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Vaccination and Mortality of Patients with a Novel Coronavirus Infection (COVID-19): A Global Approach

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Aim. The aim is to study the correlation between the vaccination rate (VR) and mortality rate of patients with COVID-19 (MpCOV).
Methods. The countries with gross domestic product per capita corrected for purchasing power parity (GDP PPP) over $ 10,000 were selected for an ecologic study. The city-states and countries with a population of <1,000,000 were excluded. The number of patients who died from COVID-19 within a week was divided by the number of patients diagnosed with COVID-19 within a week 20 days earlier to calculate MpCOV.
Results. We included 85 countries. VR (r = –0.604; p < 0.001) and GDPpcPPP level (r = –0.542; p < 0.001) significantly correlate with MpCOV. Multivariate analysis showed that VR (p = 0.001), rather than GDPpcPPP level (p = 0.202), is an independent determinant of MpCOV. There was no significant difference in MpCOV between groups of countries with VR <20 % and 20–39 % (1.96 [1.21; 4.67] vs. 1.96 [1.01; 3.36] %; p = 0.464). MpCOV was higher in countries where VR were lower when groups of countries with VR of 20–39 %, 40–59 %, 60–79 %, and ≥80 % were compared (1.96 [1.01; 3.36] vs. 1.11 [0.76; 1.64] vs. 0.50 [0.39; 1.00] vs. 0.16 [0.10; 0.21]; p = 0.003; p = 0.020, and p = 0.008).
Conclusions. An increase in VR correlates with a decrease in MpCOV.
Keywords: vaccination, SARS-CoV-2, COVID-19, mortality, vaccination rate
Conflict of interest: the authors declare no conflict of interest.

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Вакцинация и смертность больных COVID-19: глобальный подход

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Цель исследования. Изучить корреляцию между охватом вакцинацией от COVID-19 и смертностью больных этой инфекцией на национальном уровне.
Материалы и методы. В данное экологическое исследование были включены страны с величиной валового внутреннего продукта (ВВП), рассчитанного по паритету покупательной способности на душу населения (ВВПдН) выше 10 000 $ на человека. Города-государства, а также малые страны с населением менее 1 млн человек были исключены. Смертность больных COVID-19 была рассчитана как отношение количества пациентов, умерших от COVID-19 в течение недели, к количеству зарегистрированных случаев этой инфекции в течение недели, которая началась за 20 дней до первого дня недели учета смертей.
Результаты. Было включено 85 стран. Охват вакцинацией (r = –0,604; p < 0,001) и уровень ВВП (r = –0,542; p < 0,001) значимо коррелировали со значениями смертности больных COVID-19. Многофакторный анализ показал, что охват вакцинацией (p = 0,001), но не уровень ВВП (p = 0,202) является независимым предиктором исхода COVID-19. Не было значимой разницы в смертности больных COVID-19 между группами стран с охватом вакцинацией менее 20 и 20–39 % (1,96 [1,21; 4,67] vs. 1,96 [1,01; 3,36] %; p = 0,464). Смертности

больных COVID-19 была выше в группах стран с меньшим охватом вакцинацией, когда сравнивали страны с охватом вакцинацией в 20–39, 40–59, 60–79 и ≥80 % (1,96 [1,01; 3,36] vs. 1,11 [0,76; 1,64] vs. 0,50 [0,39; 1,00] vs. 0,16 [0,10; 0,21]; p = 0,003; p = 0,020 и p = 0,008).
Выводы. Увеличение охвата вакцинацией от COVID-19 коррелирует со снижением смертности больных COVID-19 на национальном уровне.
Ключевые слова: вакцинация, SARS-CoV-2, COVID-19, смертность, охват вакцинацией
Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

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Introduction

The new coronavirus infection (COVID-19) has become a major global health challenge in the 21st century. Despite the encouraging results obtained in the initial clinical trials of vaccines against it [1–3], the change of its dominant variant to the new strains led to a decrease in the ability of currently used vaccines to prevent the development of COVID-19 [4]. However, experts continue to insist that vaccination is useful and necessary, as it continues to protect against severe forms of this infection and death [4].

There is a pronounced unevenness in the coverage of vaccination among different countries: more than 80 % of the population is vaccinated in some of them and less than 10 % of the population has got the vaccine in others. If vaccination protects from severe forms of COVID-19 and death, then mortality rate of patients with COVID-19 (MpCOV) must be lower in countries with larger vaccination rate. Testing this hypothesis was the aim of our study.

Methods

An ecologic study was conducted. We analyzed the number of COVID-19 cases in a week (September 9–15, 2021) in different countries. Since, according to our research, the median time from the onset of COVID-19 to death was 20 days [5, 6], we also analyzed how many people in these countries died from COVID-19 in a week from September 29 to October 5, 2021. Thus, we calculated MpCOV in different countries by dividing the number of deaths from COVID-19 in the period from September 29 to October 5, 2021 by the number of COVID-19 cases detected during the period from September 9 to 15, 2021.

We correlated the obtained MpCOV with the percentage of vaccinated population (vaccination rate) at the end of September 2021, as well as with the level of country economic development (the level of gross domestic product per capita calculated using purchasing power parity (GDPpcPPP) for 2020), which can also influence in the effectiveness of COVID-19 treatment and mortality from COVID-19.

As a source of information on the number of COVID-19 cases, deaths and vaccinations, we used Yandex service (https://yandex.ru/covid19/stat/), which aggregates data from official sources in various countries.

The data on the GDPpcPPP of states were taken from the reference book of the International Monetary Fund.

Low-income countries (GDPpcPPP less than $10,000 per capita) were excluded, as the conditions of their health systems more likely determined mortality from COVID-19 than vaccination. We also excluded city-states and microstates (with a population of less than 1 million people), as their health systems also have features that can lead to biases.

We also excluded: countries with a pronounced unevenness in data reporting (less than 3 reports per week) in order to eliminate the associated bias; countries for which data were not presented on the analyzed service (Turkmenistan and Kosovo); and countries that had less than 200 cases of COVID-19 and did not have deaths from COVID-19 during the analyzed period, due to the impossibility of calculating MpCOV.

Results are presented as median [interquartile range]. The groups were compared out using Mann–Whitney test. Correlations between variables were computed using Spearman's rank method. Multivariate linear regression analysis was performed to estimate the effect of vaccination rate and GDPpcPPP on MpCOV. A $p \leq 0.050$ value was taken as the criterion for significance. Statistical calculations were performed using Statistica 10 (TIBCO Software, Palo Alto, CA).

Results

We included 85 countries (Figure 1).

MpCOV, vaccination rate and GDPpcPPP of the included countries were 1.08 [0.55; 2.08] %, 49.0 [28.5; 63.4] %, and $27,717 [14,916; 42,248] per capita, respectively.

Univariate analysis showed that both vaccination rates ($r = -0.604$; $p < 0.001$; Figure 2A) and GDPpcPPP levels ($r = -0.542$; $p < 0.001$; Figure 2B) significantly correlate with MpCOV. A significant correlation was also found between the vaccination rate and the level of GDPpcPPP ($r = 0.656$; $p < 0.001$; Figure 2C).

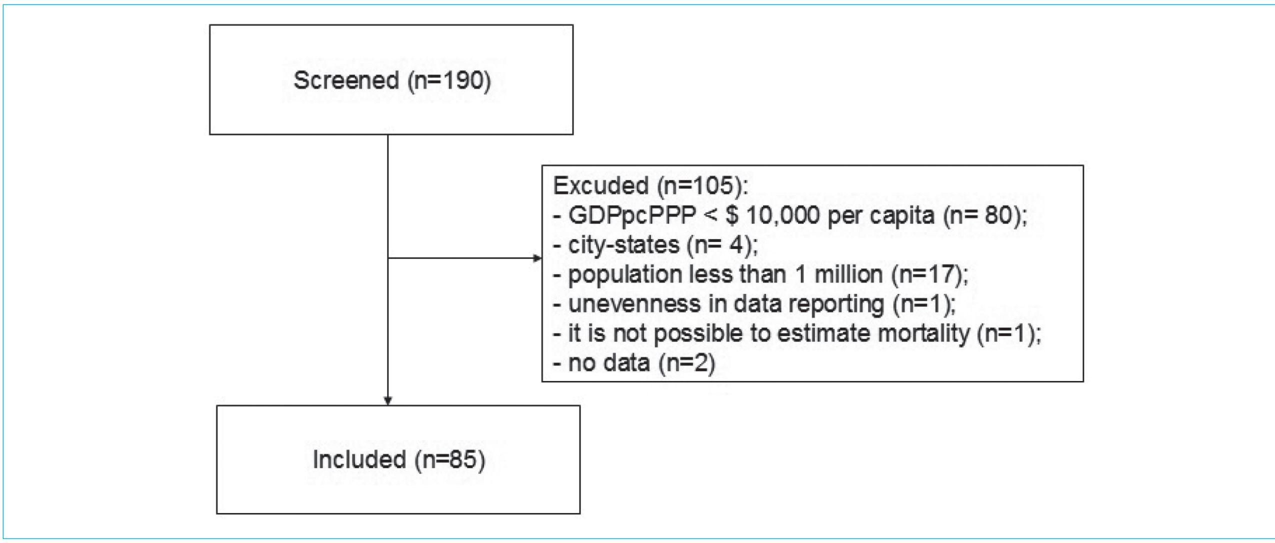

Fig. 1. Flowchart of the study. GDPpcPPP — gross domestic product per capita calculated using purchasing power parity

However, multivariate analysis showed that vaccination rate (p = 0.001; beta= –0.426 [95 % CI: (–0.188) – (–0.663)]), rather than GDPpcPPP level (p = 0.202), is an independent determinant of MpCOV.

There was no significant difference in MpCOV between groups of countries in which less than 20 % (n = 14) and 20–39 % (n = 18) of the population were vaccinated. However, MpCOV was significantly lower in the group of countries where 40–59 % of the population were vaccinated (n = 26) compared to countries where 20–39 % of the population were vaccinated. The same was true for the groups of countries where 60–79 % (n = 22) and 40–59 % were vaccinated. The minimum MpCOV was in the group of countries where ≥80 % of the population was vaccinated (n = 5; Figure 3).

Among countries where less than 40 % of population were vaccinated (n = 32), there was no significant correlation between vaccination rates and MpCOV (p = 0.883). On the contrary, such a correlation was observed among countries where more than 40 % of the population were vaccinated (r = -0.489; p < 0.001; n = 53).

In order to minimize the potential influence of economic development on the mortality of COVID-19 patients, we divided the included countries into groups with moderate (GDPpcPPP = $10,000–19,999; n = 32), high (GDPpcPPP = $20,000–39,999; n = 26) and very high (GDPpcPPP ≥ $40,000; n = 27) incomes. There were no significant correlations between the level of GDPpcPPP on the one hand and MpCOV (p = 0.765, p = 0.996, p = 0.053, respectively) and vaccination rates (p = 0.073, p = 0.657, p = 0.143, respectively) on the other in all these groups.

However, there was a significant correlation between MpCOV and vaccination rates in high- and very high-income countries (r = -0.469, p = 0.016, and r = –0.536, p = 0.004, respectively), but not in moderate-income countries (p = 0.102).

Among moderate-, high- and very high-income countries, ones with vaccination rate less than 40 % of the population accounted for 71.9, 30.8 and 3.7 %, respectively.

Discussion

The results of clinical trials of vaccines against COVID-19 inspired optimism: the effectiveness was more than 90 % [1–3]. However, the change of the dominant strain to more contagious and associated with more severe forms delta variant disrupted the plans for an early victory over COVID-19. This strain was much less neutralized by antibodies that were produced after vaccination [7, 8], which led to a drop in vaccination efficiency [9]. In addition, there is information about the dangerous side effects of vaccines [10–15]. All this gave rise to a massive campaign against vaccination. In response, supporters of vaccination said that although the vaccine became to protect against infection less, it continues to protect against death. The concept of population (herd) immunity is also actively discussed. In this regard, it becomes important to assess the impact of vaccination on the MpCOV on a national level in order to assess the effect of population immunity on it.

MpCOV depends on many factors: the age and comorbidity structure of the population, treatment approaches, the condiciton of the health care system, and, as was assumed, vaccination rate.

Since the condition of the health care system is largely determined by the level of economic development, we used the latter indicator as an indirect substitute for the former.

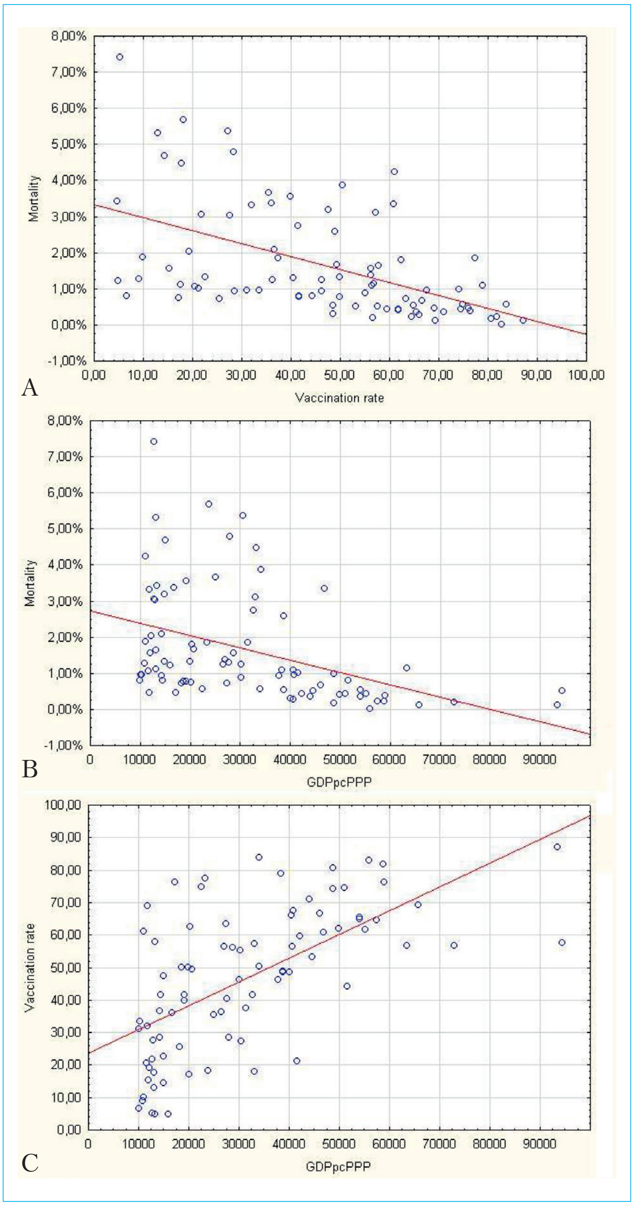

Fig. 2. Correlation between mortality rate (%) of patients with COVID-19 and vaccination rate (%) (A), between mortality rate (%) of patients with COVID-19 and gross domestic product per capita, adjusted for purchasing power parity (GDPpcPPP; $ per capita) (B), and between vaccination rate (%) and GDPpcPPP ($ per capita) (C)

In our study, we showed that MpCOV in different countries is inversely correlated with the vaccination rate in these countries. It was also shown that the latter factor depends on the level of economic development of countries. However, multivariate regression showed that vaccination rate itself rather than economic development is the main predictor of mortality rate in these patients.

Very interesting results were obtained from the analysis of subgroups. There was no significant effect of the vaccination rate on MpCOV in countries where less than 40 % of the population was vaccinated. After the vaccination rate reaches 40 %, there is a progressive decrease in MpCOV with an increase in former indicator. It seems that the effect of population immunity on protection against death of COVID-19 patients begins only with a vaccination rate of ~40 % and does not reach a plateau with an increase in vaccination.

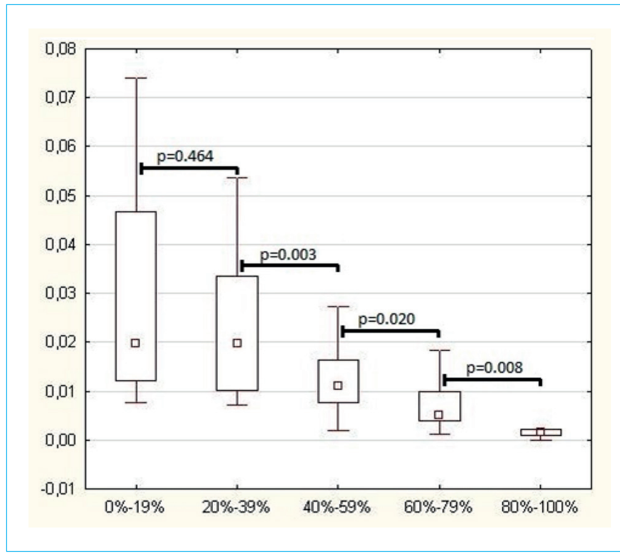

Fig. 3. Mortality rate of patients with COVID-19 in groups of countries in which 0–19, 20–39, 40–59, 60–79 and 80–100 % of the population are vaccinated

After analysis by subgroups depending on the income level, it was shown that there is no dependence MpCOV on the level of economic development within these groups, but the dependence of MpCOV on the vaccination rate was only in the groups of countries with high and very high incomes. This can be explained by the fact that most of countries in the moderate-income group had less than 40 % of the population vaccinated, and no effect of population immunity, as shown above, is among the countries with such low vaccination rates.

The strength of our study is that it is the first to describe the impact of vaccination on COVID-19 mortality at the national level and co-analysis of vaccination rate and GDPpcPPP was performed.

However, it has some limitations. We used secondary data provided by health authorities of different countries and which may be intentionally or unintentionally distorted for political purposes, due to the uneven availability of tests for COVID-19, as well as different approaches to determining the case of COVID-19 and death from COVID-19. Only a symptomatic cases with a positive polymerase chain reaction (PCR) to the causative agent of it are considered cases of COVID-19 in many countries. Asymptomatic carriers with positive PCR are also included in these cases in other countries. The cases of viral pneumonia with negative results PCR and a high degree of suspicion of COVID-19 are also included in COVID-19 cases in the third group of countries. Deaths from COVID-19 are considered in all patients who died with a positive PCR in many countries. However, the deaths from specific complications of COVID-19 (“cytokine storm”, massive lung damage, and others) are only counted for these cases in other countries.

Another limitation is related to the fact that we did not assess the age and comorbidity structure of the population and the effect of revaccination due to the impossibility of obtaining these data for all included countries.

However, we believe that these limitations did not affect the main conclusion of our study.

Conclusion

The vaccination rate is an independent factor in the reduction of MpCOV.

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