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COVID-19 in the Indian Territory of Lakshadweep – Role of MMR Vaccination in the Management of COVID-19 Pandemic

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Abstract

COVID-19 caused by SARS-CoV-2 virus, is a contagious disease which has spread across the entire world within one year and four months of its first appearance in Wuhan, China. Since then new mutated strains of SARS-CoV-2 have been detected in most of the countries including India; the first variant being detected in the United Kingdom (B 7.1.1). We had reported earlier that some regions of Indian Territory had minimal spread of COVID-19 in the population. Among them, one exception was territory of Lakshadweep which did not have even a single case of COVID-19 until December, 2020. However, the first case of COVID-19 emerged in Lakshadweep in January, 2021. The significance of spread of COVID-19 in the population which were previously immunized with MMR (Mumps Measles Rubella) vaccine with plausible role of MMR vaccination in management of COVID-19 has been evaluated in this article.
Keywords: COVID-19; SARS-CoV-2; Active case; Mortality; MMR vaccination; COVID-19 management.

1. Introduction

The spread of COVID-19, caused by SARS-CoV-2 virus, started during early part of 2020 across the world, and it continues to do so until now. In a series of papers, we demonstrated that implementation of 'Lockdown' at an early stage of the spread of COVID-19, across the country, had a profound effect on the spread of the disease in the Indian population (1-6). We reported that implementation of timely Lockdown slowed down the rate of COVID-19 and the slowdown was accompanied with an increase in doubling time of COVID-19. However, lower number of active cases of COVID-19 with lower mortality rate led us to postulate that there was prior immunity/vaccination history in the population, against related/unrelated pathogens that may have played a role in controlling its spread in the population.

In one of our recent studies, where data from a cluster of eight states were evaluated for status of COVID-19 in the population, it was observed that in all of the eight states evaluated there was a marked decrease in the number of confirmed COVID-19 cases following Lockdown, with one exception being the Union territory of Lakshadweep, where no confirmed cases of COVID-19 was recorded. The study revealed that all the states with confirmed cases of COVID-19 had very low number of active cases and mortality and there was a negative correlation between number of recovered individuals and number of active cases of COVID-19 [1].

However, the Territory of Lakshadweep which had no recorded cases of COVID-19 until December, 2020, recorded its first ever case of COVID-19 during the month of January, 2021. The plausible reason for this uncharacteristic resistance to development of COVID-19 for ten months and more since its first appearance in India was due to probable existence of strong underlying immunity in the population against SARS-CoV-2, the causative agent of COVID-19. The region of Lakshadweep has a history of vaccination against various pathogens which included Rubella, measles etc. One of the world's largest vaccination campaigns against measles and rubella was launched in February 2017 in Lakshadweep and some other states by the Government of India. Measles was a major childhood killer disease and rubella, known to cause congenital rubella syndrome (CRS), is responsible for irreversible birth defects. The aim of the largest nationwide vaccination campaign was to prevent above mentioned conditions with a safe and effective combined measles-rubella vaccine. Under the Measles-Rubella (MR) campaign, all children in the target age group (between 9 months and less than 15 years) were given a single shot of MR vaccination, irrespective of their previous measles/rubella vaccination status or measles/rubella disease status with the anticipation that the additional campaign dose would boost the already existing immunity in the subjects and thereby protect the entire community by eliminating transmission of measles and rubella. Some studies have now reported that antibody titre to MMR virus was significantly higher in those who had confirmed cases of COVID-19 [2]. This is first study undertaken to assess the status of COVID-19 in a population which was previously vaccinated against rubella, Mumps and measles.

2. Methods

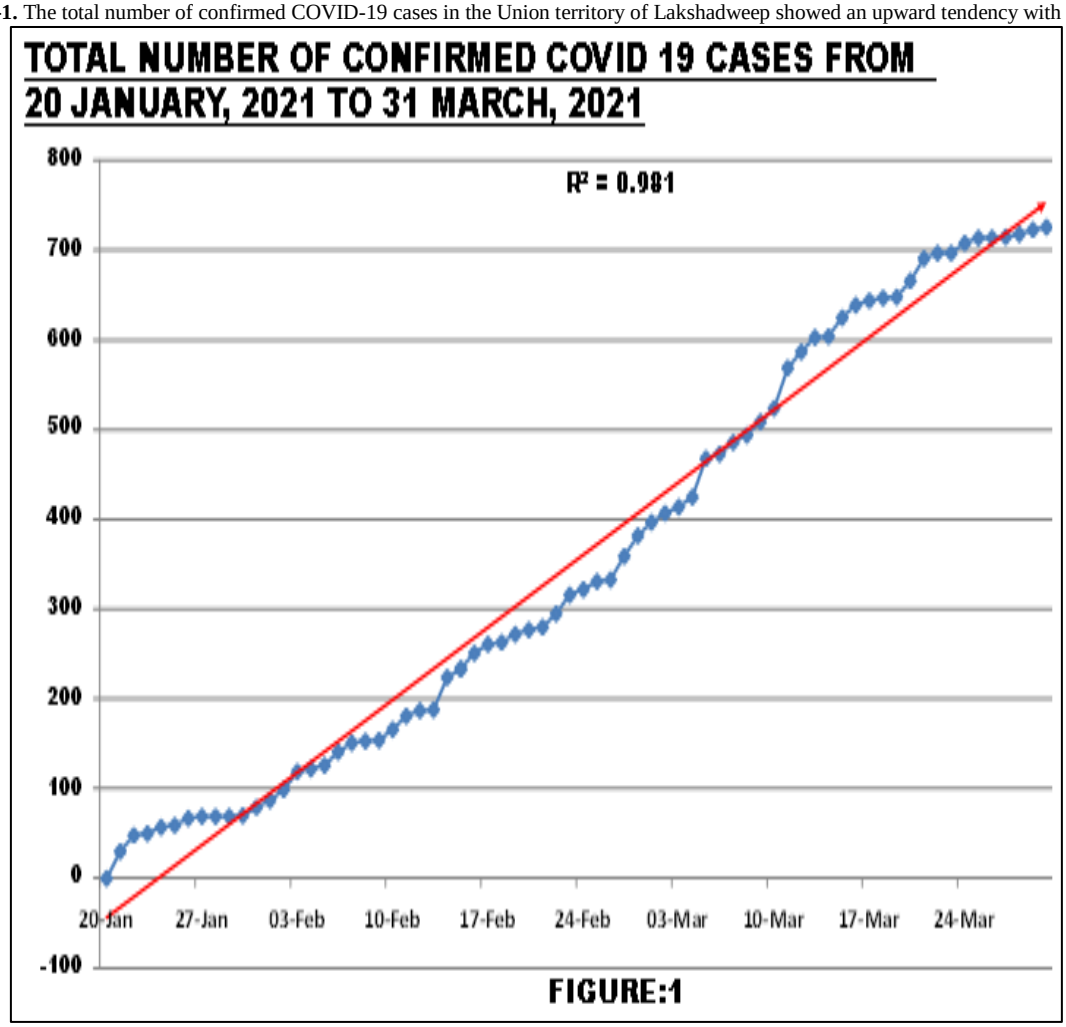
The present study was carried out on the data collected on COVID-19 from different sources that included the Ministry of Health, Government of India (web site at www. mygov.in); Health bulletin of Government of India and from other National and International News outlets. The raw data used in this study were from the month of January, 2021 when first case of COVID-19 was reported in Territory of Lakshadweep, to March 31, 2021. The Statistical analysis was performed by Microsoft Excel and power point programs and the correlation studies were performed using web based Pearson Correlation Coefficient program. The data was considered significant when p value was less than 0.05.

3. Results and Conclusions

Briefly stated that more than two month long 'Lookdown' was imposed on March 25, 2020 to control the spread of COVID-19 in all regions of India. Following the end of complete Lockdown on 31 May, 2020, the Lockdown was gradually relaxed in a phased manner of 'one month' with some restrictions being maintained in some sensitive COVID-19 'pockets' in the population. The implementation of Lockdown had a positive impact on limiting the progression of COVID-19 in the entire population [3-8], with no cases in Lakshadweep until December, 2020.

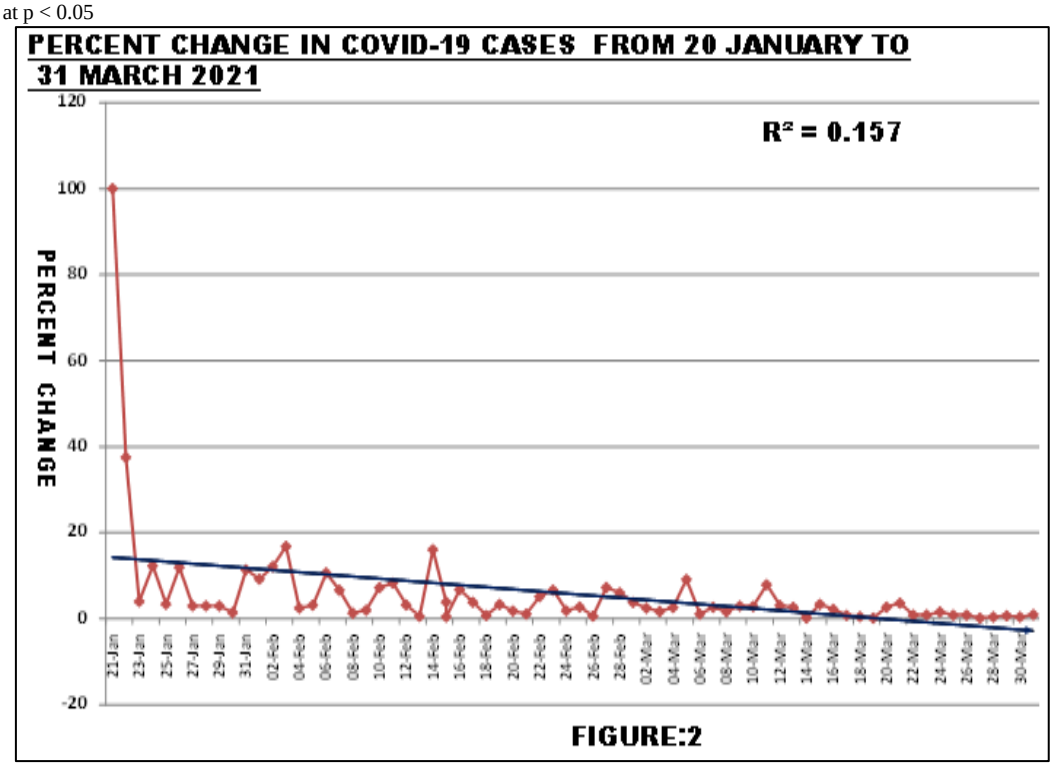
However, the first case of COVID-19 in Indian Territory of Lakshadweep was detected during 3rd week of January, 2021. The **Figure 1** reflects the distribution of COVID-19 in Lakshadweep from 20 January, 2021 until 31 March, 2021. It was clear from the graph that the total number of confirmed cases of COVID-19 showed an upward tendency though with marked volatility. The trend line of confirmed cases confirmed a gradual increase in number of COVID-19 bearing individuals. The graph also reflected that actual number of COVID-19 changed its course after 20 March, 2021.

Figure-1. The total number of confirmed COVID-19 cases in the Union territory of Lakshadweep showed an upward tendency with $p < 0.05$



Such initial increase in number of COVID-19 cases in a short time period, followed by a quick change in course was not surprising given the prior history of vaccination in the population. The late onset of COVID-19 in Lakshadweep was probably due to prior protection that existed in the population due to MMR vaccination; such immunisation may also have helped in preventing infection by the SARS-CoV-2 virus for 10 months. The percent change of COVID-19, which provided a better insight into the progression of the disease, demonstrated a downward trend in progression of the disease (Figure: 2). After showing initial volatility, the rate of progression of the disease stabilis from 22nd March, 2021. However, the trend in progression of COVID-19 was not significant at $p < 0.05$.

Figure-2. The percent change of COVID-19 in the Lakshadweep population showed a downward trend with initial volatility. The result was not significant at $p < 0.05$



In order to assess the impact of COVID-19 in the population, it was necessary to evaluate the progression of active cases of COVID-19. The first active case of COVID-19 in the population was recorded on 2nd February, 2021. The Figure: 3A which reflect the total number of active cases in the population from 2nd February, 2021 to March 31, 2021, demonstrated a volatile rise in the number of active cases of COVID-19 at the beginning, making a peak around 12-13 March, 2021 and thereafter the number declined. However, a rapid wane in total number of active cases of COVID-19 was evident by 31 March, 2021. The percent value of active cases compared to confirmed cases as demonstrated in Figure: 3B was 5.4% on 31 March, 2021 as compared to 34.49% on 14 March, 202. There was a fivefold fall in the number of active cases within a span of 16 days suggesting a strong resistance was encountered by the novel coronavirus in the population. This data further validates the fact that, though the virus was able to infect the host without facing much resistance, it was unable to cause any fatality to the host. However, the trend of progression was not statistically significant at $p< 0.05$.

Figure-3A. Total number of active cases of COVID-19 in Lakshadweep demonstrated that there was a fall in number of active cases of COVID-19 after initial rise. However, the result was not significant with $R^2 = 0.055$

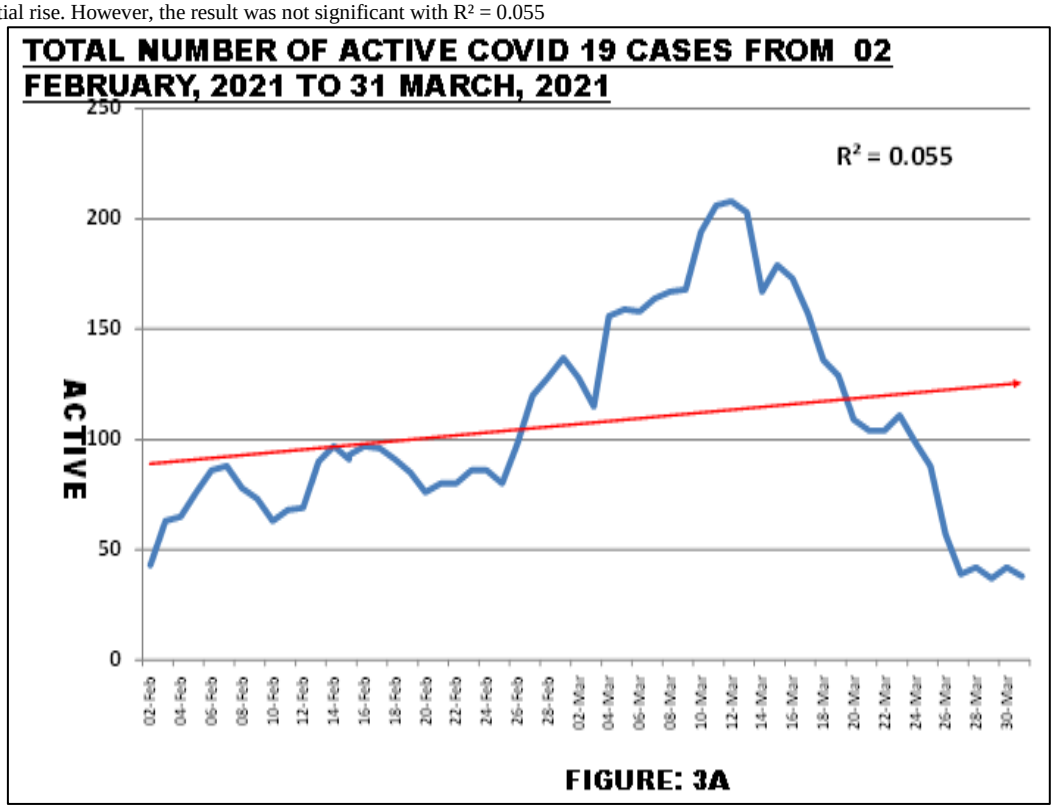
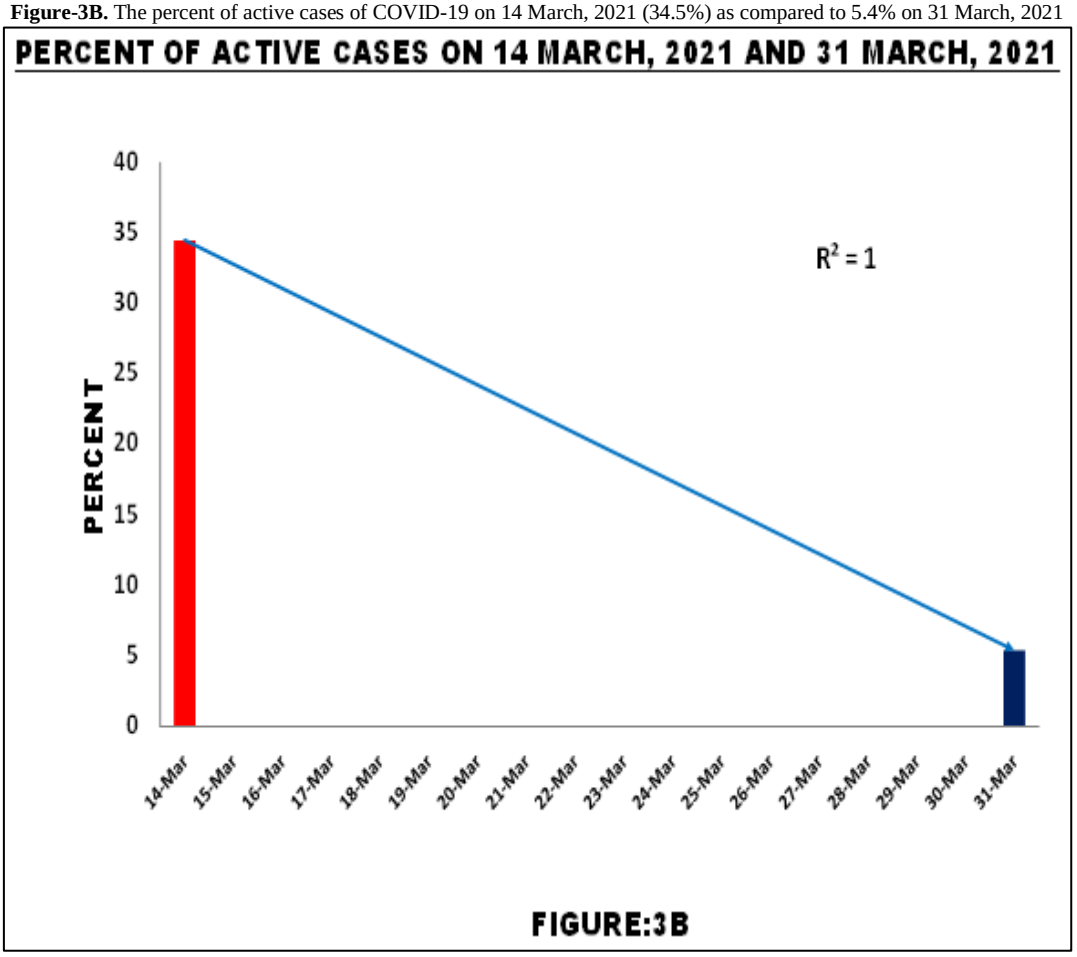
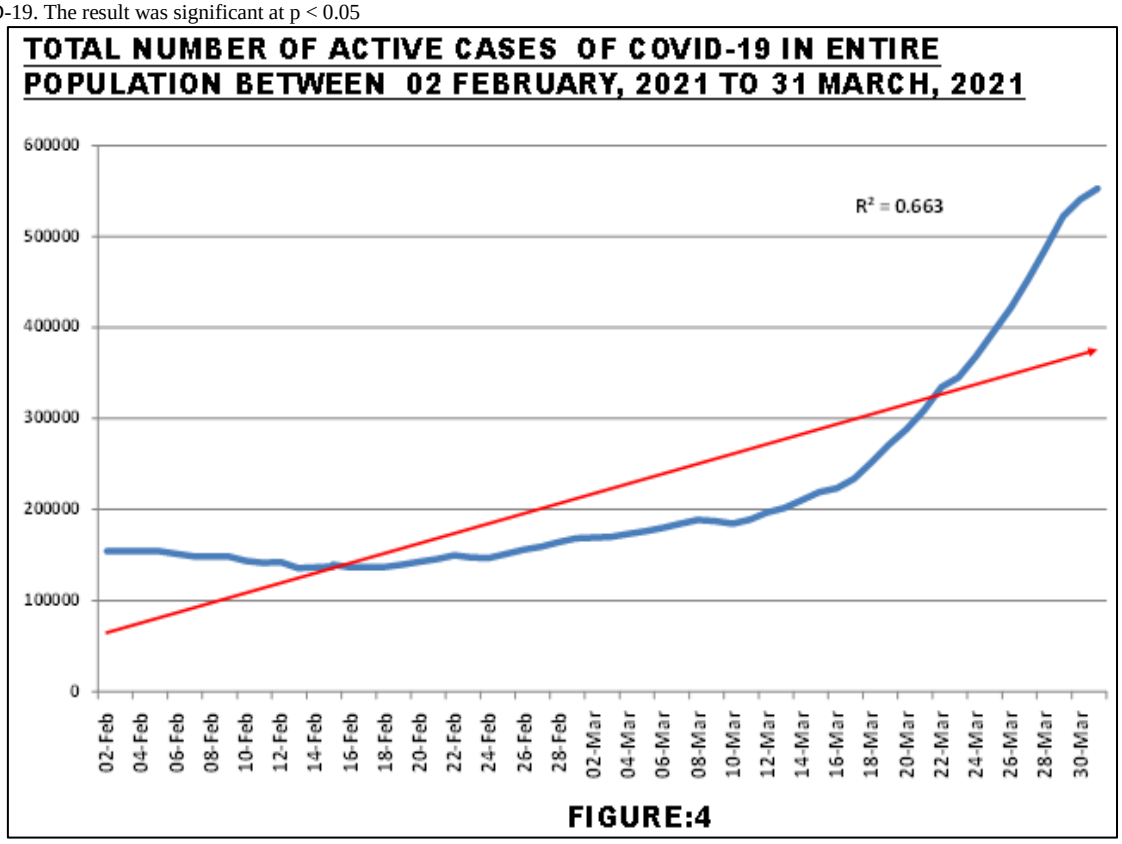


Figure-3B. The percent of active cases of COVID-19 on 14 March, 2021 (34.5%) as compared to 5.4% on 31 March, 2021



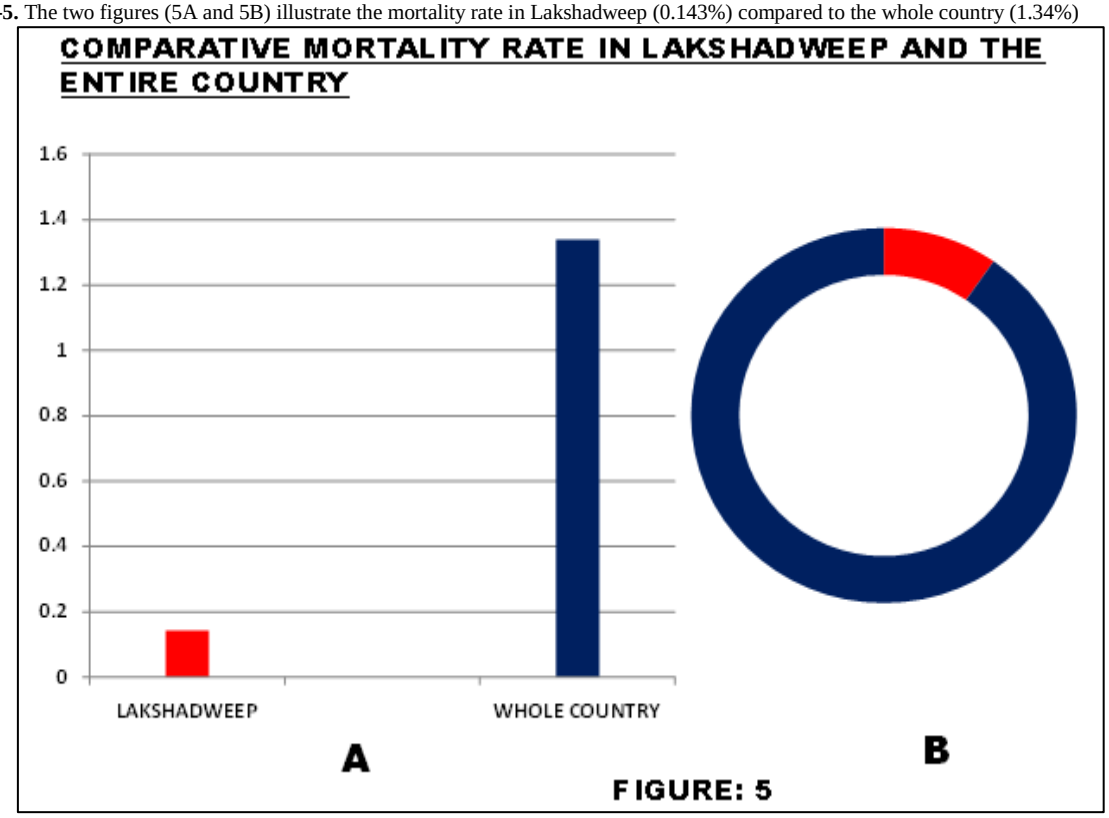
However, in comparison, active cases of COVID-19 in the entire country for the same time period reflected that, though, there was an initial decrease in the number of active cases a reversal was noted from 16 March, 2021. This was contrary to the observed downward trend of active cases in Lakshadweep (Figure: 4). The upward trend was consistently maintained until 31 March, 2021.

Figure-4. An upward trend of active cases of COVID-19 in the entire country was noted after initial regression in the number of active cases of COVID-19. The result was significant at $p < 0.05$



From analysis of data in Figure 3, it was apparent that the active cases were showing a downward trend in the population of Lakshadweep by the end of March, 2021. The rapid rise and wane of active cases, though not very significant statistically, point to plausible presence of an underlying resistance against SARS-CoV-2 virus in the population which prevented effective spread of the virus in the body after tangible infection. Interestingly, this phenomenon was also substantiated from the observation that there was very low number of mortality from COVID-19 in the population. The mortality rate from COVID-19 in Lakshadweep was ~10 fold lower compared to the rate of mortality in the entire country (Figure 5A & 5B). The low mortality rate of 0.143% in the population was due to a strong immune response developed against COVID-19 which could be coming from prior immunization of the population.

Figure-5. The two figures (5A and 5B) illustrate the mortality rate in Lakshadweep (0.143%) compared to the whole country (1.34%)



Consistent with the data on mortality from COVID-19, the active cases did not have any correlation with confirmed cases of COVID-19 (Figure: 6).This implied that most individuals having infection of SARS-CoV-2 did not develop active COVID-19 and they subsequently recovered completely from the disease. This correlation between active cases and confirmed cases was further substantiated by the correlation study of recovered/discharged individuals with that of confirmed cases of COVID-19.

Figure-6. There was no significant correlation between active cases of COVID -19 and confirmed cases of COVID-19.

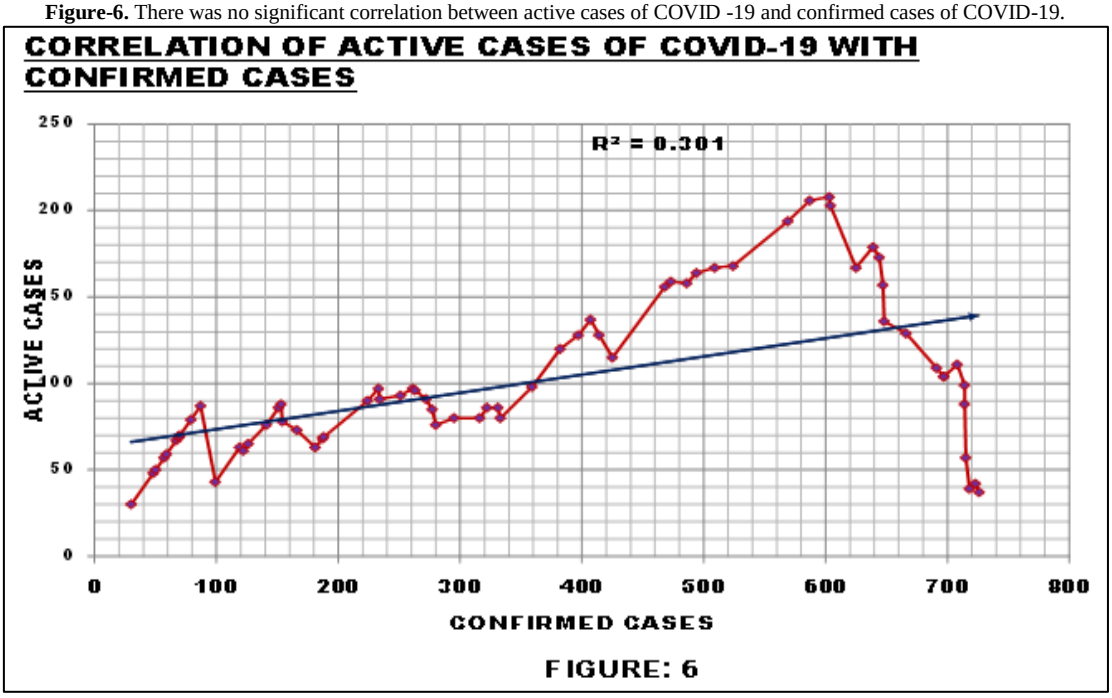
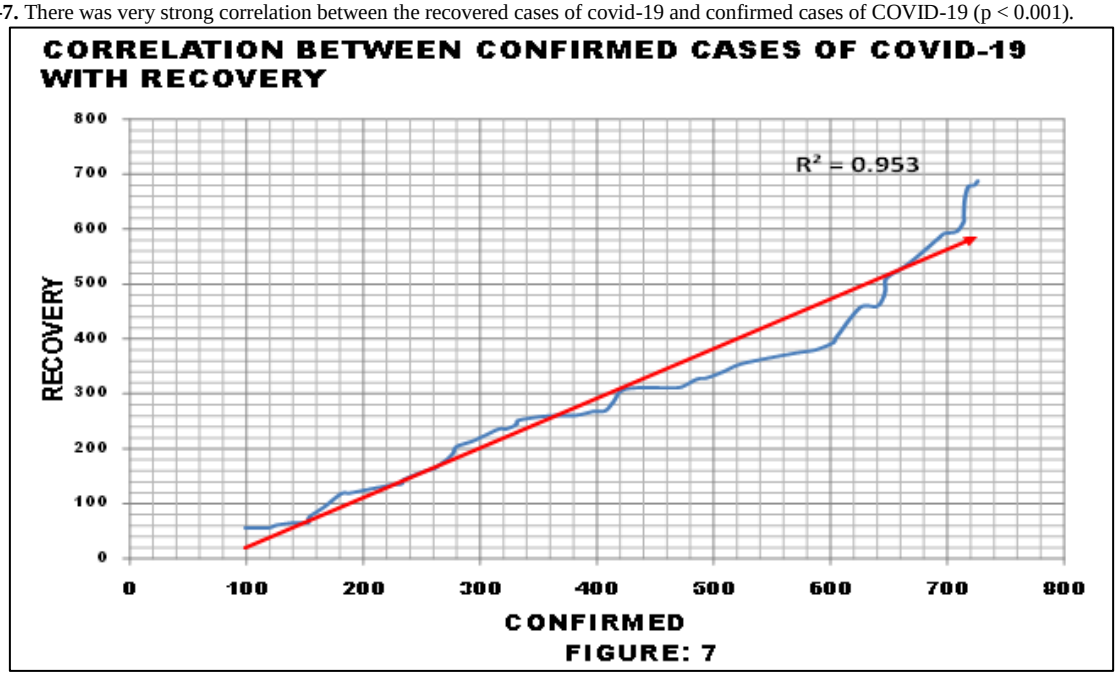
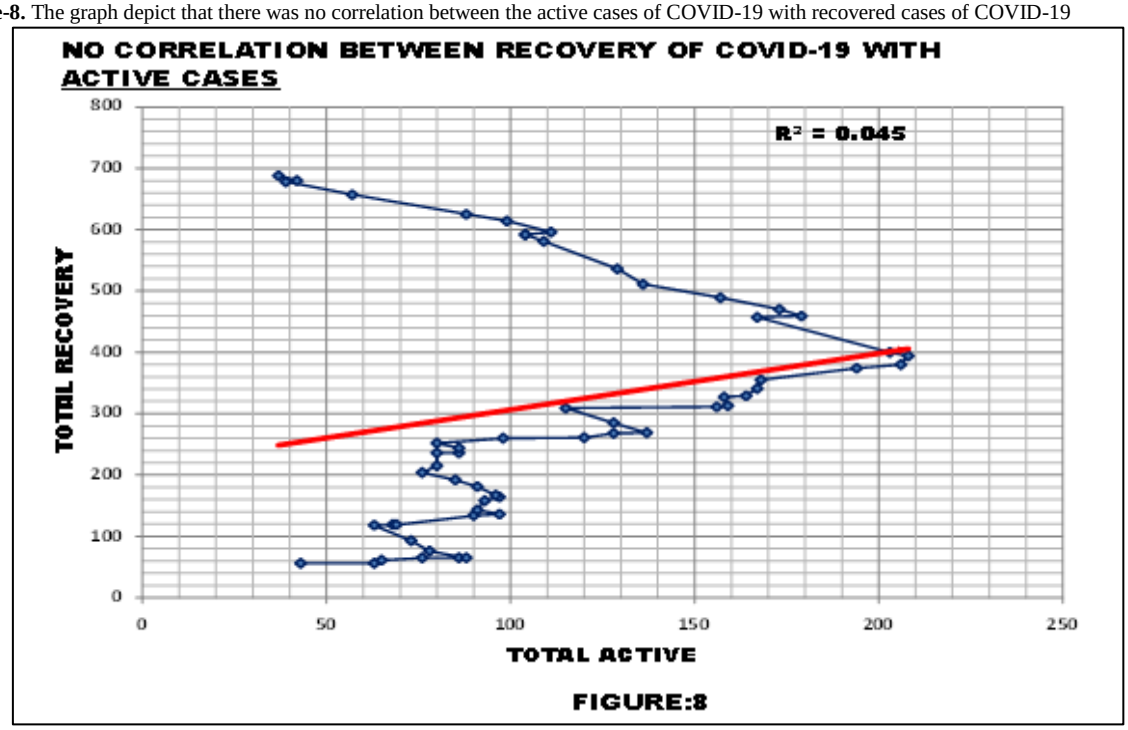


Figure-7. There was very strong correlation between the recovered cases of covid-19 and confirmed cases of COVID-19 ($p < 0.001$).



The correlation between the two variables was positive as shown in Figure: 7. The figure clearly indicated that with the increase in number of confirmed cases, the recovered individual from COVID-19 also increased showing a direct correlation between the two variables. The correlation between the two variables was highly significant at $p < 0.001$. Consistent with this data, a negative correlation was observed between total number of recovery from COVID-19 and active cases of COVID-19, as shown in figure: 8. This data implied that rapid fall in active cases after their rise, was due to their recovery from COVID-19.

Figure-8. The graph depict that there was no correlation between the active cases of COVID-19 with recovered cases of COVID-19



One major conclusion that could plausibly be drawn from this study is that prior immunization of the population against Mumps, Measles & Rubella, prevented the spread of SARS-CoV-2 in the population for 10 months when the rest of the country was seeing a reasonable spread of COVID-19 in the population. And when the virus was able to infect individuals, it caused a mild form of COVID-19 from which most of the individuals recovered. The rate of infectivity of the novel coronavirus is known to be rather high. The data published in World Health Bulletin (WHO) regarding disease causing viruses in humans including COVID-19 noted that the SARS-CoV-2 virus responsible for causing COVID-19 had highest frequency compared to other deadly viruses as shown in Figure: 9.

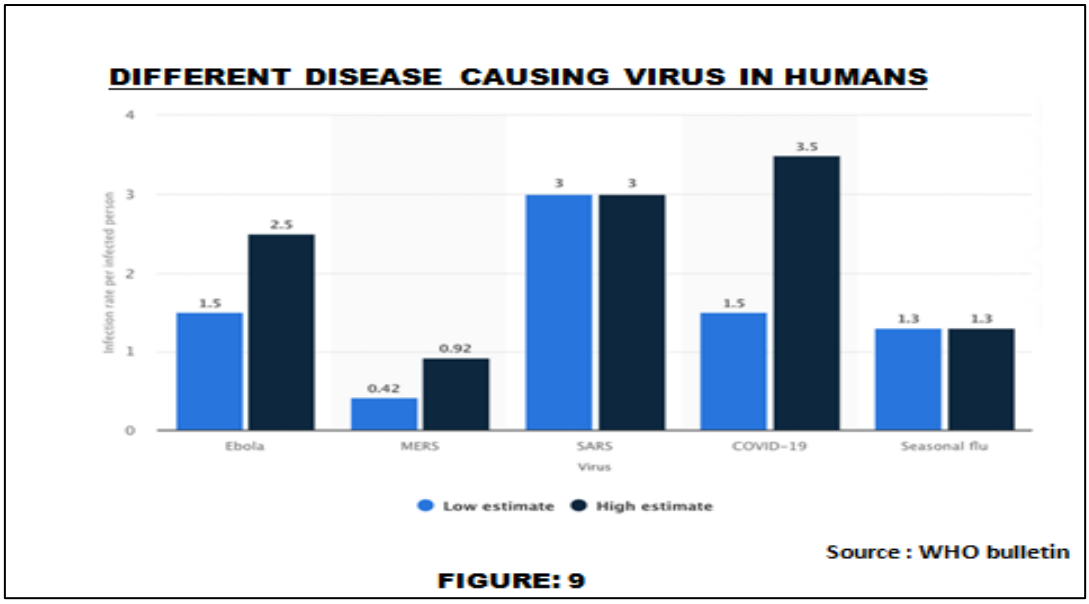


FIGURE: 9

As stated in above paragraphs that population in Lakshadweep had a prior history of immunization. And under the Measles-Rubella (MR) campaign by the Government of India in collaboration with World Health Organization (WHO) in 2017, all children in the target age group (between 9 months and less than 15 years) were given a single shot of MR vaccination, irrespective of their previous measles/rubella vaccination status or measles/rubella disease status, to boost the immunity and protect the entire community against transmission of measles and rubella. However, it appears that prior immunization could have been actively involved in protecting the population against infection by SARS-CoV-2 virus. A Study has reported that antibody against MMR vaccine was found in individuals who recovered from COVID-19 suggesting that the memory cells to MMR vaccine actively participated in neutralising the SARS-CoV-2 virus [2]. The significance of the study by Gold et al was that mumps titers related to the vaccine were significantly and inversely correlated with the severity of COVID-19-related symptoms, supporting the theorized association between the vaccine and COVID-19 severity [2]. The aim of the MMR study was to determine whether any MMR IgG titers were inversely correlated with severity in recovered COVID-19 patients previously vaccinated with the MMR vaccine (Figure: 10). A significant inverse correlation between mumps virus titers and COVID-19 severity within the MMR II group was observed in the study. Within the MMR II group, mumps titers of 134 to 300 arbitrary units (AU)/ml were found only in those who were functionally immune or asymptomatic; all with mild symptoms had mumps titers below 134 AU/ml (n17); all with moderate symptoms had mumps titers below 75 AU/ml (n11); all who had been hospitalized and had required oxygen had mumps titers below32AU/ml.

Figure-10. Analysis of MMR titers after recovery from COVID-19 (reference-8)

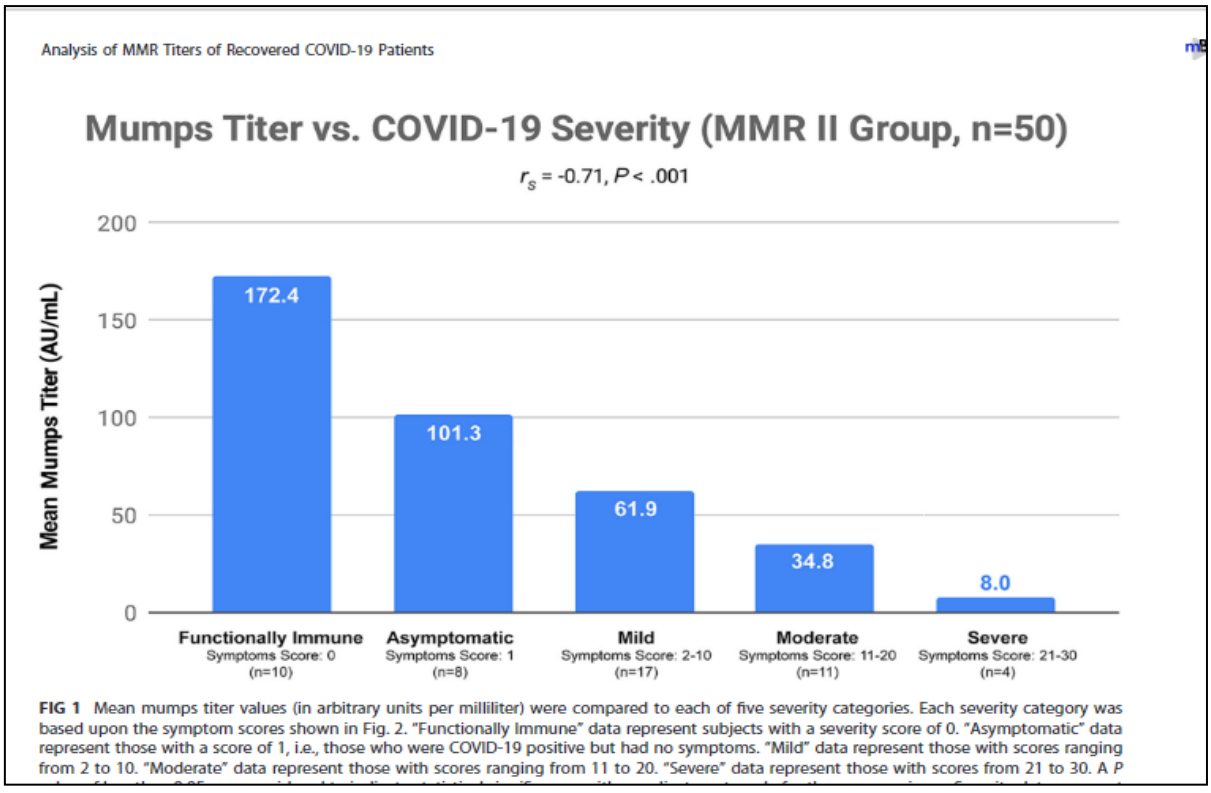


FIG 1 Mean mumps titer values (in arbitrary units per milliliter) were compared to each of five severity categories. Each severity category was based upon the symptom scores shown in Fig. 2. "Functionally Immune" data represent subjects with a severity score of 0. "Asymptomatic" data represent those with a score of 1, i.e., those who were COVID-19 positive but had no symptoms. "Mild" data represent those with scores ranging from 2 to 10. "Moderate" data represent those with scores ranging from 11 to 20. "Severe" data represent those with scores from 21 to 30. A *P*

This is first practical study which corroborates with the findings in the MMR study which had theorized association between MMR vaccine and COVID-19 severity [2] and we have shown here with data that is plausibly true. Some observations made in MMR study pointed out that: (a) younger adults with COVID-19 had death rate below 1%; (b) many people, despite prolonged close contact with someone who was COVID-19 positive, never tested positive themselves and (c) nearly half of people who test positive for COVID-19 were asymptomatic. Our study also reflected that the people in Lakshadweep were protected from developing severe COVID-19 recording very low mortality as clearly indicated in Figure: 5. On the same line, a study has shown that blood collected from SARS-CoV-1 infected individuals in the year 2015, was capable of mounting an immune response, *in vitro*, against SARS-CoV-2 infected cells in 2020 without being exposed to SARS-CoV-2 [9], suggesting a immunological memory cells generated in the SARS-CoV-1 infected individuals could act against SARS-CoV-2 probably because both were having similar backbone DNA.

It is encouraging to point out that WHO Bulletin dated 4 October 2019 had stated that as of December 2018, 168 out of 194 countries had introduced rubella vaccines and global coverage was estimated at 69%. And reported rubella cases declined 97%, from 670 894 cases in 102 countries in 2000 to 14 621 cases in 151 countries in 2018. Though no similar data is available for Mumps and Measles vaccination for the World, it could be anticipated that vaccination with MMR may prove to be useful to fight against the severity of COVID-19 and reduce mortality in different regions of the world. The present study is the first correlative field study which showed that a population which was widely vaccinated with MMR vaccine had effective protection against development of COVID-19 in the population and in cases where COVID-19 was manifested at a later stage of its spread in Lakshadweep, the SARS-CoV-2 virus was tackled efficiently by the immune system of individuals where COVID-19 was manifested.

These observations provide further insight into plausible approaches to using MMR vaccination in controlling the COVID-19 pandemic in the world using it as a primary or a secondary (booster) management dose for COVID-19, before and/or after an effective COVID-19 vaccine is widely available. In a retrospective Italian cohort study on immunity against rubella, the management strategy (booster followed by re-test and, for those who are still negative, a second booster and retest) was consistent with the goal of achieving immunological memory [10]. Analysis of immunological and epidemiological data on endemic human coronaviruses (HCoVs) showed that infection-blocking immunity wanes rapidly, but disease-reducing immunity was long-lived [11]. All these studies reinforce the importance of behavioural containment for continuing vaccination during the endemic phase. The knowledge about specific immune responses generated to maintain endemicity would help in further improving the strategy of vaccination as outlined by Altmann and Boyton [12].

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