

## ORIGINAL ARTICLE

## Does BCG vaccine prevent contract and severity of COVID-19 infection in India? A situational analysis

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<a href="#">Abstract</a>	<a href="#">Introduction</a>	<a href="#">Methodology</a>	<a href="#">Results</a>	<a href="#">Conclusion</a>	<a href="#">References</a>	<a href="#">Citation</a>	<a href="#">Tables / Figures</a>
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### Abstract

**Background:** The COVID-19 pandemic has created worldwide emergency with morbidities, mortality and panic. The BCG vaccine, usually given to prevent childhood tuberculosis, surfaced as an option as suggested by some ecological observations. However, some others studies could not establish and explain the protective effects of BCG vaccination against COVID-19 pandemic. India is one country with high BCG vaccination coverage and is among the countries with lowest COVID-19 case fatality rate. **Aims and Objectives:** We examine the relationship between the BCG coverage and COVID-19 burden in various states/UTs of India. **Materials and methods:** The information on BCG coverage and morbidity and mortality of COVID-19 was obtained from NFHS and [www.covid19India.org](http://www.covid19India.org) respectively. **Results:** The analysis suggested very weak positive relationship of BCG coverage with cases and deaths due to COVID-19. Moderate positive relationship was observed between BCG coverage and COVID-19 case fatality rate even after adjusting for health system performance. **Conclusion:** The conclusion of the study is against the role of BCG vaccination in containing the COVID-19 pandemic. The positive correlation which is not significant may be spurious and affected by many confounding factors like co-morbid conditions, testing strategies, population level immunity for other viral infections etc. Hence, the states and UTs should not be complacent by the hypothesized role of BCG vaccine in COVID-19 control. Rather, they should continue with the principles of social distancing, contact tracing, treating and surveillance of COVID-19.

### Keywords

COVID-19; SARS Cov-2; Pandemics; BCG Vaccine; Delivery of Health Care

### Introduction

The Coronavirus disease (COVID-19) is an infectious disease caused by the novel corona virus named as SARS-CoV-2. The COVID-19 pandemic originated in the city of Wuhan; the capital of Hubei province of China in December 2019 has emerged as the major public health crisis in 2020(1). The pandemic has spread to more than 200 countries with US followed by India and Brazil the

worst affected countries. As of October 2020, SARS-CoV-2 has infected 40,661,005 patients, with 1,123,180 deaths across 215 countries. India has also reported 76,49,102 COVID-19 cases and 1,19, 536 deaths during the same time period. Though majority of the individuals infected with SARS CoV-2 are asymptomatic, a low but significant proportion of infected persons have developed severe disease leading to death(2).

The impact of COVID-19 varied across countries around the globe. The empirical data has shown that some of the developed countries have reported high number of cases per million population and high case fatality rate despite imposing high-level mitigation strategies and stringent containment measures. Hence, the researchers around the world have reviewed the role of cultural norms, health infrastructure and health policies of different countries to identify the possible factors making difference in infections rate and death rate across the countries. Few ecological studies have suggested the possible role of BCG vaccination in protecting against the COVID-19(3–9). National immunization policy in some countries (Japan, South Korea, India and few others) has mandatory BCG vaccination while in several other countries (Italy, US and other developed countries) it has not(10). However, there is no consistent findings across studies reporting the possible role of BCG vaccination in protecting against the COVID-19. Few ecological studies have reported lower COVID-19 morbidity and mortality in countries with mandatory BCG vaccination during childhood compared to other countries which don't (6,11,12). However, few other studies could not establish such findings(13,14). India has got very low mortality from COVID-19 as compared to western countries(15). According to MoHFW, GoI the COVID-19 CFR in India is 1.49 at the end of October 2020. India has universal BCG vaccination policy for infants. However, the CFR varied across the states and union territories (UTs) in India.

### Aim & Objective

To study the relationship between the BCG coverage and severity of COVID-19 across states and UTs in India.

### Material & Methods

This explorative ecological observational study was carried during the month of October, 2020. We collected the state and UT wise BCG coverage information from the National Family Health Survey (NFHS) – 2, NFHS-3 and NFHS-4 reports(16). The information on cumulative COVID-19 cases and deaths was obtained from [www.covid19India.org](http://www.covid19India.org). The information was collected on October 23, 2020. Health infrastructure and health system performance can influence the BCG vaccination coverage as well as the COVID-19 infections and deaths. Infant mortality rate is considered as the proxy indicator for health infrastructure and health system performance(17). The information on IMR was collected from the Sample Registration System (SRS) March 2020 report(18). The information collected was entered in Microsoft Excel and statistical analysis was performed using SPSS version 20. The number of COVID-19 deaths and CFR were taken as proxy for severity of COVID-19. The case fatality rate was calculated by the following formula

$$CFR = \left( \frac{\text{total number of COVID-19 deaths}}{\text{total number of COVID-19 infections}} \right) * 100$$

Person correlation was performed to assess the correlation between BCG vaccination coverage and severity of COVID-19. The confounding effect of health infrastructure and health system performance (IMR) was nullified by performing partial Pearson correlation analysis. The correlation category [negligible or low,  $r < 0.5$ ; moderate,  $r = 0.5 - 0.7$ ; high,  $r > 0.7$ ] was used to report the correlation between BCG vaccination coverage and severity of COVID-19 in India(19). A p value of  $< 0.05$  was considered statistically significant.

The information was collected from reports and website available in public domain and involved statistical analysis of secondary data. Hence, permission from ethics committee is not required.

### Results

The [Table 1](#) shows the information on COVID-19 status in India as on 22nd October 2020. Maharashtra reported the highest number of cases (16,25,179) and deaths (42831) due to COVID-19. Mizoram reported the lowest number of cases (2359) and deaths (0) due to COVID-19. The CFR in India was calculated to be 1.51% as on 22nd October 2020. The median CFR was calculated to be 1.24% (Range: 0 to 3.14). Mizoram was found to have zero CFR as no death due to COVID-19 was reported as of 22nd October 2020. Punjab was found to have highest CFR (3.14%) followed by Maharashtra (2.64%) related COVID-19. The BCG vaccination coverage in India was recorded to be 91.9% (NFHS-4), 88% (NFHS-3) and 88.7% (NFHS-2). The highest BCG vaccination coverage was recorded by Goa (99.2%), Tamil Nadu (99.5%) and Goa (100%) during NFHS2, NFHS-3 and NFHS-4 survey respectively. The lowest BCG vaccination coverage was recorded by Bihar (37.7%), Nagaland (46.30%) and Nagaland (68.10%) during NFHS2, NFHS-3 and NFHS-4 survey respectively. The IMR in India is 32 per 1000 livebirths (SRS 2020). The highest (48) and lowest (4) IMR was reported from Madhya Pradesh and Nagaland respectively.

[Table 2](#) shows the correlation and partial correlation of BCG vaccination coverage with number of COVID-19 related cases, deaths and CFR. BCG coverage was not found to be correlated with COVID-19 related cases and deaths even after controlling the influence of status of health care delivery system (proxy given by IMR). However, BCG coverage was found to have low and positive correlation with COVID-19 CFR even after controlling the influence of status of health care delivery system ( $r=0.458$ ,  $p \text{ value}=0.008$ ). The correlation of BCG coverage and COVID-19 CFR was found to be statistically significant. The positive correlation of BCG coverage and COVID-19 CFR is also depicted in [Figure 1](#) (NFHS-3) and [Figure 2](#) (NFHS-2).

### Discussion

BCG vaccination is given to prevent childhood tuberculosis. Apart from giving protection against tuberculosis, the BCG is also implicated in providing non-

specific effects on various other infections especially the respiratory pathogens(20). However, the non-specific effects were not long lasting and protects for about 5-10 years till adulthood (21). The role of BCG vaccination in reducing burden of COVID-19 is still mystifying. Contrasting evidences have been reported by different studies on role of BCG vaccination coverage in reducing burden of COVID-19 in India.

Similar to our study, a study from Israel has reported no role of BCG in reducing burden of COVID-19. The study had analysed the development of COVID-19 among Israeli population borne during 1980s whose BCG vaccinations status was known(13). Similarly, Meena et al from India also could not establish the correlation between BCG vaccination coverage and COVID-19 burden across the countries in the world(14). A systematic review of all the published literature also could not find any solid evidence to recommend BCG vaccination for protection against COVID-19(22).

Our study failed to support the role of BCG vaccination (coverage) in reducing the burden of COVID-19. However, several ecological studies have reported the protective nature of BCG vaccination against COVID-19. Jain et al have attributed low COVID-19 burden in South Asian countries to mandatory BCG vaccination policy(15). Ebina et al reported the protective role of universal childhood BCG vaccination policy in low COVID-19 mortality(23). Madan et al have reported that Higher TB incidence and BCG coverage were found to be associated with lesser incidence of COVID-19 and recommended further research into pathogenesis and immune response in COVID-19(24). However, most of the studies were observational and had not taken into consideration ecological differences, prevalence of co-morbid conditions, age structure of population and testing strategies.

The finding of studies reporting protective role of BCG vaccination policy could be coincidental. Many of the studies have analysed the presence or absence of mandatory BCG vaccination policy(25). Many of the countries with mandatory BCG vaccination policy have BCG coverage of 10-15%. These studies might have missed the confounding effects of factors like testing strategy, travel restrictions etc. This raises the validity of such finding and points towards alternative explanation(21).

Our analysis showed that states and UTs with better BCG coverage have high COVID-19 CFR. This is against the widescale report of role of BCG vaccination in reducing the COVID-19 burden. This could be spurious and there could be other plausible explanations for high COVID-19 burden in states and UTs with BCG vaccination coverage in India.

## Conclusion

This study shows no inverse correlation between BCG coverage and COVID-19 burden in India. The earlier studies on cross country comparison showing protective

effect of BCG against COVID-19 may be spurious. Further research using randomized control design is needed to substantiated the facts. Till then, health system and the authority should not get complacent on management of COVID-19 pandemic and promote the practice of hygiene, social distancing, contact tracing, treating and surveillance of COVID-19 in India.

## Recommendation

The states and UTs should not be complacent by the earlier hypothesized role of BCG vaccine in COVID-19 control. Rather, they should continue with the principles of social distancing, contact tracing, treating and surveillance of COVID-19.

## Limitation of the study

The age wise information of the COVID-19 affected population is not available in any public domain. Though, BCG vaccination was stated along with universal immunization programme during 1970s, the state/UT wise vaccination coverage is available earliest in NFHS-2 report (1998-99). Hence, it was not possible to include the age specific COVID-19 affected population to correlate with BCG vaccination coverage in India. Since this is an ecological study the ecological fallacy cannot be rule out.

## Relevance of the study

This study adds to the body of the evidence that BCG vaccination status has no role in prevention of COVID-19 in adults.

## Authors Contribution

All authors contributed equally.

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**Tables**

**TABLE 1 CORRELATION AND PARTIAL CORRELATION OF BCG COVERAGE WITH COVID-19 RELATED CASES, DEATHS AND CFR IN INDIA**

State/UT	Case_22_20	Death_2_20	BCG coverage_NFHS2	BCG coverage_NFHS3	BCG coverage_NHFS4	CFR	IMR
Andhra Pradesh	796919	6524	90.20	92.40	97.20	0.82	29
Arunachal Pradesh	14077	32	54.20	57.70	70.90	0.23	37
Assam	203282	896	53.50	62.40	82.30	0.44	41
Bihar	209296	1026	37.70	64.70	91.60	0.49	32
Chandigarh	13848	212	NA	NA	95.90	1.53	13
Chhattisgarh	170130	1680	NA	84.60	98.40	0.99	41
Delhi	344318	6163	92.00	87.00	95.00	1.79	13
Goa	41586	564	99.20	96.80	100.00	1.36	7
Gujarat	164121	3670	84.70	86.40	87.90	2.24	28
Haryana	154495	1688	86.80	84.90	92.80	1.09	30
Himachal Pradesh	19844	279	94.60	97.20	94.80	1.41	19
India	<b>7763067</b>	<b>117365</b>	<b>71.60</b>	<b>78.10</b>	<b>91.90</b>	<b>1.51</b>	<b>32</b>
Jammu & Kashmir	90166	1412	85.60	90.90	95.60	1.57	22
Jharkhand	98610	859	NA	72.70	95.80	0.87	30
Karnataka	788551	10770	84.80	87.80	92.50	1.37	23
Kerala	369324	1256	96.20	96.30	98.10	0.34	7
Madhya Pradesh	164341	2842	64.90	80.50	91.60	1.73	48
Maharashtra	1625197	42831	93.70	95.30	90.00	2.64	19
Manipur	16621	127	71.00	80.00	91.20	0.76	11
Meghalaya	8677	77	46.10	65.90	85.90	0.89	33
Mizoram	2359	0	88.20	86.40	75.30	0.00	5
Nagaland	8296	21	46.10	46.30	68.10	0.25	4
Odisha	277887	1267	84.70	83.60	94.10	0.46	40
Puducherry	33832	582	NA	NA	99.90	1.72	11
Punjab	129693	4072	88.70	88.00	98.20	3.14	20
Rajasthan	180755	1800	53.90	68.50	88.20	1.00	37
Sikkim	3727	63	76.50	95.90	98.90	1.69	7
Tamil Nadu	700193	10825	98.60	99.50	94.90	1.55	15
Telangana	229001	1298	NA	NA	97.40	0.57	27

State/UT	Case_22_20	Death_2_20	BCG coverage_NFHS2	BCG coverage_NFHS3	BCG coverage_NHFS4	CFR	IMR
Tripura	30067	336	NA	81.10	82.40	1.12	27
Uttar Pradesh	463585	6790	57.50	61.00	87.60	1.46	43
Uttarakhand	59508	968	NA	83.50	92.80	1.63	31
West Bengal	337283	6308	76.50	90.10	97.50	1.87	22

NA: Not available, IMR: Infant Mortality Rate, CFR: Case Fatality Rate, NFHS: National family health survey

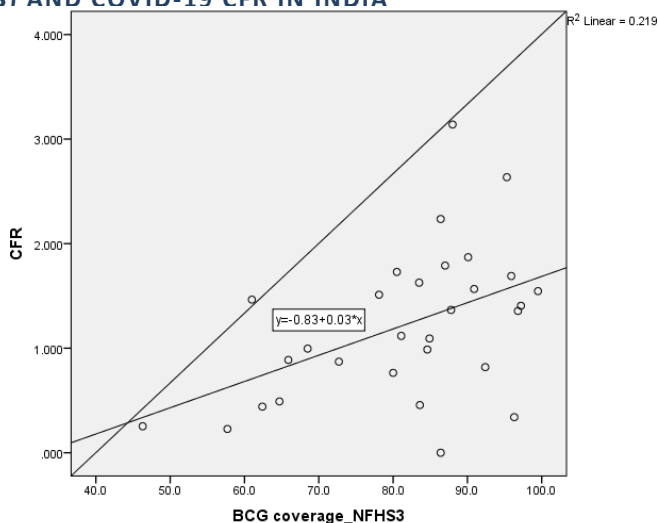
**TABLE 2 CORRELATION AND PARTIAL CORRELATION OF BCG COVERAGE WITH COVID-19 RELATED CASES, DEATHS AND CFR IN INDIA**

	Correlation co-efficient (NFHS2)	Correlation co-efficient (NFHS3)	Correlation co-efficient (NFHS4)	**Correlation co-efficient (NFHS2)	**Correlation co-efficient (NFHS3)	**Correlation co-efficient (NFHS4)
Cases	0.032	0.030	0.048	0.109	0.077	0.059
Death	0.061	0.058	0.035	0.127	0.096	0.042
CFR	0.398*	0.468*	0.461*	0.444*	0.498*	0.458*

\*\*partial correlation done for controlling the interaction of IMR \*P value <0.05

**Figures**

**FIGURE 1 SCATTERED PLOT SHOWING THE RELATIONSHIP BETWEEN BCG COVERAGE (NFHS-3) AND COVID-19 CFR IN INDIA**



**FIGURE 2 SCATTERED PLOT SHOWING THE RELATIONSHIP BETWEEN BCG COVERAGE (NFHS-2) AND COVID-19 CFR IN INDIA**

