Review

Factors Associated with Mortality Among Elderly People in the COVID-19 Pandemic (SARS-CoV-2): A Systematic Review and Meta-Analysis

Vicente Alves[1,2], Francine Casemiro[3], Bruno Araujo[1], Marcos Lima[1], Rayssa Oliveira[1], Fernanda Fernandes[1], Ana Vitória Gomes[1], Dario Gregori[2]

[1] Catholic of de Brasília, Brazil.
[2] Unit of Biostatistics, Epidemiology and Public Health at Padova University, Italy
[3] University of São Paulo, Brazil
* Correspondence: vicerap@gmail.com.

Abstract: The objective of this meta-analysis was to evaluate the factors associated with mortality of elderly Brazilians and Italians diagnosed with the new coronavirus who resided in institutions or who were hospitalized as a result of the disease; Methods: A systematic review following the recommendations of *The Joanna Briggs Institute* (JBI), where the PEO strategy was utilized - Population, Exposure and Outcome. P, being the elderly over 65 years old. E, the SARS-CoV_2 pandemic. O, mortality. The NCBI / PubMed, LILACS, EMBASE and CINAHL databases were used until July 31, 2020.; Results: There were no studies with samples of elderly Brazilians that met the inclusion criteria, which took place inside hospitals. Five Italian studies were included in the meta-analysis, with the number of elderly people varying between 18 and 1591 patients. The main morbidities presented by the elderly in the studies were: dementia, diabetes, chronic kidney disease and hypertension. Conclusions: The factors associated with the mortality of elderly Italian people diagnosed with SARS-CoV-2 who lived in institutions or who were hospitalized because of the disease were evaluated. It was found that dementia, diabetes, chronic kidney disease and hypertension are the main risk factors for mortality in elderly people with Covid-19.

Keywords: SARS-CoV-2; COVID-19 ; Non Communicable diseases (NCDs). Clinical features; Institucionalized or hospitalized elderly; meta-analisys.

1. Introduction

The Covid-19 pandemic (SARS-CoV-2) has considerable mortality in populations considered at risk, such as the elderly population. Thus, it is necessary to investigate what are the main factors that make these people more vulnerable to death. From this, the objective of this study was to synthesize the factors associated with mortality of elderly Brazilians and Italians diagnosed with the new coronavirus who resided in institutions or who were hospitalized as a result of the disease.

Several studies began to be carried out in different contexts, with scientific evidence and statistical data that pointed in certain directions. Contributing to the advancement of knowledge about its reach and the factors associated with their mortality has become a challenge for all researchers. In this specific case, it was proposed to carry out a systematic review of the studies published in Brazil and Italy between March and July of 2020, for being two countries where there was the first spread of the disease in Latin America and Europe, with the intention of raising these factors.

In Brazil, more than 80% of deaths from the new coronavirus in the elderly, who had chronic diseases and had at least one of the main risk factors constantly related to Covid-19, according to the Ministry of Health in 2020 (1). However, the data available on elderly people residing in long-term care facilities in Brazil are not accurate and not even their mortality rate within these structures, reason why one can only raise an estimate of this impact, which is a weighted percentage of 44,7%, with 107.538 deaths (2).

In Italy, the contagion outbreak started on February 20, reaching 428% of confirmed cases in the following days. Residential facilities for the elderly were the hardest hit, according to data released by the Istituto Superiore di Sanità (3). The elderly who died in these residential establishments due to Covid-19, who underwent the RT-PCR exam would be around 7.4% of all deaths in the period. When adding to this data, all those who died with flu symptoms (without any objective assessment), deaths reached 41.2%. The survey was carried out by ISS by sending a questionnaire to 3,417 establishments to which 1,356 responded to a total of 97,521 elderly residents (4).

2. Materials and Methods

Search strategy and selection criteria

It is a systematic review guided by the recommendations of *The Joanna Briggs Institute* (JBI), following the nine steps for its development: 1) Construction of the preliminary research protocol; 2) Formulation of the review question; 3) Definition of inclusion and exclusion criteria; 4) Search strategy; 5) Selection of studies for inclusion; 6) Data extraction; 7) Synthesis of the data; 8) Narrative summary; 9) References (5)

This study used articles of public and free access, located in the databases of scientific literature. Primary studies on the mortality of Italian and Brazilian elderly with a diagnosis of the new coronavirus were selected, publications in English, Italian, Spanish and Portuguese in publications that carried out quantitative and qualitative analysis. For the formulation of the research question, the PEO strategy was used - Population, Exposure and Outcome (6). It was determined that the "Population" (P) would be the elderly over 65 years, the "Exposure" (E), the SARS-CoV_2 pandemic; and the "Outcome" (O), mortality. Thus, the guiding question of this study was: "What are the factors related to the mortality of Italian and Brazilian elderly people diagnosed with the Covid-19 (SARS-CoV-2) disease?".

The inclusion criteria for the selection of articles were:

• primary studies on the mortality of elderly people diagnosed with the new coronavirus;

• studies in English, Portuguese, Spanish and Italian.

The exclusion criteria were:

• studies that were not of Italian or Brazilian elderly people;

• studies on the elderly who were not institutionalized or hospitalized; and,

• studies that did not answer the guiding question of the systematic review.

Data extraction and analysis

The search for publications happened in July of 2020 in the databases *National Center for Biotechnology Information* (NCBI / PubMed), LILACS, *Excerpta Medica Database* (EMBASE), *Cumulative Index to Nursing and Allied Health Literature* (CINAHL). The search strategy occurred by combining controlled and uncontrolled descriptors, according to the indication offered in each database. To search for articles on PubMed, controlled descriptors from *Medical Subject Headings* (MeSH) were used. *Heading-MH* was consulted for the CINHAL base. *Embase Subject Headings* (EMTREE) was used to search EMBASE and *Health Sciences Descriptors* (DeCS) were used to search LILACS. For this search, "aged", "coronavirus infections" and "mortality" were used. The Boolean operator "AND" was used in all combinations as follows: "aged AND aged 80 and over AND coronavirus infections AND mortality". There was no time limit for publication. For the selection of articles, the Rayyan application, developed by the QCRI (Qatar Computing Research Institute), was used, which helps in systematic reviews, facilitating the selection process for reading articles, which took place in three stages: in the first one, the search in the databases of data; secondly, the reading of the title and the abstract, when two researchers (FG Casemiro e BG Araújo) performed the bibliographic search and independently extracted data from the included studies. Disagreements were resolved by the third investigator (VP Alves) or by consensus. So that the purpose was to separate the studies for this third stage, in which the full reading of the articles occurred, aiming to select those that were in agreement with the inclusion criteria (7).

In the development of the search and selection of articles, from the databases to the selection of studies by reading titles and abstracts or full text, the PRISMA protocol was used (8) (Figure 1), in order to guarantee the rigor of the systematic review (7).

Figure 1: Flow diagram of the number of studies selected and included in the meta-analysis.
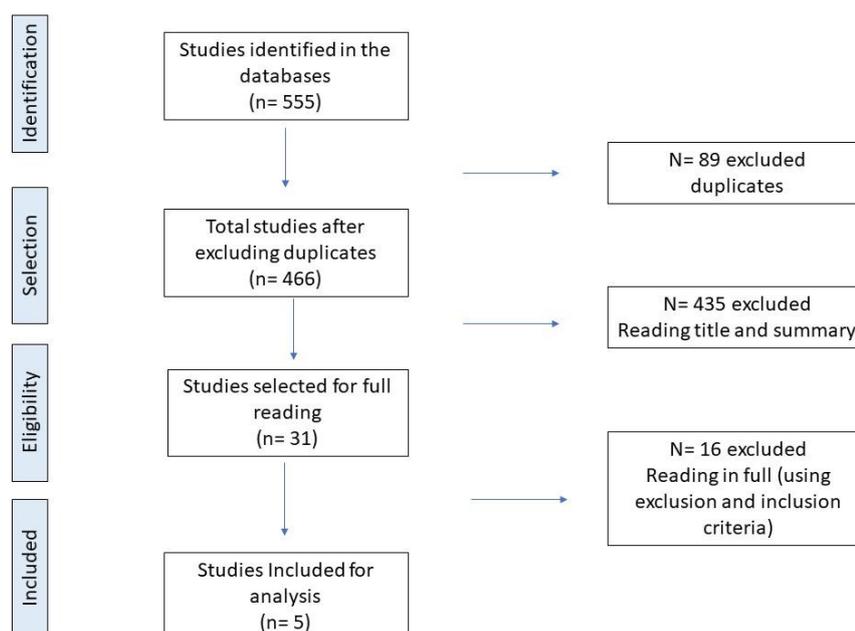
From the findings, the results were organized by performing a descriptive synthesis of the data, shown in Table 1.

The meta-analysis was conducted using the Stata software, version 16.0. Initially, the mortality rate was estimated using the number of deaths as the numerator and the total number of the analyzed sample as the denominator, multiplied by the constant 100%. The grouped meta-analysis of the mortality rate was performed using random effects models (9). Heterogeneity between studies was assessed using the I-square (I^2) (10).

Next, the factors associated with mortality were analyzed, with the outcome being death. Thus, two groups were compared (non-survivors versus survivors). The following quantitative variables were considered as predictors: age, Charlson Index, lymphocytes, CRP, glucose, albumin, ALT, AST, bilirubin, GGT, lipase, CK, LDH, sodium, potassium, clhoride, urea, creatinine, hscTnI, PT / INR , APTT, D-dimer, Ferritin, Hb, WBC, neutrophils and platelets. In the study that presented data such as median and interquartile range (IIQ) (11) transformation was done in mean and standard deviation (SD) (12). The following qualitative variables were considered to be predictors: male gender, chronic diseases, cancer, diabetes, cardiovascular diseases, COPD, immunodeficient, Chronic Kidney disease (CKD), metabolic disease, obesity, hypertension, HF, dementia and smoking. Variables related to the use of drugs and therapies were excluded from the risk factor analyzes, since this review would not address clinical trials.

The effect size was reported as standardized mean difference (SDM) for quantitative variables or relative risk (RR) for qualitative variables. All of these measures were followed up with a 95% confidence interval (13). Heterogeneity between studies was assessed using the I-square (I^2) (10). Fixed or random effect models were used depending on heterogeneity. Variables with p-value <0.05 were considered statistically significant.

The protocol for this article was published in the *International Prospective Register Of Systematic Reviews*, PROSPERO, in August 2020, under the register: CRD42020201790.

3. Results

There were no studies with samples of elderly Brazilians that met the inclusion criteria, so only Italian studies remained in the selection, which took place inside hospitals. The number of elderly people varied between 18 (14) and 1591 (15) patients. The objectives of the publications are similar when making a descriptive analysis of the elderly and the factors associated with the new coronavirus.

The main morbidities presented by the elderly in the studies were: dementia (16) diabetes (15,17), chronic kidney disease (15), hypertension (17).

Table 1: Descriptive synthesis of the data

Author / Year	Journal	Aim	Elderly sample	Sample location
(Bianchetti et al., 2020)	Journal of Nutrition, Health and Aging	To evaluate the prevalence, clinical characteristics, and outcomes of dementia in individuals hospitalized for the infection of COVID19.	627	Hospitals and nursing homes in the province of Brescia, Northern Italy.
(Stroppa et al., 2020)	Future Oncology	Describe the case of 25 cancer patients who were infected with COVID-19.	18	Piacenza's general hospital, Northern Italy.
(Deiana et al., 2020)	International Journal of Environmental Research and Public Health	Describe the clinical characteristics of patients who died after a positive test for SARS-CoV-2 infection and evaluate the influence of health conditions associated with the outcome of death.	573	Sardinia, Italy
(Bonetti et al., 2020b)	Clinical Chemistry and Laboratory Medicine (CCLM)	Describe laboratory findings in a group of Italian patients with COVID-19 in the Valcamonica area, and correlate the abnormalities with severity of the disease.	518	Emergency Department of the Valcamonica Hospital (Esine, Brescia, Lombardia, Italy)
(Iaccarino et al., 2020)	Hypertension	Check if renin-angiotensin, the system inhibitors, are related to the serious results of COVID-19.	1591	Multicenter study.

The Figure 2 shows the meta-analysis of the mortality rate found. A mortality rate of 27.7% was observed (IC95%: 15,7-41,57%), with high heterogeneity between studies (I^2: 97,71%; p<0,001).

Figure 2. Mortality rate in the elderly obtained in the meta-analysis
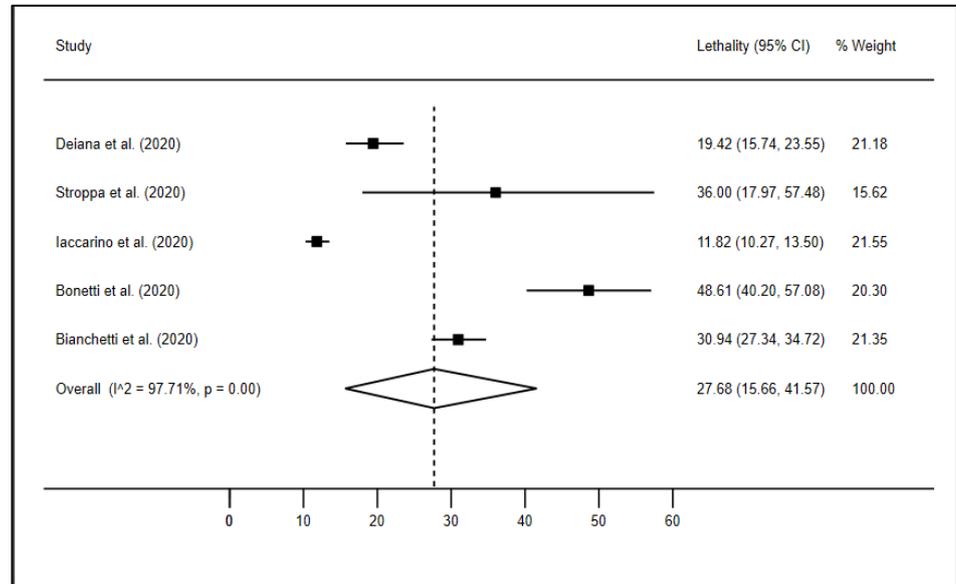
The meta-analysis was conducted for each predictor variable, being stratified into quantitative and qualitative variables.

The Table 2 shows the descriptive analysis of the quantitative variables, according to the group of survivors and non-survivors, and Table 3 the effect size, in SDM and 95% CI, of the variables in mortality.

Table 2. Descriptive analysis of quantitative variables, according to group of survivors and non-survivors

Variables	Non-survivors			Survivors		
	N	Mean	SD	N	Mean	SD
Age (years)						
Iacarinno et al. (2020)	188	79.6	0.8	1.304	64.7	0.4
Stroppa et al. (2020)	9	74.44	7.21	16	68.38	10.16
Bonetti et al. (2020)	70	75.4	14.99	74	62.63	14.97
Charlson Index						
Iacarinno et al. (2020)	188	4.37	0.14	1.403	2.63	0.05
Lymphocytes						
Stroppa et al. (2020)	9	2.67	5.32	16	0.85	0.41
Bonetti et al. (2020)	70	0.77	0.34	74	1.05	0.37
CRP						
Stroppa et al. (2020)	9	14.82	7.54	16	9.33	4.87
Bonetti et al. (2020)	70	163.17	120.32	74	79.43	98.90
Glucose						

Bonetti et al. (2020)	70	8.22	3.14	74	6.16	0.88
Albumin						
Bonetti et al. (2020)	70	34.10	3.10	74	36.53	4.16
ALT						
Bonetti et al. (2020)	70	35.33	19.68	74	33.17	18.90
AST						
Bonetti et al. (2020)	70	62.83	29.52	74	43.00	25.71
Bilirubin						
Bonetti et al. (2020)	70	13.30	8.17	74	11.07	3.93
GGT						
Bonetti et al. (2020)	70	65.08	55.82	74	53.25	44.42
Lipase						
Bonetti et al. (2020)	70	33.08	12.29	74	51.92	42.15
CK						
Bonetti et al. (2020)	70	203.50	195.67	74	116.83	104.34
LDH						
Bonetti et al. (2020)	70	524.33	166.53	74	320.08	113.60
Sodium						
Bonetti et al. (2020)	70	138.00	4.54	74	137.33	3.78
Potassium						
Bonetti et al. (2020)	70	4.05	0.73	74	3.85	0.57
Chloride						
Bonetti et al. (2020)	70	101.00	3.78	74	101.00	4.54
Urea						
Bonetti et al. (2020)	70	24.37	13.25	74	13.93	6.73
Creatinine						
Bonetti et al. (2020)	70	121.33	52.99	74	61.10	40.60
HscTnI						
Bonetti et al. (2020)	70	113.17	218.00	74	9.37	7.49
PT/INR						
Bonetti et al. (2020)	70	1.14	0.19	74	1.05	0.08
APTT						
Bonetti et al. (2020)	70	33.33	6.06	74	31.33	3.78
D-dímero						
Bonetti et al. (2020)	70	2.30	1.79	74	1.18	1.08
Ferritin						
Bonetti et al. (2020)	70	1375	1497.22	74	852.83	826.40
Hb						
Bonetti et al. (2020)	70	129.33	22.71	74	137.33	18.90
WBC						
Bonetti et al. (2020)	70	8.14	4.94	74	5.86	2.43
Neutrophils						

Bonetti et al. (2020)	70	6.59	3.99	74	4.21	2.32
Platelets						
Bonetti et al. (2020)	70	180.67	51.47	74	183.67	74.10

N: sample size in each group; SD=Standard deviation

Table 3. Meta-analysis of factors associated (quantitative variables) with mortality

Variables	SMD (95.0% CI)	I²	Z	p-value
Age (years)	3.10 (2.79; 3.40)	99.9%	19.76	**<0.001**
Charlson Index	1.74 (1.56; 1.92)	-	19.33	**<0.001**
Lymphocytes	-0.59 (-0.91; -0.28)	88.7%	3.70	**<0.001**
CRP, g/L	0.78 (0.47; 1.10)	0.0%	4.88	**<0.001**
Glucose, mmol/L	0.90 (0.56; 1.25)	-	5.16	**<0.001**
Albumin, g/L	-0.66 (-0.99; -0.32)		3.85	**<0.001**
ALT, U/L	0.11 (-0.22; 0.44)		0.67	0.502
AST, U/L	0.72 (0.38; 1.06)		4.17	**<0.001**
Bilirubin total, μmol/L	0.35 (0.02; 0.68)	-	2.09	**0.037**
GGT, U/L	0.24 (-0.09; 0.56)	-	1.41	0.160
Lipase, U/L	-0.60 (-0.93; -0.27)	-	3.52	**<0.001**
CK, U/L	0.56 (0.22; 0.89)	-	3.28	**0.001**
LDH, U/L	1.44 (1.07; 1.80)	-	7.69	**<0.001**
Sodium, mmol/L	0.16 (-0.17; 0.49)	-	0.96	0.336
Potassium, mmol/L	0.31 (-0.02; 0.64)	-	1.83	0.068
Chloride, mmol/L	0.00 (-0.33; 0.33)	-	0.00	1.000
Urea, mmol/L	1.00 (0.66; 1.35)	-	5.66	**<0.001**
Creatinine, μmol/L	1.28 (0.92; 1.64)	-	6.99	**<0.001**
hscTnI, ng/L	0.68 (0.35; 1.02)	-	3.98	**<0.001**
PT/INR	0.62 (0.29; 0.96)	-	3.65	**<0.001**
APTT, s	0.40 (0.07; 0.73)	-	2.37	**0.018**
D-dimer, g/L	0.76 (0.42; 1.10)	-	4.41	**<0.001**
Ferritin, ng/mL	0.44 (0.10; 0.77)	-	2.58	**0.010**
Hb, g/L	-0.38 (-0.71; -0.05)	-	2.28	**0.023**
WBC, ×10⁹/L	0.59 (0.26; 0.93)	-	3.47	**0.001**
Neutrophils, ×10⁹/L	0.74 (0.40; 1.07)	-	4.26	**<0.001**
Platelets, ×10⁹/L	-0.05 (-0.37; 0.28)	-	0.28	0.779

The analysis of quantitative variables showed that mortality increased with increasing age (SMD: 3.10; 95.0% CI: 2.79; 3.40), from the Charlson Index (SMD: 1.74; 95.0% CI: 1.56; 1.92), CRP (SMD: 0.78; 95.0% CI: 0.47; 1.10), glucose (SMD: 0.90; 95.0% CI: 0.56; 1.25), AST (SMD: 0.72; 95.0% CI: 0.38; 1.06), bilirubin total (SMD: 0.35; 95.0% CI: 0.02; 0.68), CK (SMD: 0.56; 95.0% CI: 0.22; 0.89), LDH (SMD:1.44; 95.0% CI: 1.07; 1.80), urea (SMD: 1.00; 95.0% CI: 0.66; 1.35), creatinine (SMD: 1.28; 95.0% CI: 0.92; 1.64), hscTnl (SMD: 0.68; 95.0% CI: 0.35; 1.02), PR/INR (SMD: 0.62; 95.0% CI:0.29; 0.96), APTT (SMD: 0.40; 95.0% CI:

0.07; 0.73), D-dimer (SMD: 0.76; 95.0% CI: 0.42; 1.10), ferritin (SMD: 0.44; 95.0% CI: 0.10; 0.77), WBC (SMD: 0.59; 95.0% CI: 0.26; 0.93) and neutrophils (SMD: 0.74; 95.0% CI: 0.40; 1.07). On the other hand, COVID-19 mortality decreased as the number of lymphocytes increased (SMD: -0.59; 95.0% CI: -0.91; -0.28), albumin (SMD: -0.66; 95.0% CI: -0.99; -0.32), lipase (SMD: -0.60; 95.0% CI: -0.93; -0.27) and Hb (SMD: -0.38; 95.0% CI: -0.71; -0.05) (Table 3).

The Table 4 shows the descriptive analysis of qualitative variables, according to the group of survivors and non-survivors, and Table 5 the effect size, in RR and 95% CI, of the variables in mortality.

The analysis of quantitative variables showed that the risk of mortality was higher in individuals with diabetes (RR: 1.90; 95.0% CI: 1.53; 2.37), DPOC (RR: 2.19; 95.0% CI: 1.54; 3.10), with chronic kidney disease (RR: 3.96; 95.0% CI: 2.65; 5.91), with hypertension (RR: 1.37; 95.0% CI: 1.24; 1.51), HF (RR: 3.27; 95.0% CI: 2.49; 4.29) and with dementia (RR: 3.67; 95.0% CI: 2.43; 5.55) (Table 4).

Table 4. Descriptive analysis of qualitative variables according to group of survivors and non-survivors

Variables	Non-survivors			Survivors		
	N	n	%	N	N	%
Male						
Bonetti et al. (2020)	70	45	64.3	74	51	68.9
Iacarinno et al. (2020)	188	125	66.5	1403	891	63.5
Stroppa et al. (2020)	9	5	55.6	16	15	94.8
Deiana et al. (2020)	81	40	50.6	336	89	26.6
Chronic diseases						
Bonetti et al. (2020)	70	49	70.0	74	43	57.3
Cancer						
Bonetti et al. (2020)	70	9	12.9	74	6	8.0
Diabetes						
Bonetti et al. (2020)	70	21	30.0	74	16	21.3
Iacarinno et al. (2020)	188	61	32.4	1403	208	14.8
Stroppa et al. (2020)	9	2	22.2	16	6	37.5
Cardiovascular diseases /coronary artery disease						
Bonetti et al. (2020)	70	38	54.3	74	33	44.0
Iacarinno et al. (2020)	188	56	29.8	1403	160	11.4
COPD						
Bonetti et al. (2020)	70	14	20.5	74	6	8.0
Iacarinno et al. (2020)	188	28	14.9	1403	94	6.7
Stroppa et al. (2020)	9	3	33.3	16	4	25.0
Immunodeficiencies						
Bonetti et al. (2020)	70	2	2.8	74	0	0.0

Chronic Kidney disease						
Bonetti et al. (2020)	70	9	12.9	74	3	4.0
Icarinno et al. (2020)	188	31	16.5	1403	56	4.0
Metabolic disease						
Bonetti et al. (2020)	70	10	14.3	74	7	9.3
Obesity						
Bonetti et al. (2020)	70	12	17.1	74	5	6.8
Iacarinno et al. (2020)	188	12	6.4	1403	90	6.4
Hypertension						
Iacarinno et al. (2020)	188	138	72.9	1403	737	52.5
Stroppa et al. (2020)	9	5	55.6	16	11	68.8
HF						
Iacarinno et al. (2020)	188	57	30.3	1403	130	9.3
Dementia						
Bianchetti et al. (2020)	194	51	26.3	433	31	7.2
Smoking						
Stroppa et al. (2020)	9	4	44.4	16	9	56.3

Table 5. Meta-analysis of factors associated (quantitative variables) with mortality

Variables	RR (95.0% CI)	I^2	Z	p-value
Male	0.98 (0.67; 1.43)	89.3	0.10	0.919
Chronic diseases	1.20 (0.94; 1.54)	-	1.48	0.139
Cancer	1.60 (0.60; 4.23)	-	0.92	0.356
Diabetes	1.90 (1.53; 2.37)	62.7	5.73	**<0.001**
Cardiovascular diseases/coronary artery disease	1.80 (0.85; 3.80)	92.0	1.53	0.125
COPD	2.19 (1.54; 3.10)	0.0	4.39	**<0.001**
Immunodeficiencies	5.28 (0.26; 108.12)	-	1.08	0.280
Chronic Kidney disease	3.96 (2.65; 5.91)	0.0	6.73	**<0.001**
Metabolic disease	1.51 (0.60-3.75)	-	0.89	0.374
Obesity	1.28 (0.78; 2.10)	60.8	0.99	0.322
Hypertension	1.37 (1.24; 1.51)	69.3	6.25	**<0.001**
HF	3.27 (2.49; 4.29)	-	8.55	**<0.001**
Dementia	3.67 (2.43; 5.55)	-	6.17	**<0.001**
Smoking	0.74 (0.32-1.71)	-	0.70	0.483

RR: Relative risk; Z= Z statistic of meta-analysis; I^2: I-square; 95.0% CI: 95% Confidence Interval.

4. Discussion

This study aimed to synthesize the factors associated with mortality of elderly Brazilians and Italians diagnosed with the new coronavirus who were institutionalized or hospitalized, but which resulted in finding only Italian studies in hospitals, due to the inclusion criteria. The data showed that diabetes, COPD, hypertension and dementia are morbidities that considerably increase the risk of death in the elderly.

ISTAT (2020), in its May 4th report, states that the impact of Covid-19 is greater in people with extremely compromised health conditions, causing the mortality of these people to happen in a shorter time. The document also reports that, in some cases, Covid-19 may not be the leading cause of death, but a contributing factor in overall mortality (18). There are a series of phenomena and dynamics that affect the current state of health of Italians, such as the aging of the population, the increase in risk factors, the DNCT, "the phenomenon of vaccination hesitation, the threat of antimicrobial resistance, the difficulties of access to innovation, the shortage of doctors, the lack of regional homogeneity and the delay in digitizing the health system that affect the system as a whole (19).

Italy has the lowest prevalence rate, by age, for COPD and cardiovascular disease (19) and these were the diseases that increased mortality among the elderly in the articles analyzed. On the other hand, the country has the highest prevalence rate by age for dementia. As aging progresses, the risk of this diagnosis increases. It is a progressive neurodegenerative syndrome characterized by a cognitive decline that limits social functions and activities of daily living (20). In addition to having an important impact on the quality of life of these people, dementia was also shown to be a risk factor for mortality in elderly people with Covid-19.

5. Conclusions

NCDs when associated with SARS-Co2 are death factors in the elderly. This data is fundamental for the elaboration of public policies, health promotion practices and prevention of chronic diseases throughout aging. In addition, the planning of prevention strategies against coronavirus for the elderly population with CNCD, COPD and dementia must have a clear and precise target to prevent so many deaths from occurring among the elderly.

The most important limitation of this research is the small number of articles found in Italy and none in Brazil, which prevented further analysis. In addition, aspects related to chronic diseases should be considered in future studies, since these aspects impact on the mortality of elderly people with COVID-19.

6. Patents

Conflicts of Interest "The authors declare no conflict of interest."

References

1.   Ministério da Saúde. Coronavírus - COVID 19 [Internet]. Coronavírus - COVID-19. 2020 [cited 2020 Dec 19]. Available from: https://coronavirus.saude.gov.br

2.   Machado CJ, Pereira CC de A, Viana B de M, Oliveira GL, Melo DC, Carvalho JFMG de, et al. Estimativas de impacto da COVID-19 na mortalidade de idosos institucionalizados no Brasil. Cien Saude Colet [Internet]. 2020 Sep;25(9):3437–44. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-81232020000903437&tlng=pt

3.   Instituto Nazionale di Statistica. Sulla Mortalità Totale Della Popolazione Residente Periodo Gennaio-Maggio 2020 [Internet]. Roma; 2020. Available from: https://www.epicentro.iss.it/coronavirus/pdf/Rapp_Istat_Iss_3Giugno.pdf

4.   Pesaresi F. Covid-19. La mortalità nelle strutture residenziali per anziani [Internet]. 7 luglio. 2020 [cited 2020 Dec 19]. Available from: https://welforum.it/covid-19-la-mortalita-nelle-strutture-residenziali-per-anziani/

5.   Aromataris E, Munn Z. Chapter 1: JBI Systematic Reviews. In: JBI Manual for Evidence Synthesis [Internet]. JBI; 2020. Available from: https://wiki.jbi.global/display/MANUAL/Chapter+1%3A+JBI+Systematic+Reviews

6.   Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetc R, et al. Chapter 7: Systematic Reviews of Etiology and Risk. In: JBI Manual for Evidence Synthesis [Internet]. JBI; 2020. Available from: https://wiki.jbi.global/display/MANUAL/Chapter+7%3A+Systematic+reviews+of+etiology+and+risk

7.   Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Syst Rev [Internet]. 2016 Dec 5;5(1):210. Available from: http://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-016-0384-4

8.   Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med [Internet]. 2009 Jul 21;6(7):e1000097. Available from: http://dx.plos.org/10.1371/journal.pmed.1000097

9.   Nikolakopoulou A, Mavridis D, Salanti G. Demystifying fixed and random effects meta-analysis. Evid Based Ment Heal. 2014;17(2):53–7.

10. Hippel PT von. The heterogeneity statistic I2 can be biased in small meta-analyses. BMC Med Res Methodol. 2015;15:35.

11. Bonetti G, Manelli F, Patroni A, Bettinardi A, Borrelli G, Fiordalisi G, et al. Laboratory predictors of death from coronavirus disease 2019 (COVID-19) in the area of Valcamonica, Italy. Clin Chem Lab Med. 2020;58(7):1100–5.

12. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14(1):1–13.

13. Martins-Filho P, Tavares CSS, Santos V. Factors associated with mortality in patients with COVID-19. A quantitative evidence synthesis of clinical and laboratory data. Eur J Intern Med. 2020;

14. Stroppa EM, Toscani I, Citterio C, Anselmi E, Zaffignani E, Codeluppi M, et al. Coronavirus disease-2019 in cancer patients. A report of the first 25 cancer patients in a western country (Italy). Futur Oncol. 2020;16(20):1425–32.

15. Iaccarino G, Grassi G, Borghi C, Ferri C, Salvetti M, Volpe M. Age and Multimorbidity Predict Death among COVID-19 Patients: Results of the SARS-RAS Study of the Italian Society of Hypertension. Hypertension. 2020;366–72.

16. Bianchetti A, Rozzini R, Guerini F, Boffelli S, Ranieri P, Minelli G, et al. Clinical Presentation of COVID19 in Dementia Patients. J Nutr Heal Aging. 2020;24(6):560–2.

17. Deiana G, Azara A, Dettori M, Delogu F, Vargiu G, Gessa I, et al. Deaths in SARS-CoV-2 positive patients in Italy: The influence of underlying health conditions on lethality. Int J Environ Res Public Health. 2020;17(12):1–10.

18. Instituto Nazionale di Statistica. Impacto dell'epidemia COVID-19 sulla mortalità totale Della Popolazione residente primo trimestre 2020 [Internet]. 2020. Available from: https://www.istat.it/it/archivio/242149

19. The European House. 14th Meridiano Sanità: Le coordinate della salute - Rapporto 2019 [Internet]. November 1. House TE, editor. Roma; 2019. Available from: https://www.ambrosetti.eu/en/research-and-presentations/xiv-rapporto-meridiano-

sanita/

20.   Confortin SC, Meneghini V, Ono LM, Garcia KC, Schneider IJC, D'Orsi E, et al. Indicadores antropométricos associados à demência em idosos de Florianópolis – SC, Brasil: Estudo EpiFloripa Idoso. Cien Saude Colet [Internet]. 2019 Jun;24(6):2317–24. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-81232019000602317&tlng=pt