Review Article ISSN 2639-9458

Microbiology & Infectious Diseases

Covid-19 Aging and Chronic Diseases

Cornelli Umberto MD, PhD[1], Belcaro Giovanni MD, PhD[2], Cesarone Maria Rosaria MD, PhD[2], Recchia Martino PhD[3], and Cotellese Roberto MD, PhD[4]

[1]*Institute of Life Techonolgy Bergamo Italy.*

[2]*IRVINE, Italy.*

[3]*Labs University G. d'Annunzio, Pescara, Chieti, Italy.*

[3]*University of Lugano, Switzerland.*

[4]*University G. d'Annunzio Pescara, Chieti, Italy.*

***Correspondence:**
Umberto Cornelli, Piazza Novelli 5 20129 Milan, Italy.
Giovanni Belcaro, 94 Strada Statale 16 Bis 65110 Spoltore (PE), Italy.
Maria Rosaria Cesarone, 94 Strada Statale 16 Bis 65110 Spoltore (PE), Italy.
Martino Recchia, Via Salaino 7 Milan- Italy.
Roberto Cotellese: Via Tassoni 102 65122 Pescara-Italy.

Received: 19 August 2020; **Accepted:** 25 September 2020

Citation: Cornelli Umberto, Belcaro Giovanni, Cesarone Maria Rosaria, et al.. Covid-19 Aging and Chronic Diseases. Microbiol Infect Dis. 2020; 4(4): 1-6.

ABSTRACT

Importance: *the common believe is that aging and concomitant chronic diseases are facilitating the infection and death from COVID-19. This may cause a limitation of the freedom of these patients and a severe discomfort on their daily living.*

Objective: *all the deaths due to COVID-19 have been analyzed in those 49 countries (49 SC) considered by WHO as reliable in terms of data recording. In the same countries the deaths for the most common chronic diseases were considered in terms of Age Standardized Death Rates (ASDRs).*

Evidence review: *Records of the WHO in terms of ASDRs were retrieved and records from Global Health Estimates of World Health Organization 2018. The deaths for COVID-19 were taken by the John Hopkins Registry up to the May 19th 2020.*

Findings: *No correlation were found with COVID-19 deaths and variables related to aging; no correlation was found with, diabetes type II, cardiovascular diseases, digestive and pulmonary diseases; only senile dementia was found positively correlated.*

Conclusions and Relevance: *COVID-19 represents an independent disease and many of the common believes that aging and concomitant diseases are increasing the risk of death should be carefully revised.*

Keywords
COVID-19, Aging, Chronic diseases.

Question: the COVID-19 deaths are supposed to be more frequent in elderly people suffering from chronic diseases.
Findings: the COVID-19 deaths are not correlated to aging and chronic diseases such as diabetes, pulmonary diseases or CVDs, the only disease increasing death for COVID-19 is senile dementia.
Meaning: the therapy for chronic diseases is facilitating the survival from COVID-19 death.

Introduction

In the literature regarding the COVID-19 pandemia it is reported very frequently that the disease in causing death particularly in elderly people [1], respiratory failure and smoking [2] diabetes [3], cardiovascular and chronic obstructive pulmonary diseases [4,5]. These data were confirmed in the report concerning COVID- 19 deaths in Italy [6]. From an analysis considering all the Italians Regions these data were not confirmed and correlation between age indexes, CVD, diabetes, obesity chronic diseases) were found to be negative as was for the vaccination for the common flu [7,8]

and other variables have been shown to be positively correlated such as the number of companies and workers in the territory, the GDP, and living in flat land or mountains, while temperature and rain fall could be ruled out [9].

The lockdown for elderly people and for who is suffering from chronic diseases is an extremely serious aspect of the prevention of the viral spreading, and these subjects are considered particularly sensible to the COVID-19 representing a source of infection for the population.

The aim of the present study is to analyze the available data on worldwide death for COVID-19 and correlate them with aging and chronic diseases.

Material and Methods

The list and the criteria of choice for the countries

In total, the countries listed by WHO in terms of ASDRs are 191. The data used for correlations were relative only to those 49 countries (selected countries or SC) considered by WHO *"with high completeness and quality of cause-of-death assignment*" that "*may be compared and time series may be used for priority setting and policy evaluation"* [10]. The list of the countries is reported in Table 3.

Criteria of choice for the variables

The Age Standardized Death Rate x 100000 population (ASDRs) were considered for some Chronic disease (Table 2).

ASDRs are free of the bias related to age distribution unlike crude data or prevalence/incidence measures. The ASDRs data listed as Global Health Estimates 2016 and published in 2018 were used [10].

For all the variables the values were relative to both genders.
The values of population aging were taken from United Nation records [11], and life expectancy was retrieved from worldometers [12].

Statistical analysis

The ASDRs are correlated during time and values concerning the last available years (2016) may represent also the values of 2020 (Table 2).

ASDRs do not consider the number of inhabitants in the country, with the consequence that values in small countries (e.g, Bahamas- about 0.4 million inhabitants) have the same weight as for larger countries (e.g. USA- about 322 million inhabitants), which can create a bias in the average values of the 49 SC.

However, despite the increase of the population, ASDRs remain significantly correlated during time ($p < 0.01$). For this reason, ASDRs values were considered sufficiently reliable.

Average values and dispersion indexes were calculated for all the variables.

In terms of correlations among variables, following a linear Pairwise Correlation analysis, the presence of some or more out outlier may compromise the r values. The impact of the outlier was minimized using the Robust fit [13] further adjusted following the method M of Huber [14].

The JMP14 Pro of SAS Institute was used for the analysis.

Results

The data concerning the population increase for both genders were reported in Table 1.

Year	Total population 10^6		
	191 countries	49 SC	% of 49 SC
2020	7391.073	1457.366	19.7

Table 1: Population: males and females in 2000 and 2016

The 49 SC represent 19.7 % the world population.
The ASDRs for the selected diseases were reported in Table 2.

Disease	GHE	2016 ASDRs values Mean ± SD	*Correlations r significant 2000 Vs 2016*
Diabetes	800	23.41 ± 31017	***0.9461***
Iron-deficiency anemia [IDA]	580	0.57 ± 0.857	***0.9032***
Tuberculosis (TBC)	30	1.43 ± 2.172	***0.9070***
STD	40	0.08 ± 0.118	***0.7620***
HIV/AIDS	100	3.54 ± 9.373	***0.9691***
Diarrheal diseases	110	1.32 ± 2.133	***0.9426***
Hepatitis	185	0.43 ± 0.316	***0.6917***
Respiratory infectious	380	16.55 ± 11.338	***0.7633***
Alzheimer	950	15.78 ± 11.193	***0.7874***
CVD	1100	179.2 ± 115.84	***0.9356***
Ischemic stroke	1141	23.99 ± 18.664	***0.8649***
Hemorrhagic stroke	1142	19.75 ± 14.088	***0.9063***
Respiratory diseases	1170	20.02 ± 9.350	***0.4146***
Digestive diseases	1210	25.481 ± 14.403	***0.8869***
Chronic kidney disease	1272	2.78 ± 2.670	***0.7626***

Table 2: ASDRs of the different diseases: mean values ± SD in 2016; *r* values in Italic bold are statistically significant at $p < 0.01$.

Legenda: GHE (Global Heath Estimation code)

All the diseases considered were significantly correlated in the past (2000 Vs 2016) which indicates that the values in 2016 can be also representative for 2020.

The values of the population, number of deaths due to COVID-19, and age indexes are reported in Table 3.

The correlation between COVID-19 and the different chronic diseases are reported in Table 4 and 5.

Country	Population X 10^6	N Deaths COVID-19	Deaths % COVID- 19	>65 years %	Old age Index %	Life Expectancy Years
Armenia	3.017	67	0.0222	113	18.5	75.55
Australia	23.578	100	0.0042	170	27.1	83.94
Austria	8.508	632	0.0743	201	31.0	82.05
Bahamas	0.368	11	0.0299	79	12.1	74.28
Belgium	11.150	9108	0.8168	197	32.5	82.17
Brazil	202.768	17983	0.0887	96	14.9	76.57
Brunei	0.406	1	0.0025	57	8.1	76.35
Canada	35.703	6028	0.1688	185	28.9	82.96
Chile	17.919	509	0.0286	126	19.2	80.74
Croatia	4.256	96	0.0226	203	35.0	79.02
Cuba	11.283	79	0.0070	157	24.9	79.18
Czechia	10.538	303	0.0288	201	33.0	79.85
Denmark	5.660	551	0.0974	204	34.6	81.40
Estonia	1.315	64	0.0486	201	33.9	79.18
Finland	5.472	301	0.0550	224	39.2	82.48
France	63.920	28025	0.4384	208	36.5	83.11
Germany	80.822	8112	0.1004	223	36.1	81.88
Grenada	0.106	0	0	104	16.2	72.59
Guatemala	15.807	43	0.0027	55	9.8	75.05
Hungary	9.877	470	0.0476	193	32.4	77.31
Iceland	0.329	10	0.0304	158	25.8	83.52
Ireland	4.610	1561	0.3386	151	24.4	82.81
Israel	8.334	278	0.0334	125	23.4	83.49
Italy	60.796	32169	0.5291	229	39.0	84.01
Japan	127.083	768	0.0060	280	51.0	85.03
Kyrgyzstan	5.895	14	0.0024	50	8.3	71.95
Latvia	2.001	21	0.0105	194	34.5	75.73
Lithuania	2.934	60	0.0204	189	33.5	76.41
Luxembourg	0.550	109	0.1983	160	22.2	82.79
Malta	0.425	6	0.0141	216	34.7	83.06
Mauritius	1.261	10	0.0079	121	19.0	75.51
Mexico	119.713	5666	0.0473	79	12.9	75.41
Netherlands	16.829	5734	0.3407	199	33.5	82.78
New Zealand	4.510	21	0.0047	170	27.5	82.80
Norway	5.166	233	0.0451	180	29.1	82.94
Rep. of Korea	50.424	263	0.0052	153	22.4	83.50
Moldova	4.03	221	0.0544	120	17.9	72.30
Romania	19.947	1141	0.0572	182	31.1	76.50
Saint Vincent & Grenadines	0.109	0	0.0000	101	16.3	72.98
Slovakia	5.421	28	0.0052	163	25.5	78.00
Slovenia	2.063	104	0.0504	204	33.5	81.55
Spain	46.344	27778	0.5994	198	32.2	83.99
Sweden	9.747	3743	0.3840	208	35.5	83.33
Switzerland	8.237	1891	0.2296	221	30.8	84.25
Macedonia	2.067	106	0.0513	142	22.1	76.26
Trinidad and Tobago	1.341	8	0.0060	116	17.8	73.90
United Kingdom	64.598	35422	0.5484	193	31.7	81.77
United States of America	318.885	91938	0.2883	167	27.6	79.11
Uzbekistan	3.049	13	0.0004	50	7.8	72.04
Total	1436.487	281799				
Average			0.1223	161	26.4	79.50
SD			0.18881	53.9	9.51	3.986
r Vs COVID-19 deaths				0.36604	0.2593	***0.4421***

Table 3: Population, number of deaths for COVID-19 and age indexes: average values ± SD.
Legenda: ond age index %= >65 years/people 20-64 years; the statistically significant correlations are reported in Italic bold character

Country	Diabetes Type II	Respiratory diseases	Digestive diseases	Respiratory infectious	CVDs	Alzheimer's disease	Stroke ischemic
Armenia	27.45	25.05	33.16	8.79	271.93	20.34	29.13
Australia	9.59	22.93	13.37	6.80	81.17	22.97	8.46
Austria	14.18	17.98	17.21	4.61	127.85	9.34	9.87
Bahamas	28.00	9.63	19.53	27.64	171.91	16.61	18.79
Belgium	5.62	28.43	19.94	16.73	95.08	22.96	10.02
Brazil	30.34	39.16	34.68	42.83	170.32	10.88	32.29
Brunei	52.97	42.74	17.98	25.52	183.75	32.19	24.77
Canada	9.10	22.40	14.88	7.78	75.83	24.33	9.00
Chile	20.53	27.14	35.99	16.27	116.59	12.41	19.68
Croatia	17.47	18.15	24.23	6.79	207.96	8.95	33.28
Cuba	12.09	26.11	21.02	29.18	161.18	19.65	24.13
Czechia	15.76	20.50	23.66	15.50	192.15	11.65	23.63
Denmark	11.39	34.40	19.83	13.66	87.75	24.57	11.47
Estonia	5.38	11.00	27.69	10.11	227.38	4.47	21.29
Finland	4.30	12.21	22.64	2.06	123.51	50.84	17.48
France	6.83	15.86	16.44	7.89	70.62	19.29	7.80
Germany	9.99	24.55	20.97	9.05	131.75	15.83	12.63
Grenada	79.99	18.53	29.10	47.88	235.43	4.91	31.28
Guatemala	68.26	26.63	59.74	54.46	135.07	3.85	18.04
Hungary	13.28	31.84	35.62	6.29	276.89	14.77	33.98
Iceland	4.50	22.15	10.63	8.24	99.91	29.37	10.07
Ireland	6,87	32.08	15.50	13.04	104.31	26.76	10.47
Israel	20.99	20.99	13.84	17.46	77.10	14.20	8.77
Italy	10.87	18.61	14.86	6.05	103.23	13.84	12.92
Japan	3.34	20.73	13.80	24.33	72.84	5.48	13.00
Kyrgyzstan	10.35	40.72	55.82	14.54	524.38	1.41	73.00
Latvia	10.89	9.61	31.20	11.76	319.89	5.27	72.08
Lithuania	5.00	10.42	43.20	11.97	307.56	4.57	55.80
Luxembourg	7.65	22.20	17.39	8.46	95.27	16.67	9.11
Malta	15.49	19.91	12.62	18.16	138.51	13.71	14.68
Mauritius	146.30	56.98	22.85	17.30	212.09	2.52	21.40
Mexico	91.40	31.00	56.27	16.62	136.57	3.56	13.46
Netherlands	7.44	26.38	12.67	10.74	89.15	32.90	11.40
New Zealand	10.51	23.91	11.33	8.34	99.26	19.76	10.53
Norway	5.99	26.49	11.76	13.16	89.54	24.34	10.31
Rep. of Korea	13.90	19.01	15.66	21.05	73.65	13.96	18.79
Moldova	8.71	18.15	78.49	23.48	490.89	3.51	79.88
Romania	6.73	22.70	43.71	22.24	322.95	4.40	49.78
Saint Vincent & Grenadines	88.45	25.98	29.48	40.75	288.02	4.04	38.17
Slovakia	9.99	14.03	36.78	28.69	206.97	22.29	30.45
Slovenia	6.57	13.13	23.76	12.75	138.49	2.90	20.79
Spain	6.82	28.71	17.77	8.19	82.13	21.51	8.79
Sweden	8.28	19.23	13.51	9.22	109.83	28.23	11.68
Switzerland	6.08	16.31	13.44	7.46	87.26	25.49	7.82
Macedonia	29.98	28.91	13.76	5.35	393.88	1.90	73.37
Trinidad and Tobago	115.58	25.97	27.66	21.97	249.50	8.03	33.93
United Kingdom	4.17	30.64	21.58	13.23	91.05	37.60	10.13
United States of America	15.27	39.69	22.75	10.90	133.48	32.44	12.87
Uzbekistan	27.40	17.28	38.94	17.68	498.40	2.10	34.89
Average	24.31	24.02	25.48	16.55	179.19	15.78	23.99
SD	31.017	9.350	14.403	11.3385	115.84	11.193	18.868
r Vs COVID-19 deaths	-0.2942	0.0858	-0.2829	-0.2624	***-0.3829***	***0.4142***	***-0.3736***

Table 4: ASDRs for different diseases in relation to the COVID-19 deaths in the 49 SC.

Disease	*Correlations value of r*		
	Vs COVID-19	Vs LE	Vs old 65>Vs
Diabetes	-0.2942	***-0.5583***	***-0.5453***
Iron-deficiency anemia [IDA]	-0.1459	***-0.3968***	***-0.4301***
Tuberculosis (TBC)	-0.3161	***-0.6241***	***-0.5870***
STD	0.1182	***-0.4722***	***-0.5275***
HIV/AIDS	-0.1745	***-0.4133***	***-0.3974***
Diarrheal diseases	-0.1086	-0.2466	***-0.3858***
Hepatitis	-0.0884	-0.3221	-0.3658
Respiratory diseases	0.0858	-0.1662	-0.3632
Alzheimer	***0.4214***	***0.5498***	0.2739
CVDs	***-0.3829***	***-0.8221***	***-0.4393***
Ischemic stroke	***-0.3736***	***-0.7220***	-0.2926
Hemorrhagic stroke	-0.3406	***-0.7898***	***-0.5646***
Respiratory diseases	0.0858	-0.1662	-0.3632
Digestive diseases	-0.2829	***-0.7263***	***-0.4679***
Chronic kidney disease	-0.2970	***-0.4115***	***-0.6513***

Table 5: Correlations between COVID-19 aging indexes and chronic diseases.

Legenda.: The statistically significant correlations ($p< 0.01$) are reported in bold Italic characters.

Three variables only were found correlated with COVID-19: Alzheimer's disease (positive), CVDs and ischemic stroke (negative). A positive correlation means that with the increase of the variable (Alzheimer's disease) the deaths for COVID- 19 increase also; a negative correlation means that with the variable increase (CVDs, stroke), the deaths for COVID-19 decrease.

The pattern of the different diseases and COVID-19 are consistently different from those related to aging.

Discussion

The results of the present finding cannot be applied worldwide since the 49 SC represent only the 20 % of the population (Table 1) and most among the developed countries.

Another limitation of the study is that in the same country there are territories with very different death rates due to the virus, so called hot areas, which can be very close to areas almost completely free virus free. One example is Italy, where there are Regions with the highest death rate in the world (Lombardia > 1.5 x 1000 inhabitants; 5 times more than USA) and also with the e lowest rate (Molise <0.07 × 1000 inhabitants; 40 times lower than USA).

China, India, Russia, and Africa were not reported in this study, however, the countries represented in this study are consistent with 85 % of deaths for COVID-19 which makes reliable the results.

When the present data are compared to those of a single country such as Italy (divided into the 20 different Regions) the conclusions were almost superimposable to the present one [7-9]. Two main topics were the reason of the study: age, and chronic diseases.

Age

Aging was not emerging as a risk factor: despite it is true that elderly people die more frequently than young people, it is not true that COVID-19 is affecting more consistently elderly people. All the indexes in relation to aging were not found statistically significant. Furthermore, the pattern of correlations of COVID-19 with chronic diseases is completely different from those characteristic for aging (LE and % of people > 65 years).

One aspect unfortunately could not be analyzed in the present study concerning the deaths in the nursing home, which now days is emerging as very dramatic. However, there are no data available for the moment.

Some aspects are for sure characteristics of people living in nursing homes, and consist of age, diseases, and absolute lack of affection, making these people living in a separate country, whose name could be the "Forgotten Purgatory".

Chronic diseases

The only disease positively correlated with COVID-19 was senile dementia. In this case, COVID-19 most probably is adding its general inflammatory condition to the one of Alzheimer's disease accelerating the death.

All the other diseases were not correlated, and instead the tendency was to show a negative correlation. This does not mean that chronic diseases my help to face COVID-19, but it indicates the therapy undertaken to control the chronic diseases can be effective in counteracting the viral damage.

The effect of flu vaccination on COVID-19 could not be measured, because data were not available for most of the 49 SC. However, considering the 20 Italian Regions were the data were available, it was emerging that flu vaccination was protective [8].

Just by curiosity, in those 25 countries were the LE is > 80 years all the correlations disappear, meaning that old age *per se* is the most important variable to determine the death, no matter about diseases.

Conclusions

In the 49 SC the death due to COVID-19 was found independent from aging or concomitant chronic diseases, such as diabetes type II, CVDs respiratory diseases, and digestive diseases. The only pathology increasing the death due to the virus was senile dementia.

Acknowledgements

We need to give our condolences to the families of COVID-19 victims, and our proximity to the people suffering from this viral infection. UC conceived the trial; UC, GB, MRC, RC were collecting the data; MR was in charge to make the statistical evaluation, UC wrote the text.

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