Impact of Tuberculosis Vaccination Policy (BCG) on Sars-Cov-2 Virulence and Potential Economic Effects

Claudiu George Bocean
Catalina Soriana Sitnikov
Anca Antoaneta Vărzaru
University of Craiova, Romania
boceanclaudiu@yahoo.com
inastinikov@yahoo.com
varzaruanca@yahoo.com

Abstract

The SARS-Cov-2 virus that generates Covid-19 has generated an unprecedented medical crisis leading to more than 100,000 deaths worldwide in less than four months since its identification. The spreading pattern of the virus in the world countries is asymmetrical, with many factors that influence its pattern. Previous research have shown that BCG vaccination with can induce non-specific protective effects against not only bacterial but also viral infections. This article aims to carry out a correlation analysis between the variables that define BCG vaccination policies and those that define the spread and deaths caused by Covid-19 and to study the spread pattern. In almost 55 days from the outbreak of the epidemic, a clear differentiation can be observed among the clusters of countries defined according to the BCG vaccination policy concerning disease rates and mortality, which leads us to the conclusion that the BCG vaccine generated non-specific immune protection.

Key words: BCG vaccination; SARS-CoV-2; Covid-19; viral infections; potential economic effects
J.E.L. classification: I15.

1. Introduction

Starting from January in China, and February and March worldwide, the SARS-CoV-2 (which produces COVID-19) has devastated medical systems and especially most countries' economies, but the effects at country level are strongly differentiated. In addition to other reasons that cause a significant differentiation among countries (average age of the population, health status of the population, strict and rapid measures of isolation, national culture regarding the protection against contagious diseases, the quality of health care systems, the quality of the medical act, the economic development degree, the geographical isolation degree etc.) a causal factor that drew the attention of many researchers was how each country carries out the vaccination programs and in particular the vaccination with the BCG vaccine.

2. Theoretical background

The BCG vaccine has been used for nearly a century in tuberculosis prophylaxis, with evidence that the vaccine facilitates increased resistance to a number of diseases and pathogens that are unrelated to the tuberculosis-producing Koch bacillus, also developing effects on autoimmune and inflammatory diseases (Moorlag et al., 2019; Shet et al., 2020; Hegarty et al., 2020). Although the BCG vaccine does not show direct antiviral action, it participates in strengthening the immune system, so that the effects of many viral infections are significantly reduced (Sharquie, 2020).

The idea that vaccination programs among children and, in particular BCG vaccine, appeared in the scientific environment due to the low incidence of SARS-CoV-2 virus among children. Samar and Salem suggest that bystander immunity induced after vaccination of children from 1-8 years may stimulate immunity to SARS-CoV-2, recommending the use of either one or a combination of vaccines to protect high-risk groups from serious complications associated with COVID-195 (Samar and Salem, 2020).

Several researchers from Johns Hopkins Bloomberg School of Public Health (Shet et al., 2020) built a simple linear regression model to evaluate the association between BCG vaccination and mortality attributed to COVID-19. They concluded that the mortality attributed to COVID-19 in countries with BCG vaccination policies was 5.8 times lower than in countries without BCG vaccination programs.

For the same purpose, we set out to carry out a correlation analysis between BCG vaccination policies and the spread of SARS-CoV-2 and deaths caused by Covid-19, in order to identify the spread pattern on country clusters, at the European Economic Area level.

3. Research methodology

In order to carry out a cluster and correlative analysis of the data, we have collected data on the vaccination mode and the spread of SARS-CoV-2 and deaths caused by Covid-19 from two sources accessed on April 9, 2020 and April 23, 2020: European Center for Disease Prevention and Control (ECDC) (ECDC, 2020) and Worldometer (Worldometer, 2020). The study included 31 countries from the European Economic Area, in order to ensure data homogeneity and a smaller differentiation of the national culture type regarding the protection against contagious diseases. Based on the data collected from ECDC, we proceeded to the distribution of the 31 countries on 3 clusters. The first cluster includes countries that have BCG vaccination programs for all children at birth. The second cluster includes countries that have BCG vaccination programs only for certain high-risk groups (such as immigrants from countries with high incidence of tuberculosis). The third cluster includes countries that do not currently have BCG vaccination programs. These clusters were associated with the data collected by Worldometer on April 9, 2020 and April 23, 2020 concerning the spread of SARS-CoV-2 and deaths caused by Covid-19 and we conducted a comparative and correlational analysis.

4. Results

Starting from the data obtained from Worldometer for the countries selected in the study we performed an analysis on the three clusters, calculating the correlation between the distribution on clusters and three indicators that illustrate the spread of SARS-CoV-2 and deaths caused by Covid-19: total cases in one million population, identified after testing, total deaths in one million population, death rate (calculated as a ratio between the total number of deaths reported as being caused by Covid-19 and the total number of cases identified after testing). Following the correlations calculus, we could find a strong association between the distribution on the clusters that characterize the BCG vaccination policy and the indicators that characterize the spread of SARS-CoV-2 and deaths caused by Covid-19. For data collected on April 9, 2020 the Pearson correlation coefficients of the BCG cluster variable with others variables are 0.580 (for the variable -total cases in one million population), 0.561 (for the variable - total deaths in one million population), and 0.377 (for the variable - death rate). For data collected on April 23, 2020 the Pearson correlation coefficients of the BCG cluster variable with others variables are 0.548 (for the variable -total cases in one million population), 0.495 (for the variable - total deaths in one million population), and 0.275 (for the variable - death rate). It can be seen that the calculated correlations remain significant over the measured time interval.

The lower correlation with the death rate variable is also determined by the fact that the total number of cases identified after the test is not equal to the number of the contaminated persons, due to the reduced and differentiated testing capacity of the countries included in the study and the multiple asymptomatic cases. In the comparative analysis we grouped the selected countries into

three clusters. In nine of the countries the general BCG vaccination of the population is recommended. Eight of the countries have not defined BCG vaccination policies, while 14 countries have BCG vaccination programs only for certain groups considered at risk. Illness and mortality rates differ significantly within the three clusters, significant differences that cannot be explained only by other causes.

Table no. 1 Distribution on clusters that characterize the BCG vaccination policy and the indicators that characterize the spread and deaths caused by Covid-19

Country	BCG cluster	Total Cases/ 1 mil. population	Deaths/ 1 mil. population	Death rate	Total Cases/ 1 mil. population	Deaths/ 1 mil. population	Death rate
		April 9, 2020			April 23, 2020		
Cluster 1 - No vaccination schedule							
Iceland	3	4829	18	0.4	5243	29	0.6
Spain	3	3261	326	10.0	4556	474	10.4
Italy	3	2375	302	12.7	3142	423	13.4
Belgium	3	2156	218	10.1	3693	560	15.2
Austria	3	1471	33	2.2	1666	58	3.5
Germany	3	1379	29	2.1	1805	64	3.5
Netherlands	3	1270	140	11.0	2085	244	11.7
Denmark	3	973	41	4.2	1394	68	4.9
Average measures		***2214***	***138***	***6.6***	***2948***	***240***	***7.9***
Cluster 2 - Vaccination recommended for specific groups only							
Luxembourg	2	4976	83	1.7	5855	133	2.3
Liechtenstein	2	2046	26	1.3	2124	26	1.2
France	2	1804	187	10.4	2449	327	13.3
Portugal	2	1369	40	2.9	2192	80	3.7
Ireland	2	1331	53	4.0	3376	156	4.6
Norway	2	1137	20	1.8	1358	35	2.6
UK	2	959	118	12.3	2034	276	13.6
Sweden	2	905	79	8.7	1659	200	12.1
Malta	2	763	5	0.6	1008	7	0.7
Slovenia	2	541	21	3.8	657	38	5.8
Czech Republic	2	511	10	2.0	667	20	2.9
Finland	2	470	8	1.6	773	31	4.0
Cyprus	2	467	8	1.8	658	11	1.6
Greece	2	188	8	4.5	236	12	5.1
Average measures		***1248***	***48***	***4.1***	***1789***	***96***	***5.3***
Cluster 3 - Vaccination recommended for entire population							
Estonia	1	910	18	2.0	1200	34	2.8
Lithuania	1	351	6	1.7	514	14	2.7
Croatia	1	343	5	1.4	483	12	2.5
Latvia	1	312	2	0.5	412	6	1.4
Romania	1	270	13	4.8	525	28	5.4
Poland	1	147	5	3.1	278	12	4.3
Slovakia	1	128	0.4	0.3	243	3	1.1
Hungary	1	101	7	6.7	236	25	10.5
Bulgaria	1	89	3	3.9	158	7	4.7
Average measures		***386***	***10***	***2.8***	***486***	***16***	***3.8***

Source: Calculations based on ECDC (2020) and Worldometer (2020) data

From table 1 it can be observed that the average number of total cases identified in one million population is 5.7 times higher (on April 09, 2020) and 6.1 times higher (on April 23, 2020) in countries that do not have vaccination programs than those with general vaccination programs. Also, the average number of deaths in one million population is 13.7 times higher (on April 09, 2020) and 14.3 times higher (on April 23, 2020) in countries that do not have vaccination programs than those with general vaccination programs. Countries from cluster 2 with BCG vaccination programs only for certain high risk groups are in an average position depending on the extension degree of these programs. Some of the countries had general vaccination programs, but they dropped them.

5. Discussions

In almost 40 days from the outbreak of the epidemic in all the countries from the European Economic Area, a clear differentiation can be observed among the clusters of countries defined according to the BCG vaccination policy in terms of disease and mortality rates, which leads us to the conclusion that the BCG vaccine generated a nonspecific immune protection effect against SARS-CoV-2 infection. The most affected are, in particular, the countries from western and southern Europe, developed countries with a solid health system, which will suffer significant human and economic losses. A dose of BCG vaccine costs between 2 and 3 dollars, which means that with a low cost of mass immunization with an improved variant of the BCG vaccine, many human life losses and potential economic losses can be prevented.

The comparative and correlational analysis undertaken by us provides illustrative information, which provides sufficient statistical evidence to determine the mobilization of resources in the field of medical research to study the effects of the BCG vaccine on the impact of COVID-19 among the population. In our opinion, it is firstly necessary to increase the immunity of the population as quickly as possible to cope with COVID-19 disease, with the help of a variant of the BCG vaccine, whose efficacy and safety have already been tested. This will allow sufficient time for medical researchers to develop a specific vaccine for SARS-CoV-2, as well as effective antiviral drugs to fight the pandemic.

Researchers predict the occurrence of a vaccine against SARS-CoV-2 in at least 12-18 months. Meanwhile, recomposition of existing and safe vaccines that induce non-specific immune benefits may be an additional tool. There is strong epidemiological evidence that BCG existing vaccines induce non-specific benefits by reducing mortality in the case of viral infections. We believe that, while developing a specific SARS-Cov-2 vaccine, it is necessary to carry out as quickly as possible an assessment of the BCG vaccination efficacy in fighting the serious effects of SARS-Cov-2, as a mean of strengthening the population immunity, and especially of the risk groups, which could lead to mitigating the effects of the current crisis (Hegarty et al., 2020).

6. Conclusions

Given its impact on reducing the incidence of respiratory viral infections, BCG vaccine use during the COVID-19 pandemic may prove beneficial. Starting from the conclusion that in countries that have benefited from general BCG vaccination programs, SARS-Cov-2 virulence is lower, producing fewer medium or severe cases, the use of the BCG vaccine may have an impact in reducing the incidence of respiratory viral infections if is used during the COVID-19 pandemic. Therefore, we believe that clinical trials should be conducted as quickly as possible to evaluate the potential beneficial effects of the vaccine in the fight against SARS-Cov-2. The economic losses generated by the COVID-19 pandemic, both direct of human lives, but especially the indirect caused by the lockdown declared by many countries, can be reduced through better management of the medical crisis, considering a 100 years old vaccine can bring a huge benefit..

7. References

- ECDC, 2020. *Tuberculosis: Recommended vaccinations.* European Centre for Disease Prevention and Control. [online]. Available at: <https://vaccine-schedule.ecdc.europa.eu/Scheduler/ByDisease?SelectedDiseaseId=14&SelectedCountryId ByDisease=-1> [Accessed 9 April 2020].
- Hegarty, P., Kamat, A., Zafirakis, H. and Dinardo, A., 2020. *BCG vaccination may be protective against Covid-19.* [online]. Available at: <https://www.researchgate.net/publication/340224580_BCG_vaccination_may_be_protective_against_Covid-19> [Accessed 6 April 2020].
- Moorlag S., Arts, R.J.W., van Crevel, R. and Netea M.G., 2019. Non-specific effects of BCG vaccine on viral infections. *Clinical Microbiology and Infection*, 25(12), pp.1473-1478.
- Samar, S. and Salem, M.L., 2020. The Mystery Behind Childhood Sparing by COVID-19. *International Journal of Biomedical Research*. 5(1), pp. 11-13.
- Sharquie, I.K., 2020. BCG is a Good Immunotherapeutic Agent for Viral and Autoimmune Diseases: Is it a New Weapon against Coronavirus (COVID-19)? *Electronic Journal of General Medicine*, 17(6):em229.
- Shet, A., Ray, D., Malavige, N., Santosham, M. and Bar-Zeev, N, 2020. *Differential COVID-19-attributable mortality and BCG vaccine use in countries.* [online]. Available at: <https://www.medrxiv.org/content/10.1101/2020.04.01.20049478v1> [Accessed 7 April 2020].
- Worldometer. 2020. *COVID-19, - Coronavirus Pandemic*. [online]. Available at: https://www.worldometers.info/coronavirus/#countries> [Accessed 9 April 2020].