The novel coronavirus disease 2019 (COVID-19) is an infectious disease that presents an urgent challenge to global health and economy. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was the seventh identified enveloped RNA coronavirus that can infect humans, with rapid human-to-human transmission capability and varied mortality, mainly due to acute respiratory distress syndrome, severe systemic complications, and multi organ failure [1]. The spectrum of clinical presentation of COVID-19 is broad and most infected individuals experience only a subclinical or mild illness [2]. Approximately 16–26% of hospitalized patients diagnosed with COVID-19 develop severe acute respiratory distress necessitating oxygen supplementation and/or intensive care. In December 2019 the first patient with COVID-19 presented in Wuhan city, Hubei province, China [3]. Subsequently, the virus spread throughout China, and then to many other countries around the world [4]. As of 22 November 2020, approximately 58.5 million cases with laboratory confirmed COVID-19 infection have been detected in more than 200 countries with over 1,300,000 deaths [5].

Despite both national and international public health responses aimed at limiting the spread of this disease, several countries have been challenged by a critical care crisis, and many others will probably follow [6]. Outbreaks often lead to abrupt surge in the demand for hospital and critical care beds with shortage of medical staff and equipment. Therefore, many countries have used forceful mitigation and control strategies, including social distancing, quarantine, and general closure. These measures, while slowing the spread of the disease and thus allowing health systems to handle it more efficiently, might also incur enormous economic and social damage.

As long as we lack an efficient vaccine or medical treatment for the coronavirus epidemic, countries will continue to face this conflict between the urgent need to halt the pandemic spread and the grave socioeconomic impact associated with its mitigation and control. Hence, accurate prediction models that amalgamate several factors or features to forecast morbidity and mortality rates in each country may assist medical health systems in allocating healthcare resources and determining the most efficient strategies to deal with this crisis.

When looking at the geographic distribution of the COVID-19 pandemic, it seems that the burden of the disease has not been the same in all countries. While some countries have been affected severely with high morbidity and mortality rates, others report substantially smaller numbers in relation to the size of their population. While the explanation for these differences may lie in the diversity of diagnostic and mitigation efforts, it is also clear that younger populations appear to be better equipped to deal with the viral infection, as the infection rate is lower and the severity of the disease is minimized [7]. In contrast, older populations tend to experience higher infection rates and severe complications, especially respiratory distress, which necessitates intensive care and oxygen supplementation [8].

Therefore, this study aimed to assess the effects of population median age and mean ambient temperature on the COVID-19 global pandemic burden. The following sections present the methodology, results, and conclusions of the study.
policies employed by each country, other factors related to inherent differences between populations and geographical areas may also play a role.

Previous studies have shown that as with other coronavirus infections, such as severe acute respiratory distress syndrome (SARS) and Middle East respiratory syndrome (MERS) [7], COVID-19 tends to be more severe and life threatening in older patients [8]. Furthermore, the US Center for Disease Control and Prevention has reported that 80% of COVID-19-related deaths occurred in people aged 65 years or older [9]. Nonetheless, whether country population median age affects infection and death rates globally is yet unknown. Previous studies have also reported the significance of meteorological conditions such as ambient temperature, humidity, and wind speed in the survival and spread of infectious diseases, including SARS and influenza. For example, a fast drop in ambient temperature was associated with increased risk for SARS [10]. Furthermore, influenza transmission was shown to be facilitated by cold and dry weather conditions [11]. In northern Europe, low ambient temperature was found to correlate with peaks of influenza virus activity [12]. Thus, it is reasonable to hypothesize that COVID-19 transmission may also be suppressed by warmer weather conditions. The current study aimed to assess the effect of country population median age and mean ambient temperature on the number of reported infections and deaths from COVID-19. We assumed that this information may become useful in analyzing existing global epidemiologic and environmental data and in planning both national and international healthcare strategies for coping with this pandemic.

PATIENTS AND METHODS

In this observational retrospective study, we analyzed widely available international public data. The global cumulative COVID-19 pandemic daily morbidity and mortality rates were obtained from the European Union open data portal [13] and from the Johns Hopkins University Coronavirus Resource Center [5]. Population median age data were obtained from the United Nations Department of Economics and Social Affairs Population official website [14]. Historical mean country temperature data (°C) from 1901 until 2019 were obtained from the Climate Change Knowledge Portal [15]. All data were uploaded onto a computerized Excel database file (Excel spreadsheet, Microsoft Excel, Version 10, Microsoft Corp, Richmond, CA, USA). Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA). Cumulative numbers of COVID-19 cases and deaths per million residents on days 14 and 28 since the time of the first reported case (considered as the epidemic outbreak) were recorded for each country, and the correlation between the number of cases and deaths and the population median age and mean ambient temperature were calculated using Pearson's or Spearman rank correlation tests, as appropriate. Data were further analyzed using a multivariate stepwise logistic regression model. A P value < 0.05 was considered statistically significant.

RESULTS

Two hundred and two countries were available for analysis, with a total of 7.78 billion residents. The total number of cases on days 14 and 28 since the epidemic outbreak were 18,285 and 148,155, respectively, while the total number of deaths on days 14 and 28 were 4,057 and 30,528, respectively. A univariate analysis showed that population median age significantly correlated with the cumulative number of cases per million residents on days 14 and 28 from the epidemic outbreak (r = 0.310, P < 0.0001 and r = 0.364, P < 0.0001, respectively) [Figure 1, Figure 2]. Population median age also significantly correlated with the cumulative number of deaths on days 14 and 28 from the epidemic outbreak (r = 0.523, P < 0.0001; r = 0.460, P = 0.002, respectively) [Figure 3, Figure 4]. Overall mean ambient tempera-
Temperature was 17.05 ± 11.7 degrees centigrade on day 14 and 17.64 ± 11.2 degrees centigrade on day 28 from the epidemic outbreak. Mean ambient temperature showed a significant inverse correlation with the cumulative number of deaths per million residents on both day 14 and day 28 ($r = -0.367$, $P < 0.0001$, $r = -0.425$, $P = 0.006$, respectively) (Data not shown). Nonetheless, we found no correlation between the mean country temperature and the cumulative number of cases either on day 14 or on day 28 ($r = -0.37$, $P = 0.634$ and $r = -0.030$, $P = 0.699$, respectively) (data not show). After a multivariate logistic regression analysis, population median age retained its statistically significant correlation with the number of cases and deaths ($P < 0.0001$ and 0.039, respectively), however mean ambient temperature lost its statistically significant correlation with death rates ($P = 0.32$ and 0.725, for days 14 and 28, respectively).

**DISCUSSION**

These results indicate that population median age significantly correlates with COVID-19 burden in each country, while mean ambient temperature shows significant inverse correlation in a univariate but not in a multivariate analysis. These findings are not surprising considering previous reports showing that COVID-19 case fatality rates are significantly higher in older people [16]. This result may be attributed to the age-related deterioration in inflammatory and immune responses and to co-morbidities, which predispose elderly individual to a more severe clinical injury by the COVID-19 infection [17]. We suggest that the cumulative number of both proven coronavirus cases and deaths per million residents are closely associated with the median age of the population in each country, so that countries with older populations experience significantly larger numbers of cases and deaths than countries with younger populations during the first month following the epidemic outbreak. A possible explanation for these findings may be that younger individuals are less vulnerable to this virus and therefore less likely to become sick and to transmit it to others. If more people in a certain population are younger, the overall spread of the disease may be slower, and it may even fade away before reaching older and more vulnerable individuals.
Meteorological variables can forecast global viral epidemic outbreaks with high correlations to actual data [18]. More specifically, ambient temperature and relative humidity seem to play a major role in the seasonal behavior of respiratory viruses [19]. Previous studies have shown that a warm ambience can reduce the ability of SARS and influenza viruses to spread [20,21]. Recently, some investigators reported that these factors may have a strong influence on COVID-19 transmission coefficient R value [18]. Moreover, they have been reported to affect total mortality rates from the viral outbreak [22]. We found mean ambient temperature to be inversely correlated with the number of deaths using a univariate analysis although not with the number of cases related to the COVID-19 pandemic. Nonetheless, after a multivariate logistic regression analysis this correlation lost its statistical significance as it was outweighed by the population median age. These data agree with a previously reported study by Yao et al. [23] that found no correlation between COVID-19 transmission and ambient temperature or UV radiation in China. According to our study, it seems that advanced population median age is a substantially more significant risk factor for morbidity and mortality from this pandemic than low ambient temperature.

As the COVID-19 pandemic progresses, epidemiological data are required to guide global intervention strategies. The data from the current study may be valuable for both national and international health systems in planning policies and allocating resources for combating this global hazard. The vast majority of developed countries who have experienced viral outbreaks implemented aggressive mitigation and control measures, including social distancing, quarantine, as well as general closure. These measures may reduce overall morbidity and mortality by flattening the curve and thus allow healthcare systems to cope better with the number of severely affected patients who need intensive medical care [24]. Unfortunately, while doing so they might also incur a substantial socioeconomic crisis which may eventually lead to high unemployment rates and economic recession. When inspecting global morbidity and mortality data from the COVID-19 pandemic, it becomes clear that not all countries have been affected equally. While some countries experienced large numbers of infections and deaths, others reported only small numbers of cases and even smaller numbers of deaths. While diagnostic, as well as mitigation and control strategies, certainly influenced the pandemic evolution in each country, other factors related to inherent differences between populations and geographical areas may also play a role. In the current study we showed that population median age has a significant influence upon morbidity and mortality rates from this pandemic so that countries with older populations are more severely affected than those with younger populations. If this paradigm is indeed true, it seems plausible that countries with older populations may require more aggressive mitigation and control strategies while those with substantially younger populations may benefit from less radical policies which would carry milder socioeconomic consequences.

Of interest, some countries (such as Japan, Taiwan, and South Korea) were found to have low COVID-19 morbidity and mortality rates despite relatively older populations. This may suggest the importance of other epidemiologic factors in the evolution and progression of this pandemic such as genetic predisposition, previous exposure to similar corona viruses (other than SARS-CoV-2) and population's behavior (e.g., wearing masks).

The current study has several limitations. Primarily, it is difficult to tell whether and to what extent differences in financial resources and strategies utilized to combat the COVID-19 pandemic may have affected morbidity and mortality rates in each country. Furthermore, one may argue that younger populations are more likely to be found in developing countries where birthrates are higher and life expectancy is lower as compared to developed countries [25]. Per definition, developing countries have lower gross domestic product (GDP) per capita and often...
less efficient health systems which may lead to lower coronavirus detection rates and therefore falsely lower numbers of cases and deaths related to this virus. While this argument is difficult to refute, it should be remembered that with less competent and more vulnerable health systems one would expect to see higher morbidity and mortality from this pandemic as the ability of these systems to cope with severe or life-threatening cases is suboptimal. Moreover, population's density is often higher and sanitary conditions less favorable in developing countries, which may also lead to higher infection and death rates.

CONCLUSIONS

Country population median age significantly correlates with COVID-19 pandemic burden while mean ambient temperature shows a significant inverse correlation in a univariate but not in a multivariate analysis. This explains why countries with older populations may suffer a heavier burden from this pandemic. This information may be valuable for health systems in planning strategies for combating this global health hazard.

Correspondence

Dr. A. Zilberlicht
Dept. of Obstetrics and Gynecology, Carmel Medical Center, Haifa 3436212, Israel
email: ariel.zilberlicht@gmail.com

References