



Population Age Structures of Nations with COVID-19 and Attributed Deaths

Ali Akbar Mahzoon¹, Saleh Ghasemi², Ali Dabbagh³, Mohammad Akbari⁴, Hadis Ashrafizadeh⁵, Hamideh Javadinasab⁶ and Mohammad Esmaeil Akbari^{7,*}

¹Office of Population, Labor Force Statistics & Census Statistical Centre of Iran (SCI), Tehran, Iran

²Shahid Beheshti University of Medical Sciences, Tehran, Iran

³Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴Economic Development and Planning Department, Faculty of Management and Economics, Tarbiat Modares University, Tehran, Iran

⁵Student Research Committee, Nursing and Midwifery School, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

⁶Ministry of Health & Medical Education, Tehran, Iran

⁷Cancer Research Center, Shahid Beheshti University of Medical Sciences Cancer Research Center, Shahid Beheshti University of Medical Science, Tehran, Iran

*Corresponding author: Cancer Research Center, Shohadaye Tajrish Hospital, Tehran, Iran. Tel/fax: +98-2122748001-2, Email: profmeakbari@gmail.com

Received 2021 March 05; Revised 2021 April 19; Accepted 2021 May 21.

Abstract

Background: The COVID-19 pandemic is one of the greatest challenges the world has faced during the last decades that has affected every aspect of human life.

Objectives: This study aimed to identify the effects of the age composition of the countries on global mortality and the final outcome of the COVID-19 outbreak.

Methods: This ecological observational study used the World Health Organization (WHO) reports for information on COVID-19 in 42 countries with more than 1000 formal COVID-19 reports. The correlation coefficient between age composition pattern and COVID-19 deaths was calculated in selected countries by SPSS.

Results: This study demonstrated a positive relationship between COVID-19-attributed death and the country population share of the 50 - 64 years age group at the significance level of 90.8%. The only age range that could affect the nationwide mortality rate was the age range of 50 - 64 years. There was not a significant correlation between COVID-19-attributed death and the population share of 65 years and over.

Conclusions: The young population is protective against COVID-19-related death, and they are productive and responsible for community needs during this pandemic crisis. Population aging and the increasing share of the elderly in population is one of the most critical social changes in the 21st century, and its consequences affect almost all sections of the society.

Keywords: COVID-19, Population Age Structures, Pandemic, Worldwide, Mortality

1. Background

During the last days of 2019, the outbreak of COVID-19 commenced in Wuhan in Hubei Province, China. The COVID-19 pandemic is one of the greatest challenges the world has faced during the last decades; the disease has not only been a heavy burden to the health system, but also it has affected the societal, economic, personal and interpersonal, sports-related, educational, industrial, and even political aspects of the human life (1, 2). While we have learned a great deal from the novel coronavirus SARS-CoV2 to date and its causes, evidence shows that mortality is higher in the elderly and close to zero in children (3).

This pandemic has some relatively unique features, including its very rapid rate of progression possibly due to

the durability of the virus on surfaces, relatively very low involvement of children, increased mortality in the elderly and immune-compromised patients, and the determining role of the immune system in the final outcome (4, 5). At the beginning of the epidemic, demographers introduced the young age structure as a safe pattern in terms of mortality. Countries are unable to develop human and economic capital infrastructure and are at risk of all kinds of internal conflicts because more than half of the world's population is under the age of 25. However, the results of studies show that so far, during the corona virus epidemic, the elderly population of countries are structurally more endangered than other age patterns (6). In the age-related mortality pattern, the areas with the most elderly people are at higher risk of more severe illness or death than the

areas with younger populations (3). What has been confirmed to date is that the risk of COVID-19-related mortality rises with age. Therefore, if the population of people infected with COVID-19 in one country is more than other countries, the CFR will be higher, even if the specific risk of death is the same for all age groups (7).

However, the role of the median age of the population on the nation-specific and worldwide outcome and mortality has not been defined yet; in other words, could the age-composition of a country or a specific society affect the trend of the outbreak, disease mortality, and the outcome in COVID-19 pandemic? The worldwide estimates of COVID-19-related age-specific mortality rates have grown by leaps and bounds since reporting began two months ago. Yet, the relationship between these rates has remained almost constant. By applying these age-related rates to individual countries, one can account for the differences that might be observed relative to a similar level of infection throughout the world (6, 8). In this article, we sought to summarize regional differences in population age structures among countries in the context of unequal age- and sex-specific death risks associated with the spread of the COVID-19 pandemic. Also, this study was designed and implemented to find the effects of the age-composition of the countries on global mortality and the final outcome of the COVID-19 outbreak.

2. Methods

This is an observational ecological study, which examines the relationship (or correlation) between an exposure and a given outcome measured in populations. Unlike other types of studies, this study does not examine individuals, and the unit under study is population groups instead of individuals. Ecological studies are generally involved in both hypothesizing and testing hypotheses (9, 10). In an ecological study (with cross-sectional design) for information on COVID-19 deaths, the World Health Organization Report No. 70 of March 30, 2020 (Monday, April 11) was used. This information included the total number of confirmed infections, the total number of deaths, the number of new infections, and deaths during one day leading up to the reporting date.

The COVID-19 case-fatality rate (CFR) is defined as the ratio of deaths (D) associated with COVID-19 divided by the number of detected COVID-19 cases (N): $CFR = D/N$. In our application, the death and case counts are cumulative counted up to a certain date. If case counts and death counts are available by age, which is our situation, the CFR can also be written as the sum of age-specific CFRs weighed by the proportion of cases in a certain age group

(7). We use a as an index to denote different age groups. The proportion of deaths for each age group was estimated through dividing the number of deaths by the total number of deaths in the country.

The 2019 World Population Outlook report was also used for demographic and major age groups.

The method used in this study is to calculate the correlation coefficient between age composition pattern and COVID-19 deaths in selected countries. The selected countries were those countries with more than 1000 formal COVID-19 reports in the WHO report, leading to recruitment of 42 countries (Table 1). Data entry and analysis were performed using SPSS, version 16.0. Pearson correlation test was used to examine the relationship between exposure and outcome. A level of 90% was considered statistically significant.

2.1. Ethical Considerations

In the present study, no intervention was performed on individuals in the community, only the reports of the World Health Organization were examined. According to the research ethics statement, the publication of information that has been made available to the public in advance and in a correct manner does not require informed consent (13).

3. Results

The scatter plot of the number of deaths caused by COVID-19 in the population share of under 15 years, the population share of 15 - 49 years, the population shares of 50 - 64 years and 65 years, or older age group are visible in Figures 1 - 4.

Based on the above scatter plots, Pearson, Kendall, and Spearman correlation coefficients between COVID-19 deaths and the following variables was calculated: (1) country population percentage under 15 years; (2) country population percentage between 15 to 49 years; (3) country population percentage between 50 to 64 years; (4) country population percentage 65 years and over.

The correlation coefficient between COVID-19-attributed death and country population percentage under 15 years was negative at the significance level of 85.2%; also, the correlation coefficient between COVID-19-attributed death and country population percentage between 15 to 49 years was negative at the significance level of 86.1%. The two latter analyses demonstrate that those countries with higher country population percentage under 49 years had lower COVID-19-attributed death rates.

Table 1. Population Share of Age Groups in Countries with More Than 1000 COVID-19 Cases (11, 12)

Country	Total Population	Below 15 Years Age	Percentage Between 15 - 49 Years	Percentage Between 50 - 64 Years	Percentage Above 65 Years	Total Confirmed Cases	Total Deaths
United States of America	331,003	18.4	46.0	19.0	16.6	122,653	2,112
Italy	60,462	13.0	41.3	22.4	23.3	97,689	10,781
China	1,439,324	17.7	49.5	20.8	12.0	82,447	3,310
Spain	46,755	14.4	44.3	21.4	20.0	78,797	6,528
Germany	83,784	14.0	41.3	23.0	21.7	57,298	455
France	65,274	17.7	42.3	19.3	20.8	39,642	2,602
Iran (Islamic Republic of)	83,993	24.7	55.1	13.6	6.6	38,309	2,640
The United Kingdom	67,886	17.7	44.4	19.3	18.7	19,526	1,228
Switzerland	8,655	15.0	44.5	21.5	19.1	14,274	257
Netherlands	17,135	15.7	43.0	21.3	20.0	10,866	771
Belgium	11,590	17.0	43.6	20.1	19.3	10,836	431
Republic of Korea	51,269	12.5	47.8	23.9	15.8	9,661	158
Turkey	84,339	23.9	52.4	14.6	9.0	9,271	131
Austria	9,006	14.4	44.3	22.1	19.2	8,813	86
Portugal	10,197	13.1	43.1	21.1	22.8	5,962	119
Canada	37,742	15.8	45.6	20.5	18.1	5,655	61
Israel	8,656	27.8	46.5	13.2	12.4	4,247	15
Norway	5,421	17.3	46.3	18.9	17.5	4,102	22
Australia	25,500	19.3	46.7	17.8	16.2	3,966	16
Brazil	212,559	20.7	53.8	15.9	9.6	3,904	114
Sweden	10,099	17.6	43.6	18.5	20.3	3,700	110
Czech	10,709	15.8	45.5	18.6	20.1	2,829	16
Ireland	4,938	20.8	47.4	17.2	14.6	2,615	46
Malaysia	32,366	23.4	55.9	13.5	7.2	2,470	34
Denmark	5,792	16.3	43.6	20.0	20.2	2,395	72
Luxembourg	626	15.6	50.0	20.1	14.4	1,950	21
Chile	19,116	19.2	51.1	17.4	12.2	1,909	6
Japan	126,476	12.4	40.1	19.0	28.4	1,866	54
Poland	37,847	15.2	46.8	19.3	18.7	1,862	22
Ecuador	17,643	27.4	52.6	12.4	7.6	1,835	48
Romania	19,238	15.5	45.2	20.1	19.2	1,760	40
Pakistan	220,892	34.8	51.6	9.2	4.3	1,625	18
Russian Federation	145,934	18.4	46.3	19.9	15.5	1,534	10
Thailand	69,800	16.6	48.9	21.6	13.0	1,524	9
Philippines	109,581	30.0	52.8	11.6	5.5	1,418	71
Saudi Arabia	34,814	24.7	60.2	11.6	3.5	1,299	8
Indonesia	273,524	25.9	53.3	14.5	6.3	1,285	114
South Africa	59,309	28.8	54.4	11.3	5.5	1,280	1
Finland	5,541	15.9	42.1	19.4	22.6	1,218	11
Greece	10,423	13.7	43.1	20.9	22.3	1,156	38
India	1,380,004	26.2	54.4	12.8	6.6	1,071	29
Iceland	341	19.4	46.6	18.3	15.6	1,020	2

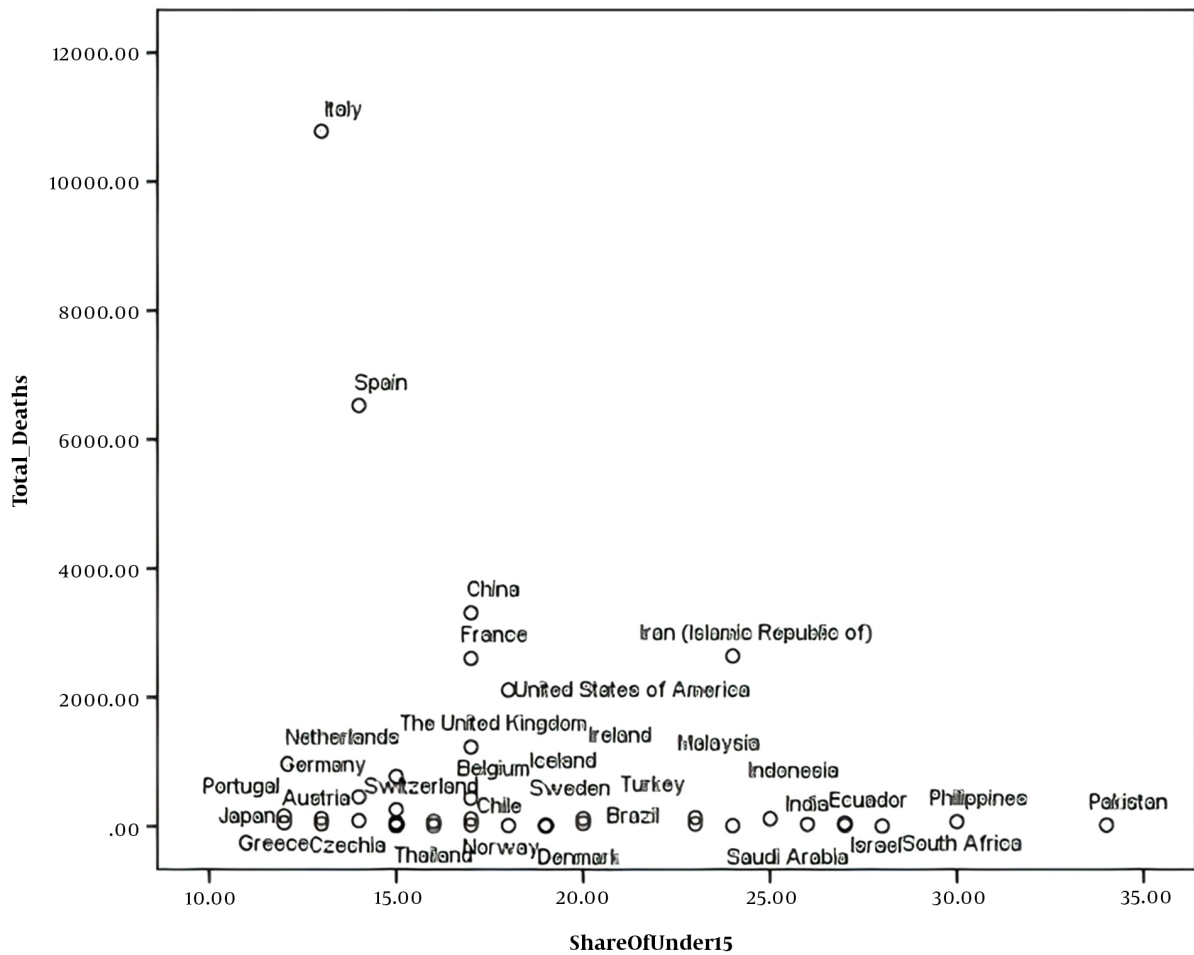


Figure 1. Distribution of mortality rates due to COVID-19 versus the share of the population under 15 years old in the selected countries.

The correlation coefficient between COVID-19-attributed death and country population percentage between 50 to 64 years was positive at the significance level of was 90.8%, which means that the latter two variables had a positive relationship.

The correlation coefficient of COVID-19-attributed death with country population percentage 65 years and over was not significant, with a significance level of 83.8, which means that we could not prove that countries with higher country population percentage 65 years and over had more COVID-19-related deaths.

4. Discussion

Various factors affect the prevalence and outbreak of COVID-19 in a country, including population health conditions, the effectiveness and efficiency of government re-

sponse, and the availability of care resources. Age structure (the share of the total population in each age group) alone cannot determine which countries will suffer the most during a pandemic. However, it can provide a good understanding of how to respond to a crisis. If the age-specific mortality rates of two countries is the same in terms of COVID-19 virus, the country with the highest elderly population will have more deaths per 1,000 people (3, 14). The available statistics show that the majority of deaths due to COVID-19 in the elderly are in the United States, Italy, Spain, France, and the United Kingdom (15). Using population pyramids, Dowd et al. (2020) showed how the age structure of the population correlates with the high mortality rate of COVID-19 (16). By keeping the prevalence of infection constant at 10% and using only age-specific mortality rates (17), they exhibited that the mortality rate of COVID-19 varies among communities due to age structure.

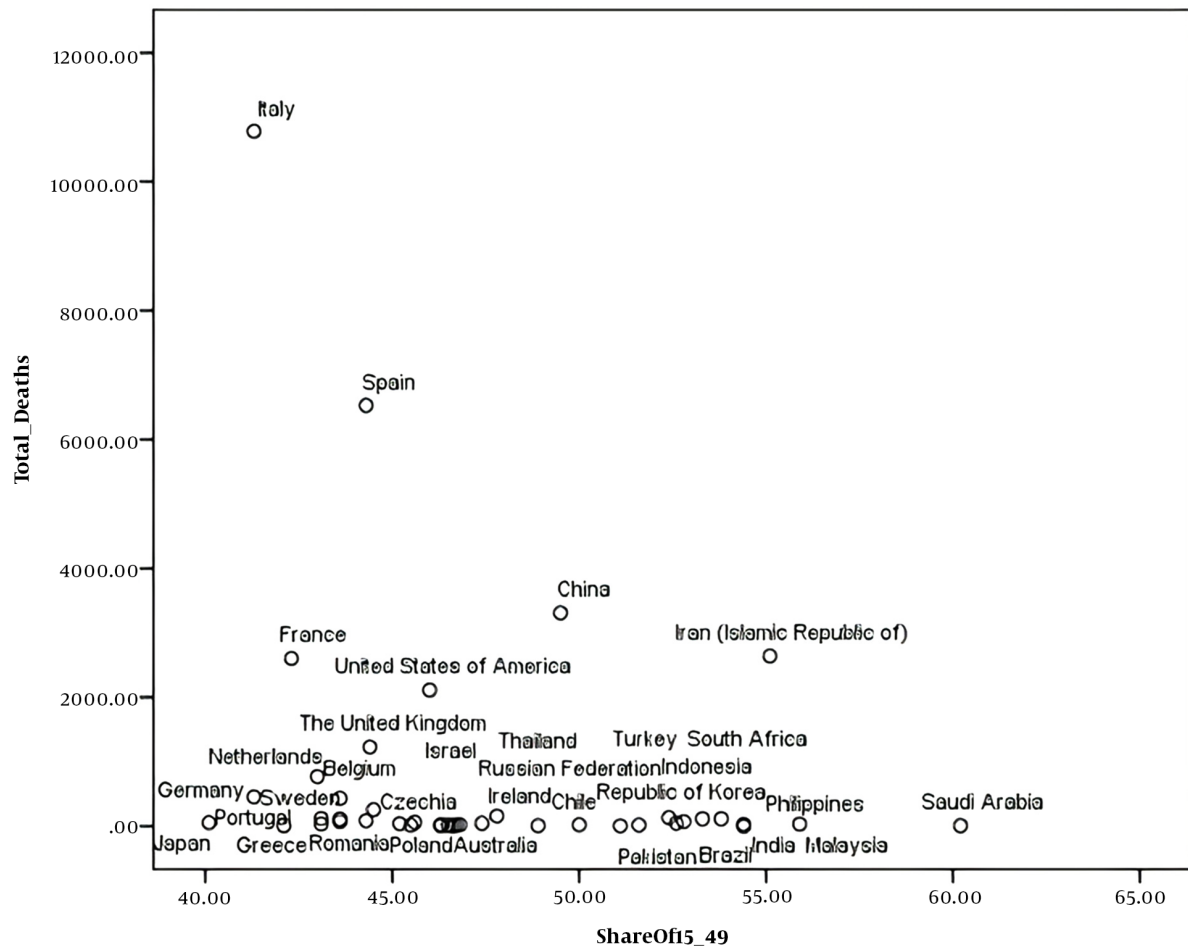


Figure 2. Distribution of mortality rates due to COVID-19 versus the share of the population aged 15 - 49 years in the selected countries.

It is worth noting that this calculation is not an epidemiological prediction. Rather, it provides a demographic perspective on the role that age population structures alone can play in the spread of the disease, assuming that other factors remain constant.

This study demonstrated a positive relationship between COVID-19-attributed death and the country population share of the 50 - 64 years age group. In other words, the only age range that could affect the nationwide mortality rate is the age range of 50 - 64 years. The correlation between COVID-19-attributed death and population share of below and above 15 years (divided at the age of 15) has been examined in previous studies, which have claimed the lower rate of COVID-19 incidence in the population below 15 years of age. The findings of Cincotta in New York City showed that deaths per million residents in the population aged 75 and older have remained about

74 to 76 times the rates among 18 to 44-year-olds over the past month. The elderly are more at risk of death than the young population (6), which is consistent with the results of the present study. The study of Medford and Trias-Llimós revealed that a higher share of deaths was observed in the 80 - 89 age group than in the other countries, except for China (18). In contrast, Onder et al. showed that in China, 17% of the population is 60 years of age and older, and only 1% of the population is 85 years of age or older. The death toll from COVID-19 in the age group of 85 years and older has been reported to be six times higher than the overall rate. As a result, if China's share of the elderly was higher, the death rate would be much higher than it is today (14). Medford and Trias-Llimós indicated that deaths in China occur at slightly younger ages than in Europe, and they are split slightly more evenly across the older ages, with 30% of deaths in age bands 60 - 69 and 70 - 79 and 20% of deaths

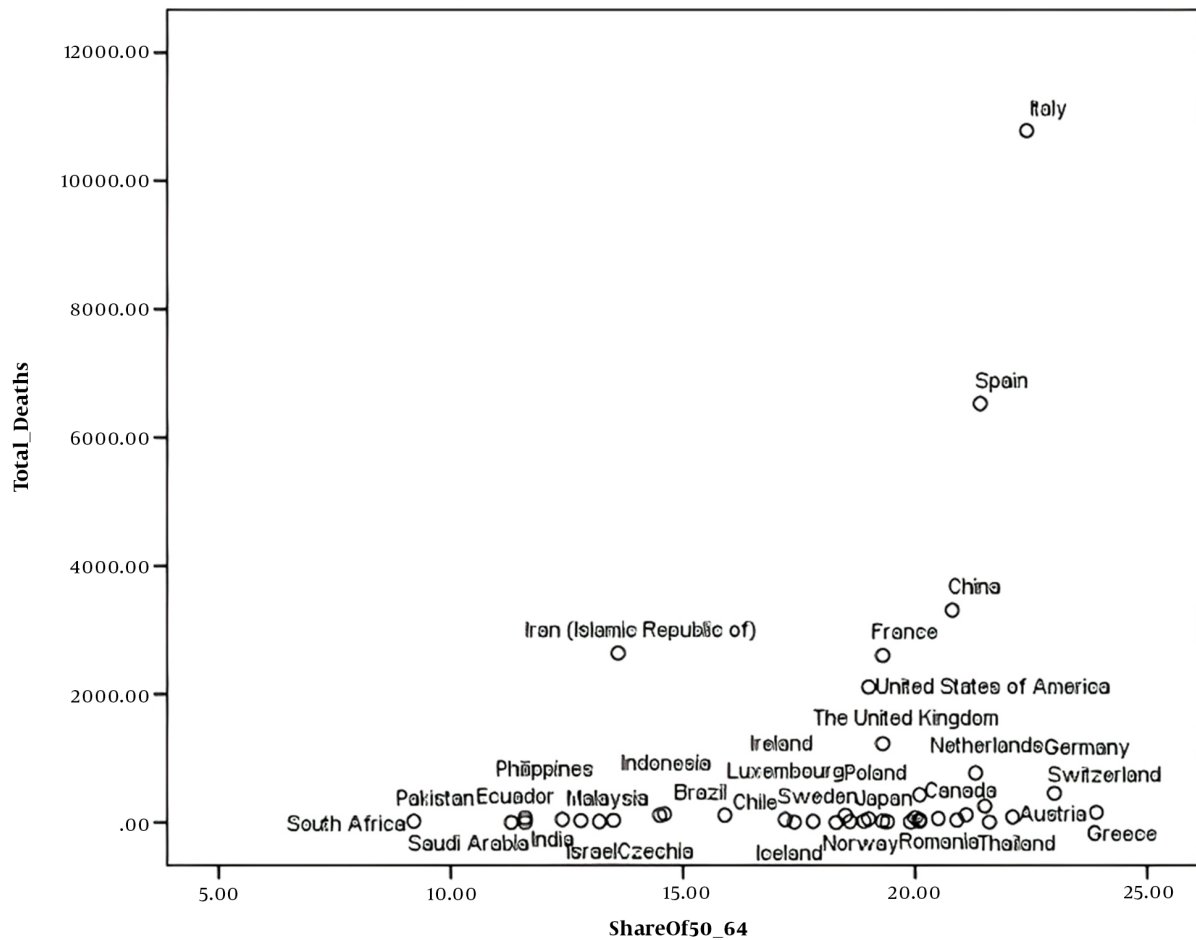


Figure 3. Distribution of mortality rates due to COVID-19 versus the share of the population aged 50 to 64 years in the selected countries.

at ages above 80. Above age 80, the proportion of deaths is 50, 58, 59, and 59% for Italy, the Netherlands, Spain, and France, respectively. These differences between the countries persist after adjustment for age structure (18).

On the other hand, age-specific incidence rate (ASIR) has been demonstrated to work as an efficient epidemiological index in epidemiological studies, which could save money, time, and effort (19, 20). Besides, age-specific mortality rate (ASMR) has been used as a critical index in studying the characteristics of previous pandemics (21-23). In this study, we could not retrieve the required data to calculate ASIR and ASMR, which is one of the shortcomings of the study.

Based on the results of this study, the young population is protective against COVID-19-related death, and they are productive and responsible for community needs during this pandemic crisis.

Cincotta exhibited that people who are less likely to die from the coronavirus are usually young people who seem likely to exhibit fewer symptoms (6). Also, according to recent studies, low CFRs in low- and middle-income countries show the distribution of young population, and high CFRs in some countries, such as Italy, is due to high elderly population and mortality in this age group (14, 24). Nowadays, any level of planning for communities is critical to be aware of their age structure. Population structure is literally equivalent to the composition of a population, and in terms of terminology, is the set of elements and features and relatively stable relationships of a population that have evolved over time (25-27).

Population aging and the increasing share of the elderly in the population is one of the most critical social changes in the 21st century, and its consequences affect almost all sections of the society (28). Population aging has

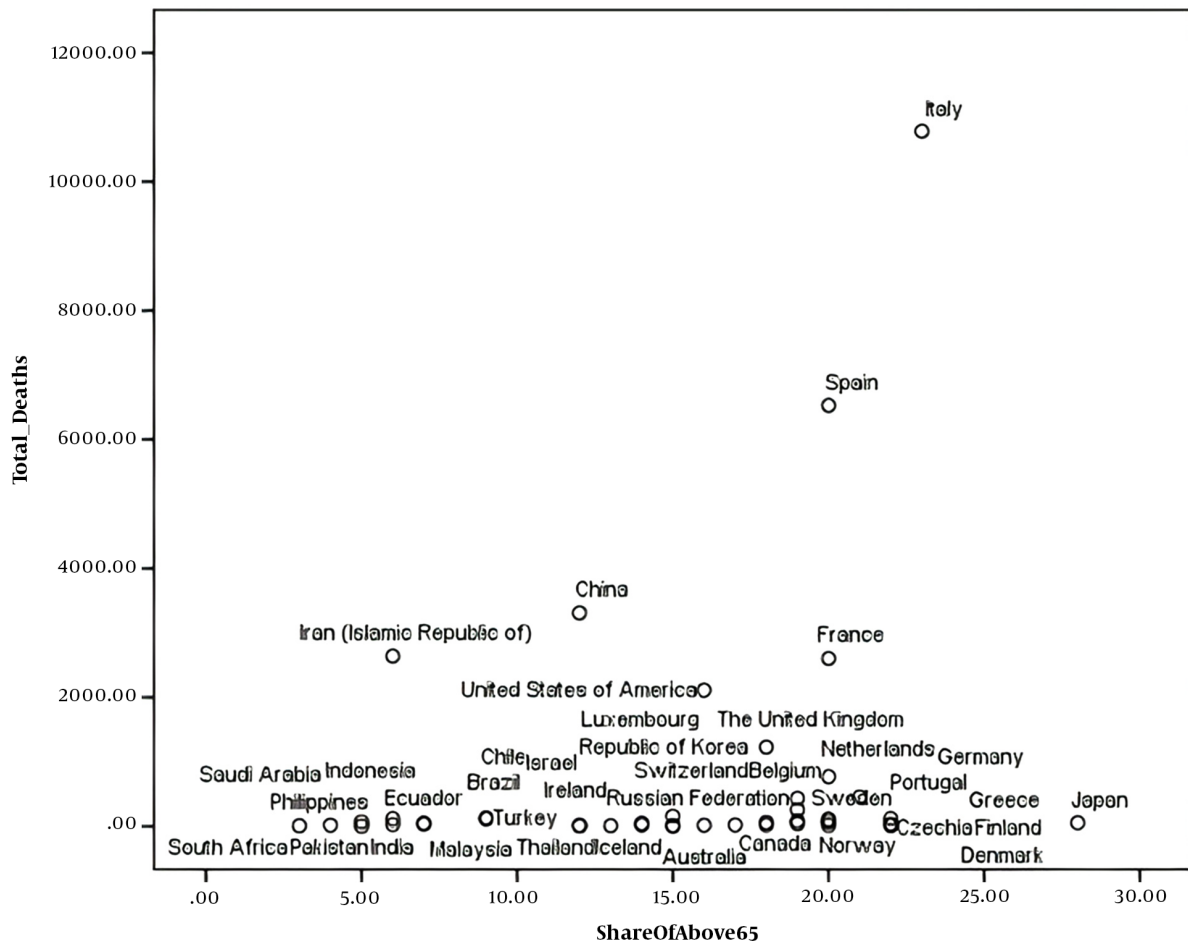


Figure 4. Distribution of mortality rates due to COVID-19 versus the share of the population aged 65 years old and over in the selected countries.

been one of the major concerns of the last century around the world. The importance of addressing the issue of population aging, which has increasingly emerged around the world, is not hidden from anyone (25, 29). The global population aging, which is now accelerating, has significant effects in cultural, economic, social, political, and medical areas, which should be fully considered. Issues such as lack of social support, lack of job and social role, living expenses, and especially high health care costs are among the numerous factors that show the need to pay special attention to old age (30-32).

Elderly people are also more vulnerable to disease. In fact, as people grow older, their risk of chronic and epidemic diseases surges. Increasing health costs of the world's elderly communities can lead to some critical challenges, especially in providing health care for the elderly (32, 33).

4.1. Conclusions

In addition to numerous economic and social challenges, the Coronavirus pandemic has highlighted the importance of social and demographic inequalities in health. Given that statistics indicate an increase in coronavirus mortality in elderlies, this affects the age structure of societies, especially those whose age pyramid is old, because the elderly are more susceptible to underlying diseases. We recommend authorities to support the policy of encouraging the total fertility rate and even change policies of United Nations agencies and non-governmental organizations regarding family planning and young population growth. Future studies are suggested to examine the relationship between exposure and outcome to examine the age pyramid structure of populations. In addition, data by age and sex should be included in regular mortality statistics. It is also necessary to compare and identify the best

policy practices to ensure consistency in data and metrics across countries.

Acknowledgments

We would like to thank the Vice-Chancellor of Research Affairs of Shahid Beheshti University of Medical Sciences, Tehran, Iran, for its assistance in the production of this research.

Footnotes

Authors' Contribution: All the authors contributed to the conception and design of the study. MEA and MA performed data analysis. HA, MEA, and MA drafted the manuscript. All the authors read and approved the final manuscript.

Conflict of Interests: The authors declare that they have no competing interests.

Funding/Support: This study has not received any funding.

References

- Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020;579(7798):265–9. doi: 10.1038/s41586-020-2008-3. [PubMed: 32015508]. [PubMed Central: PMC7094943].
- Takian A, Raoufi A, Kazempour-Ardebili S. COVID-19 battle during the toughest sanctions against Iran. *Lancet*. 2020;395(10229):1035–6. doi: 10.1016/S0140-6736(20)30668-1. [PubMed: 32199073]. [PubMed Central: PMC7138170].
- Jarosz B, Kaneda T. *Oldest areas may be hardest hit: The importance of age structure in understanding mortality during the coronavirus pandemic*. Washington, USA: Population Reference Bureau; 2020. Available from: <https://www.prb.org/resources/oldest-areas-may-be-hardest-hit-the-importance-of-age-structure-in-understanding-mortality-during-the-coronavirus-pandemic/>.
- Cdc Covid- Response Team. Severe outcomes among patients with Coronavirus disease 2019 (COVID-19) - United States, February 12-March 16, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(12):343–6. doi: 10.15585/mmwr.mm6912e2. [PubMed: 32214079]. [PubMed Central: PMC7725513].
- Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *J Infect*. 2020;80(6):e14–8. doi: 10.1016/j.jinf.2020.03.005. [PubMed: 32171866]. [PubMed Central: PMC7102640].
- Cincotta R. *Population age structure: The hidden factor in COVID-19 mortality*. Washington, USA: Environmental Change and Security Program Woodrow Wilson International Center for Scholars; 2020. Available from: <https://www.newsecuritybeat.org/2020/05/population-age-structure-hidden-factor-covid-19-mortality/>.
- Dudel C, Riffe T, Acosta E, van Raalte A, Strozza C, Myrskylä M. Monitoring trends and differences in COVID-19 case-fatality rates using decomposition methods: Contributions of age structure and age-specific fatality. *PLoS One*. 2020;15(9):e0238904. doi: 10.1371/journal.pone.0238904. [PubMed: 32913365]. [PubMed Central: PMC7482960].
- NYC Health. *COVID-19: Data*. New York, USA: NYC Health; 2020.
- Blakely TA, Woodward AJ. Ecological effects in multi-level studies. *J Epidemiol Community Health*. 2000;54(5):367–74. doi: 10.1136/jech.54.5.367. [PubMed: 10814658]. [PubMed Central: PMC1731678].
- Munnangi S, Boktor SW. *Epidemiology of study design*. Treasure Island (FL): StatPearls Publishing; 2020.
- World Health Organization. *Coronavirus disease 2019 (COVID-19) situation report-70*. World Health Organization; 2020.
- Leridon H. Population mondiale : Vers une explosion ou une implosion? *Popul Soc (Paris)*. 2020;N°573(1):1. doi: 10.3917/popsoc.573.0001.
- Journal of Educational Strategies in Medical Sciences. [A national guide to ethics in the publication of medical research works]. Tehran, Iran: Journal of Educational Strategies in Medical Sciences; 2016. Persian. Available from: <https://edcbmj.ir/content/31/>.
- Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020;323(18):1775–6. doi: 10.1001/jama.2020.4683. [PubMed: 32203977].
- Benksim A, Ait Addi R, Cherkaoui M. Vulnerability and fragility expose older adults to the potential dangers of COVID-19 pandemic. *Iran J Public Health*. 2020;49(Suppl 1):122–4. doi: 10.18502/ijph.v49iS1.3682. [PubMed: 34268218]. [PubMed Central: PMC8266024].
- Dowd JB, Andriano L, Brazel DM, Rotondi V, Block P, Ding X, et al. Demographic science aids in understanding the spread and fatality rates of COVID-19. *Proc Natl Acad Sci U S A*. 2020;117(18):9696–8. doi: 10.1073/pnas.2004911117. [PubMed: 32300018]. [PubMed Central: PMC7211934].
- Esteve A, Permanyer I, Boertien D. [The vulnerability of the Spanish provinces to COVID-19 according to their structure by age and co-residence: Implications for (de) confinement]. *Perspectives Demográfiques*. 2020;19:1–4. Spanish. doi: 10.46710/ced.pd.esp.19.
- Medford A, Trias-Llimós S. Population age structure only partially explains the large number of COVID-19 deaths at the oldest ages. *medRxiv*. 2020;Preprint. doi: 10.31219/osf.io/kb2zg.
- Alghamdi IG, Hussain J, Alghamdi MS, El-Sheemy MA. The power of the age standardized incidence rate to discover the gene link between cancer diseases: Development of a new epidemiological method to save money, time, and effort for genetic scientists. *Oncotargets Ther*. 2015;8:677–87. doi: 10.2147/OTT.S75785. [PubMed: 25878508]. [PubMed Central: PMC4386787].
- Short KR, Kedzierska K, van de Sandt CE. Back to the future: Lessons learned from the 1918 influenza pandemic. *Front Cell Infect Microbiol*. 2018;8:343. doi: 10.3389/fcimb.2018.00343. [PubMed: 3034981]. [PubMed Central: PMC6187080].
- Cilek L, Chowell G, Ramiro Farinas D. Age-specific excess mortality patterns during the 1918-1920 influenza pandemic in Madrid, Spain. *Am J Epidemiol*. 2018;187(12):2511–23. doi: 10.1093/aje/kwy171. [PubMed: 30124746]. [PubMed Central: PMC6454514].
- Ramiro D, García S, Casado Y, Cilek L, Chowell G. Age-specific excess mortality patterns and transmissibility during the 1889-1890 influenza pandemic in Madrid, Spain. *Ann Epidemiol*. 2018;28(5):267–72. doi: 10.1016/j.annepidem.2017.12.009. [PubMed: 29336941].
- Dahal S, Jenner M, Dinh L, Mizumoto K, Viboud C, Chowell G. Excess mortality patterns during 1918-1921 influenza pandemic in the state of Arizona, USA. *Ann Epidemiol*. 2018;28(5):273–80. doi: 10.1016/j.annepidem.2017.12.005. [PubMed: 29361358]. [PubMed Central: PMC5911181].
- Henriques M. Coronavirus: Why death and mortality rates differ. *BBC Future*. 2020;2.
- Evans CJ, Ison L, Ellis-Smith C, Nicholson C, Costa A, Oluyase AO, et al. Service delivery models to maximize quality of life for older people at the end of life: A rapid review. *Milbank Q*. 2019;97(1):113–75. doi: 10.1111/1468-0009.12373. [PubMed: 30883956]. [PubMed Central: PMC6422603].

26. Cabeza R, Albert M, Belleville S, Craik FIM, Duarte A, Grady CL, et al. Maintenance, reserve and compensation: The cognitive neuroscience of healthy ageing. *Nat Rev Neurosci*. 2018;**19**(11):701-10. doi: [10.1038/s41583-018-0068-2](https://doi.org/10.1038/s41583-018-0068-2). [PubMed: [30305711](https://pubmed.ncbi.nlm.nih.gov/30305711/)]. [PubMed Central: [PMC6472256](https://pubmed.ncbi.nlm.nih.gov/PMC6472256/)].
27. da Costa JP, Vitorino R, Silva GM, Vogel C, Duarte AC, Rocha-Santos T. A synopsis on aging-Theories, mechanisms and future prospects. *Ageing Res Rev*. 2016;**29**:90-112. doi: [10.1016/j.arr.2016.06.005](https://doi.org/10.1016/j.arr.2016.06.005). [PubMed: [27353257](https://pubmed.ncbi.nlm.nih.gov/27353257/)]. [PubMed Central: [PMC5991498](https://pubmed.ncbi.nlm.nih.gov/PMC5991498/)].
28. Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: The challenges ahead. *Lancet*. 2009;**374**(9696):1196-208. doi: [10.1016/S0140-6736\(09\)61460-4](https://doi.org/10.1016/S0140-6736(09)61460-4). [PubMed: [19801098](https://pubmed.ncbi.nlm.nih.gov/19801098/)]. [PubMed Central: [PMC2810516](https://pubmed.ncbi.nlm.nih.gov/PMC2810516/)].
29. Bhadra M, Howell P, Dutta S, Heintz C, Mair WB. Alternative splicing in aging and longevity. *Hum Genet*. 2020;**139**(3):357-69. doi: [10.1007/s00439-019-02094-6](https://doi.org/10.1007/s00439-019-02094-6). [PubMed: [31834493](https://pubmed.ncbi.nlm.nih.gov/31834493/)]. [PubMed Central: [PMC8176884](https://pubmed.ncbi.nlm.nih.gov/PMC8176884/)].
30. GBD Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: A systematic analysis for the Global Burden of Disease study 2017. *Lancet*. 2018;**392**(10159):1736-88. doi: [10.1016/S0140-6736\(18\)32203-7](https://doi.org/10.1016/S0140-6736(18)32203-7). [PubMed: [30496103](https://pubmed.ncbi.nlm.nih.gov/30496103/)]. [PubMed Central: [PMC6227606](https://pubmed.ncbi.nlm.nih.gov/PMC6227606/)].
31. GBD Population Fertility Collaborators. Population and fertility by age and sex for 195 countries and territories, 1950-2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;**392**(10159):1995-2051. doi: [10.1016/S0140-6736\(18\)32278-5](https://doi.org/10.1016/S0140-6736(18)32278-5). [PubMed: [30496106](https://pubmed.ncbi.nlm.nih.gov/30496106/)]. [PubMed Central: [PMC6227915](https://pubmed.ncbi.nlm.nih.gov/PMC6227915/)].
32. Lunenfeld B, Stratton P. The clinical consequences of an ageing world and preventive strategies. *Best Pract Res Clin Obstet Gynaecol*. 2013;**27**(5):643-59. doi: [10.1016/j.bpobgyn.2013.02.005](https://doi.org/10.1016/j.bpobgyn.2013.02.005). [PubMed: [23541823](https://pubmed.ncbi.nlm.nih.gov/23541823/)]. [PubMed Central: [PMC3776003](https://pubmed.ncbi.nlm.nih.gov/PMC3776003/)].
33. Atella V, Piano Mortari A, Kopinska J, Belotti F, Lapi F, Cricelli C, et al. Trends in age-related disease burden and healthcare utilization. *Ageing Cell*. 2019;**18**(1). e12861. doi: [10.1111/acer.12861](https://doi.org/10.1111/acer.12861). [PubMed: [30488641](https://pubmed.ncbi.nlm.nih.gov/30488641/)]. [PubMed Central: [PMC6351821](https://pubmed.ncbi.nlm.nih.gov/PMC6351821/)].