



# The Open Microbiology Journal

Content list available at: <https://openmicrobiologyjournal.com>



## REVIEW ARTICLE

### Vaccination Schedules and COVID-19 Risk

Mohamed Farouk Allam<sup>1,\*</sup>, Fady Andraous<sup>1</sup> and Ghada Essam El-Din Amin<sup>1</sup>

<sup>1</sup>Department of Family Medicine, Faculty of Medicine, Ain Shams University, El-Abaseya, Egypt

#### Abstract:

A significant difference in the number of novel coronavirus 2019 (COVID-19) cases and mortality has been noted among different World Health Organization (WHO) regions and countries. We compared the vaccination schedules for 2 countries from WHO Europe Region (Italy and Spain) and 2 countries from WHO Regional Office for the Eastern Mediterranean (Iran and Egypt). Both Iran and Egypt included the Sabin vaccine as part of the obligatory vaccination programs; meanwhile, Italy and Spain used the Salk vaccine. Recently, Iran and Egypt added a single dose of the Salk vaccine to the 6-7 doses of Sabin vaccine because of the new evidence showing that the use of the Salk vaccine in conjunction with Sabin vaccine achieves better mucosal immunity. Italy and Spain used an acellular vaccine against pertussis. Meanwhile, Iran and Egypt used a whole-cell vaccine. Taking into consideration the lower number of deaths in Iran and Egypt compared to Italy and Spain, we could hypothesize that the whole-cell pertussis vaccine could have a cross-immunity against COVID-19. Further research is warranted to identify the main reasons for the lower number of COVID-19 cases and deaths in certain countries in order to control COVID-19.

**Keywords:** Coronavirus, COVID-19, Pertussis, BCG, Measles, Vaccine, Review.

#### Article History

Received: May 28, 2020

Revised: September 13, 2020

Accepted: September 16, 2020

#### 1. NON-SYSTEMATIC REVIEW

In December 2019, the Chinese health authorities declared an outbreak of the novel coronavirus 2019 (COVID-19). A significant difference in the number of COVID-19 cases and mortality has been noted among the different World Health Organization (WHO) regions and countries.

This discrepancy could be attributed to several factors such as prevalence of testing in a population, lack of reporting in some countries, the population demographics and particularly the number of elderly making up the population and finally, the vaccination schedule. Various vaccines were discussed in the literature to be possible protective measures against COVID-19 [1, 2].

Table 1 summarizes the vaccination schedules of 2 countries from WHO Europe Region (Italy and Spain) and 2 countries from WHO Regional Office for the Eastern Mediterranean (Iran and Egypt).

Recently, it was hypothesized that the BCG vaccine may potentially be protective against COVID-19, particularly in youth below the age of 18 [6, 7]. For instance, countries that do not include the BCG vaccine, such as Italy and Spain, have reported a large number of COVID-19 cases as well as deaths.

Spain included BCG vaccine in its routine vaccination program till the early 1980s [8]. However, Iran which includes BCG in its obligatory vaccination schedule has also reported a large number of cases of COVID-19. Of note, Wuhan (China), where this pandemic was first found, also includes the BCG vaccine in its routine vaccination schedule [9]. Therefore, the protective effect of BCG against COVID-19 may not correlate. From 12 April 2020 to date WHO has not confirmed if the BCG vaccine is protective against COVID-19 [10]. A recent cohort study of 5933 adults aged 35 to 41 years showed no statistically significant difference in the proportion of positive COVID-19 test results in the BCG-vaccinated group vs the unvaccinated group [11].

Both Iran and Egypt included the Sabin vaccine (live attenuated oral poliomyelitis vaccine) under the obligatory vaccination program; meanwhile, Italy and Spain used Salk vaccine (inactivated IM poliomyelitis vaccine). Sabin vaccine simulates natural infection because it induces both circulating antibodies and intestinal resistance. Thus it immunizes susceptible contacts through secondary spread. On the contrary, Salk vaccine gives only circulating antibodies [12, 13]. Recently, Iran and Egypt added a single dose of the Salk vaccine at 5 months of age to the 6-7 doses of Sabin vaccine because of the new evidence showing that the use of Salk vaccine in conjunction with Sabin vaccine achieves better mucosal immunity [4, 13].

\* Address correspondence to this author at Department of Family Medicine, Faculty of Medicine, Ain Shams University, Egypt; Tel/Fax: + (2) 011 43 55 99 46; E-mail: farouk.allam@med.asu.edu.eg

**Table 1. Comparison between 2 countries from who europe region and 2 countries from WHO regional office for the eastern mediterranean regarding COVID-19 data and vaccination schedules.**

Variable/Country	Italy	Spain	Iran	Egypt
Number of Population	60,454,503	46,756,254	84,074,125	102,474,273
Number of Cases	246,776	329,721	301,530	93,356
Number of Deaths	35,129	28,441	16,569	4,728
BCG Vaccine (Coverage Rate)	No (0%)	No (0%)	Yes (99%)	Yes (95%)
Poliomyelitis Vaccine (Coverage Rate)	Inactivated IM vaccine (95%)	Inactivated IM vaccine (93%)	Live attenuated oral vaccine (99%)	Live attenuated oral vaccine (95%)
Pertussis Vaccine (Coverage Rate)	Acellular (95%)	Acellular (93%)	Whole (99%)	Whole (95%)
Measles Vaccine (Coverage Rate)	2 Doses (89%)	2 Doses (94%)	2 Doses (99%)	2 Doses (94%)
Influenza Vaccine* (Coverage Rate)	1 Dose (53.1%)	1 Dose (54.9%)	Not included	Not included

\* Recommended for elderly people  $\geq 65$  years old.

These differences in the vaccination schedules among the 4 studied countries and the number of COVID-19 cases suggest that Sabin vaccine could have produced cross-immunity at the community level, explaining the comparative number of cases and deaths.

Italy and Spain used an acellular vaccine for infants and children against pertussis. Meanwhile, Iran and Egypt use a whole-cell vaccine. Taking into consideration the low number of deaths in Iran and Egypt compared to Italy and Spain, we could hypothesize that the whole-cell pertussis vaccine could have a cross-immunity against COVID-19. Of note, Pakistan, where the whole-cell pertussis vaccine is included in its routine vaccination schedule also reported a relatively high number of COVID-19 cases (total 277,402) but low number of deaths (total 5,924) [3]. This observation calls for further research of the possible protective effect of the whole-cell pertussis vaccine against COVID-19; especially that the pertussis vaccine has a weaning protective effect which could explain the lower number of COVID-19 cases before 18 years of age [14].

Reviewing the vaccination schedules of Italy, Spain, Iran and Egypt, it is noted that all 4 countries include 2 doses of measles vaccine in their obligatory vaccination schedules - thus the measles vaccine does not correlate with any protective effect against COVID-19.

Recently, it was suggested that prior immunity to influenza virus could raise immunity against COVID-19. This hypothesis is supported by the immunity for both viruses, and by the previous studies showing cross reactivity of immunity between influenza and coronavirus due to the similarity in their genetic structures [15]. Both Italy and Spain include seasonal influenza vaccine in their vaccination schedules for elderly people ( $\geq 65$  years old) and for patients with chronic diseases like diabetes mellitus and bronchial asthma [4, 5]. The Iranian and Egyptian health authorities recommend seasonal influenza vaccine for elderly people and healthcare workers; however the vaccine is not included in the obligatory vaccination schedules [4]. Although Iran had more confirmed cases of COVID-19 than Italy, the rate of mortality was much lower compared with Italy and Spain. Of note, the number of cases and deaths due to

COVID-19 according to the number of general populations in Iran and Egypt is much lower compared with number of cases and deaths in Italy and Spain [3, 4]. These comparative results could exclude that the seasonal influenza vaccine may be protective against COVID-19 or is effective for declining the severity among the cases.

Undoubtedly, this ecological study is important being the only raising hypothesis, thus new analytical studies are warranted to confirm the findings [16]. The correlation between the vaccination schedules and the number of COVID-19 cases or deaths may not be enough for demonstrating a clear causation, as the data for subgroup analyses is not available yet.

## CONCLUSION

In conclusion, the live attenuated oral poliomyelitis vaccine may potentially explain the relatively low number of cases and deaths due to COVID-19 in some countries, particularly countries from WHO Eastern Mediterranean Region. The whole-cell pertussis vaccine could also offer a protective effect against COVID-19, mainly for youths. Further research is warranted to identify the main reasons for the lower number of COVID-19 cases and deaths in certain countries in order to control the outbreak of COVID-19.

## CONSENT FOR PUBLICATION

Not applicable.

## FUNDING

None.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

## ACKNOWLEDGEMENTS

Declared none.

## REFERENCES

- [1] Cascella M, Rajnik M, Cuomo A, *et al.* Features, Evaluation and Treatment Coronavirus (COVID-19). StatPearls. Treasure Island, FL: StatPearls Publishing 2020. Updated 2020 Mar 20 Internet Available at: <https://www.ncbi.nlm.nih.gov/books/NBK554776/>
- [2] McIntosh K. Coronavirus disease 2019. Available at: <https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19>
- [3] Available at: <https://www.worldometers.info/coronavirus/>
- [4] WHO vaccine-preventable diseases: monitoring system 2019 . Available at: [https://apps.who.int/immunization\\_monitoring/global\\_summary/countries?countrycriteria%5Bcountry%5D%5B%5D=IRN&commit=OK](https://apps.who.int/immunization_monitoring/global_summary/countries?countrycriteria%5Bcountry%5D%5B%5D=IRN&commit=OK)
- [5] OECD Data. Influenza vaccination rates Available at: <https://data.oecd.org/healthcare/influenza-vaccination-rates.htm>
- [6] de Vrieze J. Can a century-old TB vaccine steel the immune system against the new coronavirus? *Science* 2020. [<http://dx.doi.org/10.1126/science.abb8297>]
- [7] Sharma AR, Batra G, Kumar M, *et al.* BCG as a game-changer to prevent the infection and severity of COVID-19 pandemic? *Allergol Immunopathol (Madr)* 2020; S0301-0546(20): 30106-. Available at: <https://www.mscbs.gob.es/profesionales/saludPublica/prevPromocion/PlanTuberculosis/docs/PlanTB2019.pdf>
- [9] Hu Y, Chen Y. Evaluating Childhood Vaccination Coverage of NIP Vaccines: Coverage Survey versus Zhejiang Provincial Immunization Information System. *Int J Environ Res Public Health* 2017; 14(7):E758 [<http://dx.doi.org/10.3390/ijerph14070758>] [PMID: 28696387]
- [10] WHO Scientific Brief 2020. Available at: [https://apps.who.int/iris/bitstream/handle/10665/331745/WHO-2019-nCoV-Sci\\_Brief-BCGvaccination-2020.1-eng.pdf?sequence=1&isAllowed=y](https://apps.who.int/iris/bitstream/handle/10665/331745/WHO-2019-nCoV-Sci_Brief-BCGvaccination-2020.1-eng.pdf?sequence=1&isAllowed=y)
- [11] Hamiel U, Kozler E, Youngster I. SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adults. *JAMA* 2020; 323(22): 2340-1. [<http://dx.doi.org/10.1001/jama.2020.8189>] [PMID: 32401274]
- [12] Bockstal V, Tiemessen MM, Achterberg R, *et al.* An inactivated poliovirus vaccine using Sabin strains produced on the serum-free PER.C6® cell culture platform is immunogenic and safe in a non-human primate model. *Vaccine* 2018; 36(46): 6979-87. [<http://dx.doi.org/10.1016/j.vaccine.2018.09.068>] [PMID: 30314910]
- [13] Parker EP, Molodecky NA, Pons-Salort M, O'Reilly KM, Grassly NC. Impact of inactivated poliovirus vaccine on mucosal immunity: implications for the polio eradication endgame. *Expert Rev Vaccines* 2015; 14(8): 1113-23. [<http://dx.doi.org/10.1586/14760584.2015.1052800>] [PMID: 26159938]
- [14] Schwartz KL, Kwong JC, Deeks SL, *et al.* Effectiveness of pertussis vaccination and duration of immunity. *CMAJ* 2016; 188(16): E399-406. [<http://dx.doi.org/10.1503/cmaj.160193>] [PMID: 27672225]
- [15] Salem ML, El-Hennawy D. The possible beneficial adjuvant effect of influenza vaccine to minimize the severity of COVID-19. *Med Hypotheses* 2020; 140:109752 [<http://dx.doi.org/10.1016/j.mehy.2020.109752>] [PMID: 32361099]
- [16] Susser M. The logic in ecological: I. The logic of analysis. *Am J Public Health* 1994; 84(5): 825-9. [<http://dx.doi.org/10.2105/AJPH.84.5.825>] [PMID: 8179056]

© 2020 Allam *et al.*

This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International Public License (CC-BY 4.0), a copy of which is available at: <https://creativecommons.org/licenses/by/4.0/legalcode>. This license permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.