freeman-Tukey double arcsine transformation was used to stabilize the variances (Barendregt, Doi, Lee, Norman, & Vos, 2013). The heterogeneity of the estimates of the sample size effect throughout these studies was quantified by the I^2 statistic. The heterogeneity between the studies was assessed by Cochran's Q test and I^2 statistics. As the prevalence of mortality can vary according to the types of conditions: SARS-CoV1 and SARS-CoV2 and a general population, subgroup analyzes were used to assess whether mortality under each condition influenced a joint assessment. The prevalence of comorbidity in the elderly population has already been analyzed, considering only the SARS-CoV2 group, in view of the missing or incomplete SARS-CoV1 data. The results are presented in forestplot with 95% confidence intervals (95% CI) or scattered plots with point estimates and 95% CI. All analyzes were performed using R statistical software version 4.0 (R Core Team, 2020), with meta package version 4.11-0 (Balduzzi, Rücker& Schwarzer, 2019).

Quality Assessment: We used the Newcastle–Ottawa scale to assess the quality of the included studies (Wells *et al*., 2019). Relevant organizational websites including the Joanna Briggs Institute publish a Reviewers' Manual, which is designed to support individuals who are undertaking systematic reviews following JBI methodologies and methods (Munn, Moola, Lisy, Riitano, & Tufanaru, 2015).

This checklist contains 9 questions, which we divided into 3 domains: participants (questions 1, 2, 4, and 9), outcome measurement (6 and 7), and statistics (3, 5, and 8). A study was rated as having high quality when the methods were appropriate in all 3 domains. Quality assessment was also performed by 2 independent reviewers, and any uncertainties were resolved by consulting a third reviewer.

RESULTS

Selection and evaluation of studies: The initial search identified 625 studies with the descriptors used. After title and abstract analysis, we excluded 603 studies which were ineligible based on inclusion criteria (Figure 1). The present systematic review included a total of 15 studies (Table 1).
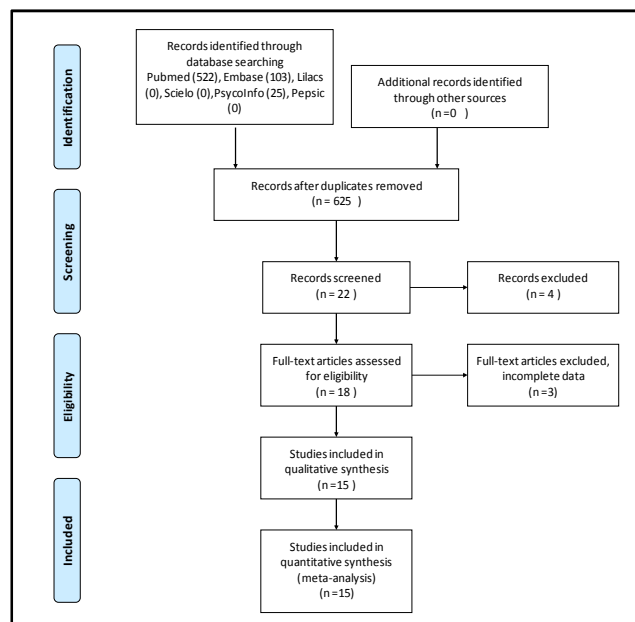
Note. PRISMA = PreferredReportingItems for Systematic Reviews and Meta-Analyses.

Figure 1. Study Flow Diagram usingthe PRISMA framework

Table 1 shows the characteristics of the 15 studies used for systematic review and meta-analysis carried out in this study, which involved the elderly and SARS-CoV, with information from the authors, the location of data collection, the sample size, the mean age and the comorbidities found. Most studies were carried out in China, 2 in the United States, 2 in Saudi Arabia, 1 in Iran, 1 in Italy, 1 in Korea and 1 in the Middle East. Only 4 studies did not bring information related to comorbidities. The main comorbidities found in the studies were cardiac disease, pulmonary disease, diabetes, neurological disease, kidney disease, hepatic disease and cancer.

Included studies: Fifteen studies were included, eight from China, two from the USA, two from Saudi Arabia, one from Italy, one from Iran, one from Korea, one from Middle East. The total population corresponded to 64643 participants, with 18107 elderly with 1622 comorbidities and 2270 deaths by SARS-CoV1 and 2, the mortality in young people was 1011 deaths in fifteen studies. Of the 15 articles initially included, only 11 contained the necessary data on comorbidities and mortality and therefore were considered for analysis of linear correlation (Table 2 and Figure 2). The 11 studies included 2651 elderly people, nine with SARS-CoV2 and two with SARS-CoV1. Observe a moderate correlation (r = 0.83) between the presence of comorbidities and mortality. Thus, in the elderly population investigated as explained comorbidities, approximately 70% (r^2 = 0.69) of mortality cases (Figure 2).

Prevalence of mortality and comorbidity in the elderly population: General mortality explained 62% of mortality in the elderly population studied (95% CI, 0.23-0.90; i2 = 100%; 14 studies). The prevalence indicators were: SARS-CoV2 0.60 (95% CI; 0.14-0.94; i2 = 100%; 11 studies); SARS-CoV1 0.69 (95% CI, 0.35-0.90; i2 = 92%; 3 studies). The difference between these two subgroups for random effect was Q = 0.07, d.f. = 1, p-value = 0.7889. Mortality occurred in 15.452 of the 18.117 elderly people with SARS-CoV2 investigated (Figure 2). A comorbidity in the elderly population with SARS-CoV2 was 95% (95% CI, 0.58-1.00; i2 = 100%; 9 studies) and Q = 497.94, d.f. = 8, p-value = <0.0001 and covered 614 elderly with comorbidities out of a total of 2,592 with SARS-CoV2 included (Figure 3).

The methodological quality of the selected studies: The quality of the studies was analyzed by the Newcastle-Ottawa Scale (table 3). The Newcastle-Ottawa Scale is graduated by a system with stars graduation that goes from 0 to 9 delimited in three domains: selection, comparability, and outcome. Higher grades represent better quality. Studies of excellent quality were considered that obtained high score in all 3 domains. In the table 3 the studies by Leung (2020), Hu *et al*., (2004), Chen T *et al*., 1 (2020), Chen T *et al*., 2 (2020), Nikpouraghdam *et al*., (2020), Ahmed (2017), Yang *et al*., (2020), Wu *et al*., (2020) and Liu *et al*., (2020) obtained excellent methodological quality when submitted to Newcastle-Ottawa Scale evaluation.

The study bias risk was analyzed by Critical Appraisal Checklist for Analytical Cross-Sectional Studies, the scale consists in 7 questions: 1. Were the criteria for inclusion in the sample clearly defined? 2. Were the study subjects and the setting described in detail? 3. Was the exposure measured in a valid and reliable way? 4. Were objective, standard criteria used for measurement of the condition? 5. Were confounding factors identified? 6. Were strategies to deal with confounding factors stated? 7. Were the outcomes measured in a valid and reliable way? 8. Was appropriate statistical analysis used? The answers by analytical cross-sectional studies Critical Appraisal Tool Answers were: Yes, No, Unclear or Not/Applicable (Table 4). According to a risk analysis by the JBI Critical Apprisal Checklist for Analytical Cross-Sectional Studies, all studies describe a description of the inclusion criteria, however, the studies by Porcheddu *et al*., (2020) does not describe in detail how resources in the sample. All studies have defined standards for measuring the variables. The studies by Procheddu *et al*. (2020), Chen Y *et al*., (2020), CDC USA, (2020) and CDC Korea (2020) did not identify the confounding factors and none of these studies used strategies to deal with confounding factors.

Table 1. Characterization of studies

Author	Location	Population (n)	Age (years)	Sars-CoV	Comorbidities in Elderly Population
Leung, 2020	China	Elderly patients (n=154)	75	Sars-CoV-2	Diabetes (n=28), Hypertension (n=43), Cardiopulmonary disease (n=65), Neurological disease (n=7), Kidney disease (n=7), Hepatic disease (n=2), Endocrine disease (n=4), Rheumatological disease (n=4), Hematic disease (n=3)
Hu et al., 2004	China	Elderly patients (n=40), young patients (n=62) Total (n=102)	45,8±15,4	Sars-Cov-1	-
Porcheddu et al., 2020	China/Italia	Elderly patients (n=13997), Young Patients (n=31563), Total 45560	49,76±14,71	SARS-CoV-2	-
Chen T et al. 1, 2020	China	Elderly patients (n=153), young patients (n=121), Total (n=274)	62,0	SARS-CoV-2	Smoking (n=38), Hypertension (n=93), Diabetes (n=47), Cardiovascular disease (n=23), Pulmonary disease (n=18), Cancer (n=7), Hepatitis B (n=11), Neurological disease (n=4), Kidney disease (n=4), Rheumatological disease (n=4), Gastrointestinal disease (n=3), autoimmune disease (n=2)
Garout et al., 2018	Saudi Arabia	Elderly patients (n=19), young patients (n=33), Total (n=52)	49,71±18,47	SARS-CoV-1	Hypertension (n=14), Diabetes (n=14), Renal disease (n=11)
McMichael et al., 2020	USA	Elderly (n=95), Young (n=34), Total (n=129)	Elderly in asylum (81,0), Health care professionals (42,5), Visitors (62,5)	SARS-CoV-2	Hypertension (n=58), Cardiac disease (n=51), Kidney disease (n=36), Diabetes (n=34), Obesity (n=30), Respiratory disease (n=30), Cancer (n=11), Autoimmune disease (8), Hepatic disease (5)
Chen Y et al., 2020	China	Elderly (n=34), young (n=4), Total (n=38)	70,0 (65 min-81 max)	SARS-CoV-2	Hypertension (14), Diabetes (11), Cardiac disease (6), Respiratory disease (5), Neurological disease (7), Fracture (1), Hepatic disease (1), Kidney disease (1)
US Department of Health and Human Services/Centers for Disease Control and Prevention, 2020	USA	Elderly (n=1200), Young (n=1249), Total (n=2449)	≥85,0 (6%), 65–84 (25%), 55–64 (18%), 45–54 (18%), 20–44 (29%)	SARS-CoV-2	-
Chen T et al. 2, 2020	China	Elderly (n=55), Young (n=148), Total (n=203)	54,0 (20 min-91 max)	SARS-CoV-2	Hypertension (n=21), Diabetes (n=12), Respiratory disease (n=2), Kidney disease (n=2), Cardiac disease (n=11), Neurological disease (n=8), Hepatic disease (n=2)
Korean Society of Infectious Diseases and Korea Centers for Disease Control and Prevention, 2020	Korea	Elderly (n=54)	75,5 (35 min-93 max)	SARS-CoV-2	Cardiac disease (n=32), Diabetes (n=16), Neurological disease (n=10), Respiratory disease (n=7), Cancer (n=7), Renal disease (n=5), Hepatic disease (n=2), Psychologic disease (n=7)
Nikpouraghdam et al., 2020	Iran	Elderly (n=1989), Young (n=10881), Total (n=12870)	55.50 ±15.15	SARS-CoV-2	Respiratory disease (n=60), Hypertension (n=59), Cardiac disease (n=37), Kidney disease (n=18), Cancer (n=17)
Ahmed, 2017	Saudi Arabia	Elderly (n=259), Young (n=401), Total (n=660)	53.9±17.9	SARS-CoV-1	-
Yang et al., 2017	Middle East	Total (n=1841)	Death (61,08±18.0, Alive (46.94±17.0)	SARS-CoV-1	944 patients with comorbidities
Wu et al., 2020	China	Elderly (n=40), Young (n=161), Total (n=201)	51,0 (43-60)	SARS-CoV-2	Hypertension (n=39), Diabetes (n=22), Cardiovascular disease (n=8), Hepatic disease (n=7), Neurological disease (n=7), Kidney disease (n=5), Endocrine disease (n=2), Cancer (n=1)
Liu et al., 2020	China	Elderly (n=18), Young (n=38), Total (n=56)	Elderly (68,00), Young (47,00), General (53,75)	SARS-CoV-2	Hepatic disease (n=1), Kidney disease (n=1), Hypertension (n=10), Diabetes (n=4), Cardiac disease (n=3)

Table 2. Comorbidities and mortality in the elderly population among the included studies

| Author	Condition	Elderly	Comorbidities	Mortality
Leung	SARS-CoV2	154	80	89
Hu et al.	SARS-CoV1	40	45	23
Chen et al.	SARS-CoV2	153	93	194
Garout et al.	SARS-CoV1	19	19	18
McMichael et al.	SARS-CoV2	95	89	23
Yifei Chen et al.	SARS-CoV2	34	25	34
TieLong Chen et al.	SARS-CoV2	55	55	19
Korean Society	SARS-CoV2	54	54	54
Nikpouraghdam et al.	SARS-CoV2	1989	160	214
Wu et al.	SARS-CoV2	40	40	40
Liu et al.	SARS-CoV2	18	18	1
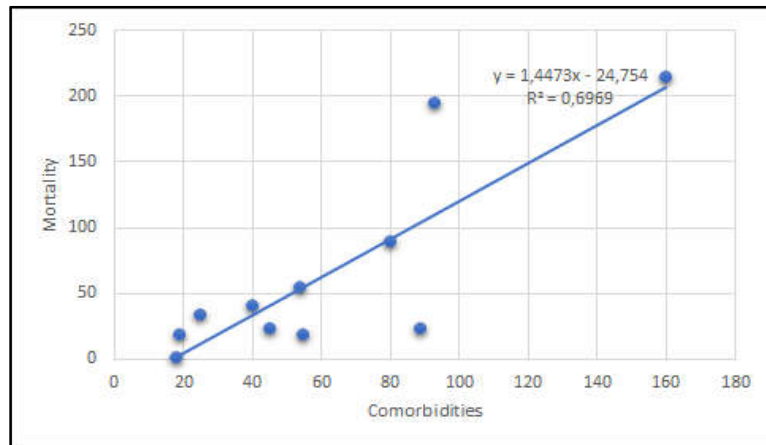
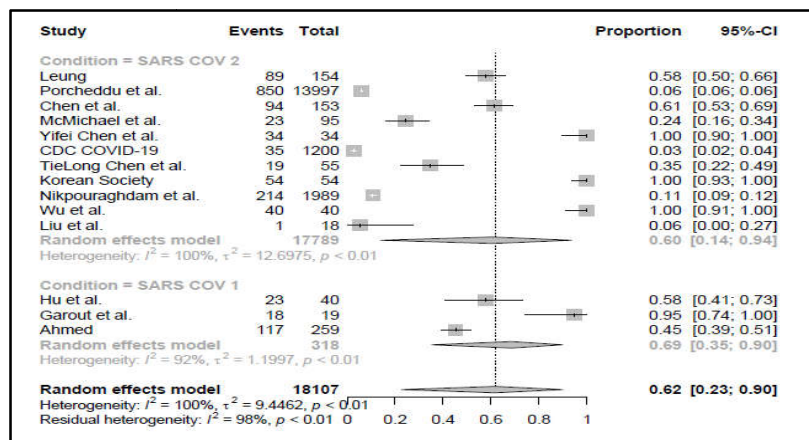**Figure 2. Linear correlation between comorbidities and mortality in the elderly population**

Figura 3. Forestplot of meta-analysis of prevalence of mortality in the elderly population
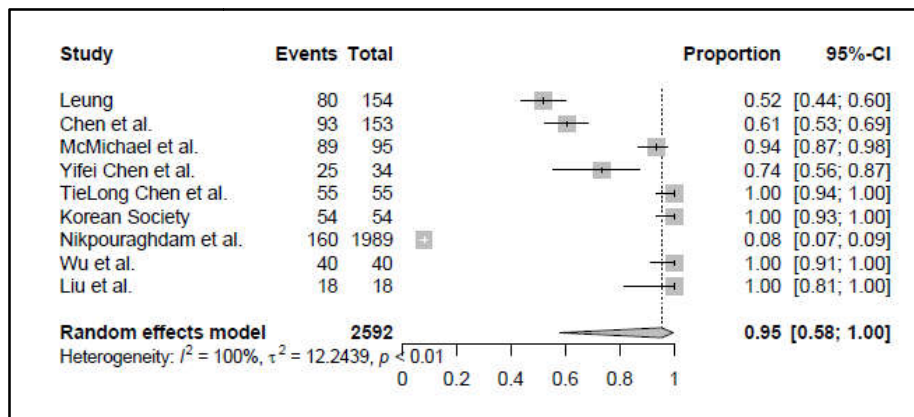

Figure 4. Forestplot of meta-analysis of prevalence of comorbidities in the elderly population

Table 3. Methodological quality of the studies by Newcastle-Ottawa Scale

| Author | Year | Selection | | | | Comparability | | Outcome | | Total |
		Representativeness of the sample	Sample size	Non-respondents	Ascertainment of the exposure	The study controls for the most important factor	The study control for any additional factor	Assessment of the outcome	Statistical test	
Leung	2020	*	*	*	**	*		*	*	8
Hu et al.,	2004	*	*	*	**	*		*	*	9
Porcheddu et al.,	2020	*	*		**	*	*	*		6
Chen T et al. 1,	2020	*	*	*	**	*	*	*	*	9
Garout et al.,	2018	*			**	*		*	*	6
McMichael et al.,	2020	*	*	*	**	*		*		7
Chen Y et al.,	2020	*			**			*	*	5
CDC USA	2020	*	*	*	**			*		6
Chen T et al. 2	2020	*	*	*	**	*	*	*	*	9
CDC Korea	2020	*	*		**			*		5
Nikpouraghdam et al.,	2020	*	*	*	**	*		*	*	8
Ahmed	2017	*	*	*	**	*	*	*	*	9
Yang et al.,	2017	*	*	*	**	*	*	*	*	9
Wu et al.,	2020	*	*	*	**	*	*	*	*	9
Liu et al.,	2020	*	*	*	**	*		*	*	8

Table 4. Study bias risk included according to JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies

Author	Year	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?
Leung	2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hu et al.,	2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Porcheddu et al.,	2020	Yes	No	Yes	Yes	No	No	Yes	No
Chen T et al. 1,	2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Garout et al.,	2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
McMichael et al.,	2020	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Chen Y et al.,	2020	Yes	Yes	Yes	Yes	No	No	Yes	Yes
CDC USA	2020	Yes	Yes	Yes	Yes	No	No	Yes	No
Chen T et al. 2,	2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CDC Korea	2020	Yes	Yes	Yes	Yes	No	No	Yes	No
Nikpouraghdam et al.,	2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ahmed	2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Yang et al.,	2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wu et al.,	2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Liu et al.,	2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes

As for the statistical analysis of the studies by Porcheddu *et al.*, (2020), McMichael *et al.*, (2020) CDC USA (2020) and CDC Korea (2020) did not use appropriate statistical analysis methods (Table 4).

DISCUSSION

There is much diversity in the results of studies on pre-existing pathological conditions in elderly people infected with SARS-CoV and their potential associated risk for mortality. Although the epidemiological data already released on this infection clearly show a greater number of serious and fatal cases in older people and those with pre-existing comorbidities, the main drivers of the high mortality rates are still not completely understood. Some viable hypotheses emerge that mainly include changes in the immune cell repertoire, inflammatory activity and epigenetic changes. But much remains to be elucidated. It is known that during aging, the immune system undergoes changes, especially by two mechanisms. One is a gradual decline in immune function known as immunosenescence, which makes it difficult to recognize, effectively signal and release invading pathogens. The other classic change in the immune system is the appearance of a low-grade state of chronic inflammation called "inflammaging", demonstrated by a two to four-fold increase in serum levels of inflammatory mediators that are considered predictive markers of mortality, regardless of comorbidity pre-existing (Candore, Caruso, & Colonna-Romano, 2010; Franceschi *et al.*, 2000).

One of the most interesting aspects for geriatricians and gerontologists is the high prevalence of comorbidities observed in the elderly and how it influences their clinical-functional status and, more especially, their state of vulnerability to diseases including those of infectious origin. In the present review, data on the main comorbidities presented by elderly victims of SARS-CoV are in line with global reports on the prevalence of chronic diseases in older people. For some time now, the WHO has been warning about the impact of these diseases, especially non-communicable ones, such as those of cardiovascular, pulmonary, renal and metabolic origin, which it considers one of the main health problems today (WHO, 2015). Considering all the cases recorded in the studies included in the analysis (SARS CoV-1 and SARS CoV-2), there was a moderate correlation (70% - $r^2 = 0.69$) between the presence of comorbidities and mortality in the elderly population. In one of the largest case series published so far on SARS CoV-2, the data for the elderly population was alarming. Of the 72,314 cases reported by the Chinese Center for Disease Control and Prevention, case fatality was 8.0% (312 out of 3,918) in patients aged 70 to 79 years and 14.8% in patients aged ≥80 years (208 out of 1,408) (Wu; McGoogan, 2020). The main limitations of this review are the wide variety of characteristics of the populations studied and the absence of separate analysis of each pathology furthermore the present review did not separate the population by gender.

CONCLUSION

In summary, the evidence described in this study is consistent with most previous studies, supporting the fact that advanced age is associated with simultaneous comorbidities, thereby increasing the fatality rate of SARS-CoV cases. Thus, considering that the COVID-19 pandemic presents new and emerging challenges as it evolves, it will be imperative to implement initial prevention and risk management strategies.

REFERENCES

Abbara, A., Collin, S. M., Kon, O. M., Buell, K., Sullivan, A., Barrett, J. and Davidson, R. N. 2019. Time to diagnosis of tuberculosis is greater in older patients: a retrospective cohort review. *ERJ open research*, *5*4, 2-12.

Ahmed A. E. 2017. The predictors of 3- and 30-day mortality in 660 MERS-CoV patients. *BMC infectious diseases, 17*1, 615.

Balduzzi, S., Rücker, G., & Schwarzer, G. 2019. How to perform a meta-analysis with R: a practical tutorial. *Evidence-Based Mental Health*, *22*4, 153-160.

Barendregt, J. J., Doi, S. A., Lee, Y. Y., Norman, R. E., & Vos, T. 2013. Meta-analysis of prevalence. *J Epidemiol Community Health*, *67*11, 974-978.

Candore, G., Caruso, C., & Colonna-Romano, G. 2010. Inflammation, genetic background and longevity. *Biogerontology*, *11*5, 565-573.

CDC 2020. https://www.cdc.gov/mmwr/ volumes/69/wr/mm 6912e2.htm 26 March 2020, date last accessed.

CDC 2020. Severe Outcomes Among Patients with Coronavirus Disease 2019 COVID-19 — United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep, 69, 343-346.

Chen, T., Wu, D., Chen, H., Yan, W., Yang, D., Chen, G. and Wang, T. 2020. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *Bmj*, *368*, 1-12.

Cheng, Y., Luo, R., Wang, K., Zhang, M., Wang, Z., Dong, L. and Xu, G. 2020. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney international*, *97*5, 829-838.

D'Adamo, H., Yoshikawa, T., &Ouslander, J. G. 2020. Coronavirus disease 2019 in geriatrics and long□term care: the ABCDs of COVID□19. *Journal of the American Geriatrics Society*, *68*5, 912-917.

DerSimonian, R., & Laird, N. 1986. Meta-analysis in clinical trials. *Controlled clinical trials*, *7*3, 177-188.

Franceschi, C., Bonafè, M., Valensin, S., Olivieri, F., De Luca, M., Ottaviani, E., & De Benedictis, G. 2000. Inflamm□aging: an evolutionary perspective on immunosenescence. *Annals of the new York Academy of Sciences*, *908*1, 244-254.

Gao, L., Jiang, D., Wen, X. S., Cheng, X. C., Sun, M., He, B. and Cai, G. Q. 2020. Prognostic value of NT-proBNP in patients with severe COVID-19. *Respiratory research*, *21*, 1-7.

Garout, M.A., Jokhdar, H.A.A., Aljahdali, I.A., Zein, A.R., Goweda, R.A., & Hassan-Hussein, A. 2018. Mortality rate of ICU patients with the Middle East Respiratory Syndrome - Coronavirus infection at King Fahad Hospital, Jeddah, Saudi Arabia. *Cent Eur J Public Health,* 262, 87-91.

Godaert, L., Bartholet, S., Gazeuse, Y., Brouste, Y., Najioullah, F., Kanagaratnam, L., ... &Dramé, M. 2018.

Misdiagnosis of chikungunya virus infection: comparison of old and younger adults. *Journal of the American Geriatrics Society*, *669*, 1768-1772.

Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA editors. Cochrane Handbook for Systematic Reviews of Interventions version 6.0 updated July 2019. Cochrane, 2019. https://www.training.cochrane.org/handbook.

Hu, X., Deng, Y., Wang, J., Li, H., Li, M., & Lu, Z. 2004. Short term outcome and risk factors for mortality in adults with critical severe acute respiratory syndrome SARS. *Journal of Huazhong University of Science and Technology*. 24, 514–517.

Hung. L.S. 2003. The SARS epidemic in Hong Kong: what lessons have we learned? *J R Soc Med*, 96, p. 374 – 378.
Jiang, S., Xia, S., Ying, T., & Lu, L. 2020. A novel coronavirus 2019-nCoV causing pneumonia-associated respiratory syndrome. *Cellular & molecular immunology*, *175*, 554-554.

Korean Society of Infectious Diseases and Korea Centers for Disease Control and Prevention 2020. Analysis on 54 Mortality Cases of Coronavirus Disease 2019 in the Republic of Korea from January 19 to March 10, 2020. *Journal of Korean medical science*, 3512, e132.

Leung C. 2020. Risk factors for predicting mortality in elderly patients with COVID-19: A review of clinical data in China. *Mechanisms of ageing and development*, 188, 111255. Advance online publication.

Liu, W., Tao, Z. W., Wang, L., Yuan, M. L., Liu, K., Zhou, L. and Ming, Y. 2020. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chin Med J Engl,* 133 9, 1032-1038.

Liu, K., Chen, Y., Lin, R., & Han, K. 2020. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *The Journal of infection,* 80 6, e14–e18.

Lloyd-Sherlock, P., Ebrahim, S., Geffen, L., & McKee, M. 2020. Bearing the brunt of covid-19: older people in low and middle income countries. *BMJ. [Internet]*, 368, m1052.

McMichael, T.M., Clark, S., Pogosjans, S., Meagan, D.V., …&Duchin, J. S. 2020 COVID-19 in a Long-Term Care Facility — King County, Washington, February 27–March 9, 2020. *MMWR Morb Mortal Wkly Rep*, 69 12, 339-342.

Munn, Z., Moola, S., Lisy, K., Riitano, D., &Tufanaru, C. 2015. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *International journal of evidence-based healthcare*, *13*3, 147-153.

Nikpouraghdam, M., Farahani, A. J., Alishiri, G., Heydari, S., Ebrahimnia, M., Samadinia, H., ... &Dorostkar, R. 2020. Epidemiological characteristics of coronavirus disease 2019 COVID-19 patients in IRAN: A single center study. *Journal of Clinical Virology*, 127, 104378.

Porcheddu, R., Serra, C., Kelvin, D., Kelvin, N., &Rubino, S. 2020. Similarity in Case Fatality Rates CFR of COVID-19/SARS-COV-2 in Italy and China. The Journal of Infection in Developing Countries, 1402, 125-128.

R Core Team 2020. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/.

Sohrabi, C., Alsafi, Z., O'Neill, N., Khan, M., Kerwan, A., Al-Jabir, A. and Agha, R. 2020. World Health Organization declares global emergency: A review of the 2019 novel coronavirus COVID-19. *International Journal of Surgery*, 76, 71–6.

TieLong Chen, Dai, Z., Mo, P., Li, X., Ma, Z., Song, S., Chen, X., Luo, M., Liang, K., Gao, S., Zhang, Y., Deng, L., &Xiong, Y. 2020. Clinical characteristics and outcomes of older patients with coronavirus disease 2019 COVID-19 in Wuhan, China 2019: a single-centered, retrospective study. *J GerontolA Biol Sci Med Sci,* 2020, 1–8.

Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J. and Zhao, Y. 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *Jama*, *32*11, 1061-1069.

Wells, G., Shea, B., O'Connell, D., Peterson, J., Welch, V., ... &Losos, M. The Newcastle□Ottawa Scale NOS for assessing the quality of nonrandomised studies in meta□analyses. The Ottawa Health Research Institute, Ottawa 2019. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm [acesso 22.03.19]

World Health Organization. 2015. World aging and health report. United States, 30, 12.

World Health Organization. 2020a. Coronavirus disease 2019 COVID-19 Situation Report - 69 [Internet]. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200329-sitrep-69-covid-19.pdf.

World Health Organization. 2020b. Coronavirus disease 2019 COVID-19 situation report – 52. https://www.who.int/docs/default-source/coronaviruse/20200312-sitrep-52-covid-19.pdf?sfvrsn=e2bfc9c0_2.

Wu, C., Chen, X., Cai, Y., Zhou, X., Xu, S., Huang, H. and Song, J. 2020. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA internal medicine*.1-10

Wu, Z., & McGoogan, J. M. 2020. Characteristics of and important lessons from the coronavirus disease 2019 COVID-19 outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *Jama*, *32*13, 1239-1242.

Yang, X., Yu, Y., Xu, J., Shu, H., Liu, H., Wu, Y. and Wang, Y. 2020. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*, 85, 475-481.

Yang, Y. M., Hsu, C. Y., Lai, C. C., Yen, M. F., Wikramaratna, P. S., Chen, H. H., & Wang, T. H. 2017. Impact of Comorbidity on Fatality Rate of Patients with Middle East Respiratory Syndrome. *Scientific reports*, 71, 11307.

Yfei Chen, Zhao, M., Wu, Y., & Zang, S. 2020. Epidemiological analysis of the early 38 fatalities in Hubei, China, of the coronavirus disease 2019. *Journal of global health*, 101, 011004.

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z. and Guan, L. 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*, 39510229, 1054–1062.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J. and Niu, P. 2020. A novel coronavirus from patients with pneumonia in China, 2019. *New England Journal of Medicine*, 382, 727-33.

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