Influence of Covid-19 Vaccination Coverage on Case Fatality Rate

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Research Article

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Abstract

**Background:** Recent evidence suggested that an increase in Covid-19 attack rate is correlated to increased case fatality rate (CFR) Covid-19 disease severity. An increase in the attack rate was suggested to lead to an increase in the viral load a proposed mechanism leading to this association. In this context, we conduct this study to look for the influence of decreasing the number of Covid-19 cases through vaccination on CFR.

**Material and methods:** We collected data concerning all countries/territories that implement Covid-19 vaccination at least for the last hundred days ending on 3d of April 2021. They were sixteen in number. Descriptive data analysis used included mean value, standard deviation, and graphical presentation by using Stem-Leaf charts and bar charts.

Inferential data analyses used included the One-Sample Kolmogorov-Smirnov (K-S) test and general linear model procedure (GLM).

**Results:** Findings showed that in a highly significant association the mean CFR decreased in countries with > 18 Covid-19 vaccine doses per 100 inhabitants.

**Conclusion:** Vaccination coverage may constitute another factor that determines temporal and spatial variances in CFR.

Introduction

Several factors were suggested to be associated with temporal and spatial variances in the Covid-19 case fatality rate (CFR, the ratio between the number of deaths and number of confirmed cases). Among these factors are comorbidity risk, demographic, socio-economic, and political variables, the age distribution of the community.[1]

COVID-19 vaccine has a substantial impact in reducing the incidence, hospitalizations, and deaths, especially among vulnerable individuals with comorbidities and risk factors associated with severe COVID-19. [2]

Important measures to monitor countries’ vaccination progress include measuring daily or 7- day average decrease in the number of cases, measuring daily or 7- day average decrease in the number of deaths, and measuring the number of confirmed COVID-19 hospital admissions.[3]

The positive association between the number of Covid-19 cases /million population inhabitants and CFR was raised in recent literature.[4][5][6] An increase in attack rate was suggested by these literature to be correlated to disease severity. The suggested hypothesis is that clustering of cases and viral overload lead to increased mortality rate and CFR.
We conduct this study to look for the influence of decreasing the number of Covid-19 cases through the Covid-19 vaccine on CFR. This will test such a hypothesis in another way since vaccination leads to a decrease in the number of cases.

**Material And Methods**

We selected all countries / territories that implement Covid-19 vaccination for at least the last hundred days ending on 3d of April 2021. They were sixteen in number. Publically available data derived concerning April 3, 2021, include total doses, vaccine doses / 100 people, total deaths, and accumulative Covid-19 cases. Data regarding total deaths and accumulative Covid-19 cases at the time when that country or territory initiated the Covid-19 vaccination was also derived accordingly. Data is included within the supplementary file.

CFRs were computed as total accumulative deaths divided by accumulative total cases x 100.

Statistical Analysis: The statistical data analysis approaches were used with (SPSS) ver. (21).

1. Descriptive data analysis which included mean value, standard deviation, and Graphical presentation by using Stem-Leaf charts and bar charts.
2. Inferential data analyses: These were used to accept or reject the statistical hypotheses, which included the following:
   
a. The One-Sample Kolmogorov-Smirnov (K-S) test.
b. General linear model procedure (GLM)

**Results And Findings**

Table (1): Normal distribution function test due to different groups in relation to CFR marker
### One-Sample Kolmogorov-Smirnov Test

| Groups                     | Test Statistic | At 12:37pm CEST, 03/04/2021 | At day 1 of starting vaccine |
|----------------------------|----------------|-----------------------------|-----------------------------|
| > 18 Doses / 100 people    | No.            | 9                           | 7                           |
| Kolmogorov-Smirnov Z       | 0.506          | 0.921                       |
| Asymp. Sig. (2-tailed)     | 0.96           | 0.364                       |
| C.S. (*)                   | NS             | NS                          |
| Test distribution of data follows Normal Shape |

| ≤ 18 Doses / 100 people    | No.            | 9                           | 7                           |
| Kolmogorov-Smirnov Z       | 0.566          | 0.749                       |
| Asymp. Sig. (2-tailed)     | 0.906          | 0.630                       |
| C.S. (*)                   | NS             | NS                          |

(*): NS: Non Sig. at P>0.05

Table (1) shows the normal distribution function (goodness of fit test). It represents a one-sample "Kolmogorov-Smirnov" test procedure comparing the observed cumulative distribution function for studied readings with a specified theoretical distribution, which proposed a normal shape (i.e. bell shape).

The results show that the distribution of studied readings regarding CFR marker distribution function in different locations. Since (P-value) is accounted at (P>0.05), this enabled us for applying the convention statistical methods (the parametrical methods).

Table (2): mean values, and standard deviation for the (CFR) marker, according to the assignable factors
In table (2) results shows that mean CFR is less in countries with > 18 vaccine doses / 100 people compared to countries ≤ 18 vaccine doses / 100 people.

We found that countries and territories that have a level of coverage of > 18 doses/ 100 person showed decreased mean CFR compared to the countries’ corresponding CFRs at the time of initiating the vaccine. The mean CFR was also decreased from 1.875 to 1.449. On the other hand, CFR for countries with a coverage rate of ≤ 18 doses per 100 inhabitants showed a lesser extent of decrease in mean CFR from 3.315 to 3.283.

Table (3) shows testing and analyzing the studied marker CFR with different sources of variation (SOV), such as the two different dose categories, countries starting vaccine time, interaction factor represented by applying the GLM of fixed effects model, and testing effectiveness of the other source of variations which were not included in the studied model (i.e. the intercept). In addition to that table (3) shows the (R^2), which represents percentage interpretation of the number of variations among the studied marker represented by the effectiveness of the assignable and interaction factors.

Results show significant differences accounted at P<0.05 related to studied vaccine dose categories /100 people, while no significant differences at P>0.05 were accounted for both the time that countries starting the vaccine, and the interaction factor. In addition to that, the intercept (the other sources of variations not included in the studied model) recorded highly significant effectiveness at P<0.01.

It was concluded that countries with a higher dose of Covid-19 vaccine indexed as >18 doses /100 people reported the lower CFR marker on April 3,2021 compared to day 1 of starting vaccine.

Table (3): General linear model of fixed effects model with interaction for testing Marginal mean values for different Source of Variation in a compact form
### Table 1: Analysis of Variance (ANOVA) Table

| Source of Variation          | Type III Sum of Squares | d.f. | Mean Square | F     | Sig.  | C.S. (*) |
|-----------------------------|-------------------------|------|-------------|-------|-------|----------|
| Intercept                   | 193.788                 | 1    | 193.788     | 45.91 | 0.000 | HS       |
| Vaccine dose category/100   | 21.109                  | 1    | 21.109      | 5.001 | 0.033 | S        |
| people                      |                         |      |             |       |       |          |
| Time starting the vaccine   | 0.412                   | 1    | 0.412       | 0.098 | 0.757 | NS       |
| Interaction                 | 0.306                   | 1    | 0.306       | 0.073 | 0.790 | NS       |
| Error                       | 53.71                   | 28   | 4.221       |       |       |          |
| Total                       | 2246.3                  | 32   |             |       |       |          |

R - Squared = 0.157

(*) HS: Highly Sig. at P<0.01; S: Sig. at P<0.05; NS: Non Sig. at P>0.05

### Discussion

The possible limitations in this study include: (1) The COVID-19 vaccine doses administered per 100 people may not equal the number of people that are vaccinated if the vaccine requires two doses, (2) Change in testing coverage within a country or across countries, (3) difficulty in estimating asymptomatic cases, (4) difficulty in estimation of actual Covid-19 deaths for a variety of reasons, (5) differed Covid-19 preventive approaches across countries and within the same country from time to time, (6) Covid-19 pandemic stage difference across countries, and (7) the contact-reducing interventions in place.

The severity of COVID-19 has been widely reported to be influenced by many factors e.g. age, sex, and underlying comorbidities.[7]

In one study vaccination reduced the overall attack rate from 9.0% to 4.6% over 300 days, which constitutes about a 50% reduction. Vaccination markedly reduced adverse outcomes, with non-ICU hospitalizations 63.5%, ICU hospitalizations 65.6%, and deaths decreasing by and 69.3% (95% CrI: 65.5% – 73.1%), respectively, across the same period.² It is clear that the relative reduction in mortality overcomes the relative reduction in morbidity. This might indicate that the attack rate has a role in mortality per se.

Furthermore, our findings support the recent evidence of the role of the number of accumulative cases within a certain community in determining CFR.⁴,⁵,⁶

It was suggested that an increase in fatality rate as the number of infected people increases is related to the overwhelming of the healthcare system.¹,⁸ This should be tested deeply as far as clusters of Covid-19 infections are associated with an increase in fatalities.⁹,¹⁰
Furthermore, although the number of hospital beds per 1000 people had a negative association with COVID mortality in certain countries including European countries, North America, Mexico, Brazil, Bolivia, and USA, these findings were not global. The number of hospital beds per 1000 people did not have such a negative association in many Asian countries (excluding Japan) and in African countries. [11] They displayed comparatively low mortality regardless of their limited bed capacity. The controversy in these findings might be biased by a high attack rate in some countries which makes these beds insufficient. On the other hand low attack in other countries probably led to low CFRs regardless of the bed capacity.

This study shed a light on the importance of Covid-19 vaccination coverage in decreasing CFR, an unmeasured factor before. Although vaccines might protect from the severe disease[12] which can decrease the CFR per se, the early detection of such findings in relatively low vaccination coverage together with the low number of infections that encountered in vaccinated patient. These infections if encountered in vaccinated patients are certainly very low and incomparable to infections in non-vaccinated patients.

### Conclusions

Covid-19 vaccination leads to a decrease in CFR in significant association possibly due to a decrease in AR.

The attack rate is a possible missed factor explains variances of CFRs among countries or among the same country at different times.

### Declarations

• Ethics approval and consent to participate: 'Not applicable
• Consent for publication: I certify that this study have not been previously published. The publisher has my permission to publish this study. With the consent, I give the publisher copyright license

Availability of data and materials: We used publically available data. Patients were not involved.

All data generated or analysed during this study are included in this published article [and its supplementary information files].
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